Srpsko lekarsko društvo
Serbian Medical Society

Sekcija za kliničku farmakologiju „dr Srđan Đani Marković"
Section of Clinical Pharmacology „dr Srđan Đani Marković"

Organizuju nacionalni kongres
Organize the National congress

XIV NEDELJA BOLNIČKE KLINIČKE FARMAKOLOGIJE

XIV WEEK OF THE HOSPITAL CLINICAL PHARMACOLOGY

24. - 25. decembar 2022.
December 24th - 25th, 2022

ZBORNIK SAŽETAKA
BOOK OF ABSTRACTS
Beograd, 24. - 25. decembar 2022.

Izdavač
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Za izdavača
Prof. dr Boris Milijašević

Glavni i odgovorni urednik
Prim. dr Dragana A. Kastratović - Maca

Urednici:
Prof. dr Boris Milijašević
Dr Srđan Z. Marković - Đani

Grafičko-tehničko uređenje
Prof. dr Boris Milijašević

Štampa
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PROGRAM
PROGRAMME

XIV NEDELJA BOLNIČKE KLINIČKE FARMAKOLOGIJE
XIV WEEK OF THE HOSPITAL CLINICAL PHARMACOLOGYS

SUBOTA, 24. decembar 2022. / SATURDAY, 24th December 2022

10:00-10:30 **Četrnaest godina rada Sekcije za kliničku farmakologiju „dr Srđan Đani Marković" Srpskog lekarskog društva**
Fourtheen years of activity of the Section for Clinical Pharmacology „dr Srdjan Djani Marković" of the Serbian Medical Society
Dragana Maca A. Kastratović, Srdjan Djani Z. Marković, Slobodan M. Janković, Boris Ž. Milijašević, Radmila M. Veličković-Radovanović, Momir M. Mikov, Mira H. Vuković, Viktorija M. Dragojević-Simić, Branka M. Terzić, Biljana P. Radojević, Biljana Savić, Zoran M. Todorović, Aleksandar L. Rašković, Ivana Miličević, Snežana Panić, Olga J. Horvat, Dejana T. Ružić-Zečević, Ivana P. Timotijević-Marković

10:30-11:00 **Antibiotska terapija bolničke pneumonije izazvane multirezistentnim uzročnicima**
Antibiotic therapy of hospital pneumonia caused by multidrug-resistant bacteria
Slobodan M. Janković

11:00-11:30 **Prijavljivanje neželjenih reakcija na lekove: znanje, stavovi i praksa lekara u Kliničkom centru Vojvodine**
Adverse drug reaction reporting: doctor's knowledge, attitudes and practice at Clinical centre of Vojvodina
Aleksandar L. Rasković, Nebojša P. Stilinović, Ana D. Tomas-Petrović, Katarina M. Panjković, Milica M. Paut-Kusturica, Dušan V. Prodanović

11:30-12:00 **Istorijski osvrt na regulative u transfuziji**
Historical Background and the Legislation of Transfusion Medicine
Ljubinka I. Nikolić, Ljiljana M. Zdelar-Stojanović, Teodora S. Crvenkov, Dušanka M. Rajković, Emina S. Čolak

12:00-12:30 **Elektrolitni poremećaji izazvani lekovima**
Drug-induced electrolyte abnormalities
Radmila M. Veličković-Radovanović

12:30-13:00 **Troškovi lečenja ulkusne bolesti**
Costs of Treatment Peptic Ulcer Disease
Boris Ž. Milijašević, Marija B. Blagojević, Nataša Z. Tomić, Dragana S. Milijašević, Radmila N. Popović, Zdenko S. Tomić

13:00-13:30 **Dugodelujući antipsihotici u lečenju psihoza**
Long-acting antipsychotics in the treatment of psychoses
Žana B. Stanković

13:30-14:00 **Ponovljeni pokušaji suicida samotrovanjem u Vojvodini**
Repetitive suicide attempts by poisoning in Vojvodina
Vesna M. Mijatović, Dušan V. Prodanović, Ana-Marija T. Vejnović, Aleksandra S. Dickov

14:00-14:30 **Primena antibiotika kod ECMO pacijenata**
Use of antibiotics in ECMO patients
Zoran M. Todorović

14:30-15:00 **Paroksetin smanjuje kardiotoksičnost doksorubicina**
Paroxetine attenuates doxorubicin-induced cardiotoxicity
Nina M. Žigon, Marija D. Kosić, Vladislav M. Pajović

15:00-15:30 **Uticaj pola primaoca i davaoca i farmakogenomike na doziranje takrolimusa: pilot studija**
The influence of gender of both donor and recipient as well as pharmacogenomics on tacrolimus dosing: pilot study
Viktorija M. Dragojević-Simić, Nemanja K. Rančić, Bojana M. Cikota-Aleksić, Jelena Tadić, Neven Vavić

15:30-16:00 **Korelacija farmakoloških i psiholoških faktora u psihofarmakološkom procesu lečenja**
Correlation of pharmacological and psychological factors in the psychopharmacological treatment process
Ivana P. Timotijević-Marković, Mirjana M. Todorović, Katarina B. Crnić

16:00-16:30 **Uticaj vitamina D3 na objektivne pokazatelje zdravstvenog stanja kod pacijenata sa sarkoidozom**
The effect of vitamin D3 on objective indicators of health status in patients with sarcoidosis
Mira H. Vuković, Branislav S. Gvozdenović, Mihailo I. Stjepanović

16:30-17:00 **Nanonosač produžava kliničku upotrebu leka**
Nanocarrier extends the clinical use of the drug
Đura J. Nakarada, Srđan Z. Marković, Dragana A. Kastratović, Miloš D. Mojović

NEDELJA, 25. decembar 2022. / SUNDAY, 25th December 2022

10:00-10:30 **Uloga budućih propisivača antibiotika u pristupu *Jedno Zdravlje* u vezi sa antibakterijskom rezistencijom – perspektive u Srbiji**
The role of prospective prescribers of antibiotics in the *One Health* approach to antibacterial resistance - perspectives in Serbia
Olga J. Horvat, Milica M. Paut-Kusturica, Ana D. Tomas-Petrović, Zorana R. Kovačević

10:30-11:00 **Bakterije zaboravljaju rezistenciju – da li smo mi to zaboravili?**
Bacteria forget resistance - have we forgotten it?
Branka M. Terzić

11:00-11:30 **Transmiterski disbalans: put u suicidalni rizik**
Transmitter imbalance: the path to suicidal risk
Mirjana M. Todorović, Ivana P. Timotijević-Marković, Katarina B. Crnić

11:30-12:00 **Bulnexo, nove terapijske mogućnosti u lečenju opijatskih zavisnika**
Bulnexo, new therapeutic possibilities in the treatment of opiate addicts
Katarina B. Crnić, Ivana P. Timotijević-Marković, Mirjana M. Todorović

12:00-12:30 **Stručni savet kliničkog farmakologa pacijentima o vakcinaciji protiv COVID-19**
Expert advice of a clinical pharmacologist to patients on vaccination against COVID-19
Dragan R. Milovanović, Dejana T. Ružić Zečević, Marko M. Folić, Nikola V. Rosić, Mirjana L. Milojević-Čorbić, Srđan M. Stefanović, Slobodan M. Janković

12:30-13:00 **Značaj suplementacije oralnim preparatima gvožđa kao vid *Patient Blood Menagement*-a u ginekologiji i akušerstvu**
Significance of iron supplementation as a form of *Patient Blood Management* in gynecology and obstetrics
Ljiljana M. Zdelar-Stojanović, Ljubinka I. Nikolić, Dušanka M. Rajković, Teodora S. Crvenkov, Bojana O. Petrović

13:00-13:30 **Uloga intravenske primene gvožđa u korekciji sideropenijske anemije**
The role of intravenous iron administration in the correction of iron deficiency anemia
Teodora S. Crvenkov, Ljubinka I. Nikolić, Dušanka M. Rajković, Ljiljana M. Zdelar Stojanović, Bojana O. Petrović

13:30-14:00 **Značaj premedikacije u transfuziji**
Significance of pre-transfusion medications in blood transfusion
Dušanka M. Rajković, Teodora S. Crvenkov, Ljiljana M. Zdelar Stojanović, Bojana O. Petrović, Ljubinka I. Nikolić

14:00-14:30 **Tumor markeri i metode određivanja**
Tumor markers and methods of determination
Mirjana M. Petrović, Danko R. Grujić, Lidija A. Šarac, Ljiljana M. Jelisavčić, Rada V. Štulić

14:30-15:00 **Troškovi i potrošnja kontrastnih sredstava u Srbiji od 2011. do 2020. godine**
Costs and consumption of contrast agents in Serbia from 2011 to 2020
Nemanja K. Rančić, Miroslav S. Mišović, Igor M. Sekulić, Dejan Ž. Kostić, Aleksandra M. Kovačević, Milijana N. Miljković, Snežana S. Mugoša, Viktorija M. Dragojević-Simić

15:00-15:30 **Izazovi u doziranju vankomicina kod oštećenja mozga izazvanih traumom**
Challenge in vancomycin dosing in traumatic brain injuries
Milijana N. Miljković, Viktorija M. Dragojević-Simić, Aleksandra M. Kovačević, Dušica M. Stamenković, Tatjana N. Đurašinović, Dejan Ž. Kostić, Nemanja K. Rančić

15:30-16:00 **Potrošnja rezervnih antibiotika u Vojnomedicinskoj akademiji pre i tokom pandemije Covid-19**
Reserve antibiotics consumption in military medical academy, before and during covid-19 pandemic
Aleksandra M. Kovačević, Viktorija M. Dragojević-Simić, Nemanja K. Rančić, Aneta V. Perić, Milijana N. Miljković, Vesna D. Šuljagić

16:00-16:30 **Infliksimab u lečenju toksične epidermalne nekrolize izazvane ko-trimoksazol-om: prikaz slučaja**
Infliximab in the treatment of co-trimoxazole-induced toxic epidermal necrolysis: a case report
Nikola V. Rosić, Dragan R. Milovanović, Dejana T. Ružić-Zečević, Marko M. Folić, Mirjana L. Milojević-Čorbić, Srđan M. Stefanović, Slobodan M. Janković

16:30-17:00 **Diskusija i zaključci**
Discussion and Conclusions
Dragana A. Maca Kastratović, Slobodan M. Janković, Viktorija M. Dragojević Simić, Aleksandar L. Rašković, Radmila M. Veličković-Radovanović, Boris Ž. Milijašević

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ZBORNIK SAŽETAKA

BOOK OF ABSTRACTS

HOSPITAL PHARMACOLOGY
International Multidisciplinary Journal

Četrnaest godina rada Sekcije za kliničku farmakologiju „dr Srđan Đani Marković" Srpskog lekarskog društva

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Sekcija za kliničku farmakologiju Srpskog lekarskog društva (SKFSLD) osnovana je 19. Februara 2009, sa ciljem da implementira i unapredi bolničku primenu znanja kliničke farmakologije u sve medicinske oblasti.

Na predlog Predsedništva i Naučnog odbora SKFSLD uz jednoglasnu podrsku Predsedništva SLD ustanovljena je godisnja nagrada za primenjenu bolničku farmakologiju „dr Srđan Đani Marković". Nagrada je jednoglasnom odlukom Predsedništva i Naučnog odbora SKFSLD dodeljena za 2020 Dr Srdjanu Djaniju Markoviću - našem Sekretaru, istraživaču lekaru, ECRIN correspodentu i monitoru, idejnom ocu i članu Uređivačkog odbora stručno - naučnog časopisa Hospital Pharmacology – International Multidisciplinary Journal. Za 2021 godinu godisnja nagrada za primenjenu bolničku farmakologiju „dr Srđan Đani Marković" je jednoglasnom odlukom Predsedništva i Naučnog odbora SKFSLD dodeljena prof prim dr Slobodanu Jankoviću – našem Predsedniku naučnog odbora SKFSLD, članu Uređivačkog stručno - naučnog časopisa Hospital Pharmacology – International Multidisciplinary Journal, osnivač i rukovodilac bolničke kliničke farmakologije kliničkog centra Kragujevac, rukovodiocu i istraživaču u više od 100 međunarodnih i nacionalnih naučnih projekata, autoru više od 600 naučnih radova i visokog ranga citiranosti, mentoru velikog broja doktorskih disertacija.

Tokom ovih 14 godina članovi SKF "Dr Srdjan Đani Marković" radili su veoma vredno kroz:

1. Kontinuiranu medicinsku edukaciju. Kursevi su akreditvani kao Prva kategorija kod Zdravstvenog saveta Srbije, sto je slušaocima donelo maksimalan broj poena u Lekarskoj komori Srbije za licencu za rad. Kursevi su namenjeni lekarima, farmaceutima, ekolozima, biohemičarima, tehničarima.
2. Simpozijume Nedelja Bolnićke kliničke farmakologije I-XIV. Tema Simpozijuma je Integracija nauke i prakse, učesnici izlažu svoje radove kroz usmene prezentacije, postere, okrugle stolove, komercijalna predavanja, 2020-22 on line. Svake godine učestvuje oko 100 lekara svih medicinskih specijalnosti, farmaceuta, biohemičara. Gosti predavači bile su kolege iz Francuske, USA, Nemačke, Grčke, Bugarske, Austrije.
3. Predavanja po pozivu u saradnji sa Akademijom medicinskih nauka, održali su: Prof Dr David T. W. Wong (USA), Primarius Dragana Maca Kastratović, Prof Dr Edoardo Spina (Italy), Prof Dr Jacques Demotes Mainard (France), Prof Pharm Christine Kubiak (France), Emil Miltchev Gatchev (Bulgaria), Vangelis G. Manolopoulos (Greece), Markus Zeitlinger (Austria), itd. Tokom 2022 nije bilo predavanja po pozivu iz inostranstva. Predavači po pozivu iz Republike Srbije su redovni učesnici Simpozijuma NBKF.
4. Naučno-stručni časopis pokrenuli smo 2014 na predlog Dr Srdjana Djanija Markovića, kao online, open access, free full text Hospital Pharmacology International Multidisciplinary Journal, dostupan na http://www.hophonline.org.
5. Uspesi. Tokom ovih 10 godina svi lekari SKFSLD postizali su značajne uspehe na radnim mestima, kroz doktorske disertacije, akademske/profesionalne pozicije. Profesori Momir Mikov, Radmila Veličković-Radivojević, Ivana Timotijević-Marković, Mihajlo Jakovljević primljeni su u AMNSLD. Profesor Primarijus Slobodan Janković postao je clan Akademije medicinskih nauka BIH. Nagradu za izuzetna ostvarenja u bolničkoj farmakologiji dobili su Dr Srdjan Djani Marković za 2020, Prof Prim dr Slobodan

Janković za 2021 godinu.
6. The Pharmacology International, časopis IUPHAR-a, više puta je objavljivao tekstove o radu SKFSLD.
7. Ostvarenje razvoja kliničke farmakologije i dalje će ići kroz KME, podršku mlađim lekarima da uče kliničku farmakologiju i primene znanja u bolnicama. Podstičemo kolege da svoje stručno-naučne rezultate publikuju u stručno-naučnom časopisu Hospital Pharmacology – International Multidisciplinary Journal. Starije kolege razvijaće i nadalje nacionalnu i međunarodnu saradnju u oblasti primenjene nauke, sa naglaskom na uključivanje mlađih kolega u multidisciplinarne timove.

Fourteen years of activity of the Section for Clinical Pharmacology „dr Srdjan Djani Marković" of the Serbian Medical Society

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The Section for Clinical Pharmacology "Dr Srdjan Djani Marković" of the Serbian Medical Association was established on February 19, 2009, with the aim of implementing and improving the hospital application of knowledge of clinical pharmacology in all medical fields.

At the suggestion of the Presidency and the Scientific Committee of the CCPSMS, with the unanimous support of the Presidency of the SMS, the annual award for applied hospital pharmacology „dr Srdjan Djani Marković" was established. The award was given by a unanimous decision of the Presidency and the Scientific Committee of SCPSMS for 2020 to Dr Srdjan Djani Markovic - our Secretary, researcher, doctor, ECRIN correspondent and monitor, the father of the launch and a member of the Editorial Board of the scientific journal Hospital Pharmacology - International Multidisciplinary Journal (www.hophonline.org). For the year 2021, the annual award "Dr Srdjan Djani Marković" was awarded by a unanimous decision of the Presidency and the Scientific Board of the SKFSLD to Prof. Dr. Slobodan Janković - our President of the Scientific Board, a member of the editorial professional and scientific journal Hospital Pharmacology - International Multidisciplinary Journal, founder and head of Cenre for hospital clinical pharmacology of the University Clinical Center Kragujevac, principal investigator and researcher in more than 100 international and national scientific projects, author of more than 600 scientific papers with high citation rank, mentor of a large number of doctoral dissertations.

During these 14 years, the members of SCPSMA have worked very hard through:

1. Continuous medical education. The courses were accredited as the first category with the Health Council of Serbia, which brought the students the maximum number of points in the Medical Chamber of Serbia for a work license. The courses are intended for doctors, pharmacists, biochemists, technicians.
2. Symposiums Week of Hospital Clinical Pharmacology I-XIV. The topic of the Symposium is the inte gration of Science and Practice, participants present their works through oral presentations, posters, round tables, commercial lectures, 2020 on line. About 100 doctors of all medical specialties, pharmacists and biochemists participate every year. Guest lecturers were colleagues from France, USA, Germany, Greece, Bulgaria, Austria.
3. Lectures by invitation in cooperation with the Academy of Medical Sciences, were held by: Prof. Dr. David TW Wong (USA), Primarius Dragana Maca Kastratović, Prof. Dr. Edoardo Spina (Italy), Prof. Dr. Jacques Demotes Mainard (France), Prof. Pharm Christine Kubiak (France), Emil Miltchev Gatchev (Bulgaria), Vangelis G. Manolopoulos (Greece), Markus Zeitlinger (Austria), etc. During 2022, there were no lectures by invitation from abroad. Lecturers invited from the Republic of Serbia are participants in the Symposium.
4. Based on the idea of Dr Srdjan Djani Markovic the scientific-professional journal SCPSMS was launched in 2014, as an online, open access, free full text Hospital Pharmacology International Multidisciplinary Journal, available at http://www.hophonline.org.
5. Successes. During these 10 years, all SCPSMA physicians have achieved significant success in the workplace, through doctoral dissertations, academic / professional positions. Professors Momir Mikov,

Radmila Veličković Radivojević, Ivana Timotijević Marković, Mihajlo Jakovljević were admitted to the AMNSLD. Professor Primarius Slobodan Jankovic became a member of the Academy of Medical Sciences of BiH. The award for outstanding achievements in hospital pharmacology was awarded to Dr Srdjan Djani Marković for 2020, Prof. Prim. Dr Slobodan Janković for 2021.

6. The Pharmacology International, a journal of IUPHAR, has repeatedly published articles on the work of SCP "Dr Srdjan Djani Marković" Serbian Medical Society.

7. The realization of the development of clinical pharmacology will continue to go through KME, supporting junior doctors to learn clinical pharmacology and applying knowledge in hospitals. We encourage colleagues to publish their professional-scientific results in the professional-scientific journal Hospital Pharmacology - International Multidisciplinary Journal. Senior colleagues will continue to develop national and international cooperation in the field of applied science, with an emphasis on the inclusion of younger colleagues in multidisciplinary teams.

Antibiotska terapija bolničke pneumonije izazvane multirezistentnim uzročnicima

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Kvantitativni odnos između farmakokinetičkog parametra (kao što je AUC, vršni nivo) i mikrobiološkog parametra (kao što je MIC) je označen kao PK/PD indeks (PDI).

Postoje tri glavna indikatora efikasnosti antibiotika: (1) procenat 24-časovne koncentracije leka slobodnog leka u plazmi iznad MIC (fT> MIC); (2) odnos površine ispod krive koncentracije slobodnog leka u plazmi/vreme tokom perioda od 24 sata i MIC (fAUC: MIC); i (3) odnos maksimalne koncentracije antibiotika u plazmi i MIC (Cmax: MIC). Kod kritično bolesnih pacijenata volume distribucije hidrofilnih antibiotika (beta-laktama, glikopeptida, aminoglikozida, linezolida) se povećava usled ekstravazacije tečnosti iz kapilara, edema i intenzivne terapije kristaloidnim rastvorima. Sa druge strane, zapremina distribucije lipofilnih antibiotika (npr. fluorohinolona i makrolida) se ne menja značajno kod kritično obolelih pacijenata.

Studije su pokazale da su MIC-ovi kod kritično obolelih pacijenata veći nego kod pacijenata na običnim odeljenjima; stoga je neophodno davati veće doze antibiotika, trudeći se da minimalne koncentracije budu 4 puta veće od uobičajenih vrednosti MIC-a.

Doze antibiotika kod kritično obolelih stoga treba izračunavati na osnovu trenutnih vrednosti farmakokinetičkih parametara propisanog antibiotika (prvo treba proceniti zapreminu distribucije, ukupni klirens i vezivanje za proteine za konkretnog pacijenta) i podataka o rezistenciji na antibiotike izolovanog uzročnika, uključujući obrazac i MIC-ove. Deterministički farmakokinetički model bez odeljaka treba koristiti kao jednostavan alat za izračunavanje doze.

Antibiotic therapy of hospital pneumonia caused by multidrug-resistant bacteria

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The quantitative relationship between a pharmacokinetic parameter (such as AUC, peak level) and a microbiological parameter (such as MIC) is labelled as a PK/PD index (PDI).

There are three main indicators of an antibiotic effectiveness: (1) percentage of 24-hour plasma free drug concentration above MIC (fT> MIC); (2) the ratio of the area under the free drug concentration curve in plasma / time over the 24-hour period and the MIC (fAUC: MIC); and (3) ratio of maximum plasma antibiotic concentration and MIC (Cmax: MIC). In critically ill patients the volume of distribution of hydrophylic antibiotics (beta-lactams, glycopeptides, aminoglycosides, linezolid) increases due to extravasation of fluid from capillaries, edema and intensive therapy with crystalloid solutions.On the other hand, the volume of distribution of lipophylic antibiotics (e.g., fluoroquinolones and macrolides) does not change significantly in critically ill patients.

Studies have shown that MICs in critically ill patients are higher than in patients in regular wards; therefore, it is necessary to give higher doses of antibiotics, trying to keep the minimum concentrations 4 times higher than the usual MIC values.

Doses of antibiotics in critically ill patients should therefore be calculated on the basis of current values of pharmacokinetic parameters of the prescribed antibiotic (volume of distribution, total clearance and protein binding should be first estimated for the concrete patient) and of data about resistance of the isolated causative agent, including pattern and MIC. Non-compartmental deterministic pharmacokinetic model should be used as straightforward tool for dose calculation.

Prijavljivanje neželjenih reakcija na lekove: znanje, stavovi i praksa lekara u Kliničkom centru Vojvodine

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Uvod: Neželjene reakcije na lek (NRL) su jedan od vodećih uzroka morbiditeta i mortaliteta, povećanja bolničkih prijema, kao i finansijski teret kako za pacijenta tako i za zdravstveni sistem. Zdravstveni radnici imaju presudnu ulogu u sistemu farmakovigilance i neophodni su im odgovarajuće znanje i veštine u oblasti zdravstvene bezbednosti, naročito za ranu identifikaciju, detekciju, upravljanje i prijavljivanje NRL.

Cilj:Ispitivanje znanja, stavova i prakse lakara zaposlenih u Kliničkom centru Vojvodine o prijavljivanju NRL.

Materijal i Metode: Istraživanje je bilo prospektivno i sprovedeno je na lekarima zaposlenim u Kliničkom centru Vojvodine, u opštini Novi Sad u periodu 29. oktobra do 4. decembra 2021. godine. Upitnik je sadržao socio-demografska pitanja, zatim test znanja, ponuđene stavove o prijavljivanju NRL i pitanja o svakodnevnoj praksi prijavljivanja NRL. Prikupljeni podaci obrađeni su u programu IBM SPSS v.23.

Rezultati: Učestvovalo ukupno 150 lekara zaposlenih u okviru različitih klinika i centara Kliničkog centra Vojvodine (KCV). Medijana testa znanja iznosila je 5 od ukupno 10 bodova. Lekari smatraju da ne poseduju dovoljno znanja iz oblasti farmakovigilance, te da su edukativne radionice (62,7%) i obavezna predavanja na osnovnim studijama medicine (78%) iz ove oblasti od velikog značaja. Postoji visoka stopa neprijavljivanja NRL (68%), a učestalost prijave ogleda se na godišnjem nivou. Ne postoji korelacija demografskih parametara (godine radnog staža, postdiplomske kvalifikacije, članstvo u profesionalnim organizacijama) sa većim znanjem lekara o prijavljivanju NRL. Identifikovana je povezanost ovih parametara i prakse prijavljivanja NRL. Utvrđeno je da stariji lekari, zatim lekari sa završenim doktorskim i specijalističkim studijama, kao i oni koji su članovi profesionalnih organizacijama češće prijavljuju NRL.

Zaključak: Doktori poseduju nepotpuno znanje o prijavljivanju NRL i izražen je trend neprijavljivanja NRL. Neophodne su dodatne studije na većem broju ispitanika za potpuno utvrđivanje suštine problema.

Ključne reči: lekari, prijavljivanje neželjene reakcije na lek, farmakovigilanca

Adverse drug reaction reporting: doctor's knowledge, attitudes and practice at Clinical centre of Vojvodina

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Introduction: Adverse drug reactions are one of the main causes of morbidity and mortality around the world, increased hospital admissions, and financial burden for patients and health care system. Health care professionals play a vital role in the pharmacovigilance system, especially in detection, identification, managing and reporting of adverse drug reactions (ADR).

Objectives: The study aimed to examine the knowledge, attitudes and practices of doctors at Clinical centre of Vojvodina towards adverse drug reaction reporting.

Methods: The prospective research was conducted on doctors employed at the Clinical Center of Vojvodina, Novi Sad municipality. Respondents completed an anonymous questionnaire that was conducted in one month period. The questionnaire contained socio-demographic questions, knowledge test, given attitudes on ADR reporting and questions about everyday reporting practice. The collected data were processed in IBM SPSS version 23.

Results: A total of 150 respondents completed the survey. The survey tool showed acceptable validity and reliability. The median knowledge score was 5 out of 10 points. Doctors were of the opinion that they did not have adequate knowledge on ADR reporting and that prevention measures are needed. Underreporting was very high (68%). The results showed a clear link between higher reporting rates and parameters such as work years, postgraduate qualifications and professional membership.

Conclusion: Underreporting of ADRs by doctors is highly prevalent. Further studies are needed to find the main cause of this trend. Initiatives to educate and train doctors on ADR reporting and simplifying the reporting procedure may improve reporting practices.

Key words: doctors, adverse drug reaction reporting, pharmacovigilance

Istorijski osvrt na regulative u transfuziji

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Uvod: Od prvih pokušaja upotrebe krvi u terapeutske svrhe, do naučno zasnovanih postulata upotrebe krvi prošlo je više od 300 godina. Svaka generacija lekara, suočena sa potrebom za kliničkom transfuzijom radi spasavanja života, doprinela je bezbednosti i prihvatanju transfuzije rešavajući nedostatak laboratorijske opreme, zakonodavstva, pa čak i adekvatno obučenog medicinskog osoblja.

Cilj: Cilj istraživanja bio je da se ukaže na istorijski razvoj i na postojeću regulativu za značajnu kliničku oblast, Kliničku transfuziologiju kao posebnu celinu.

Materijal i metode: Online pretraga istorijskog i medicinskog razvoja transfuzije i međunarodnih i domaćih propisa iz oblasti transfuziologije. Pretraživanje literature je obavljeno korišćenjem baza podataka PubMed, Cochrane, Embase i Scopus. Pretraga je obavljena po sledećim ključnim rečima: transfuziologija, regulativa, lekarsko obrazovanje, istorija transfuzije.

Tema: Prvu uspešnu transfuziju sa čoveka na čoveka direktno iz vene u venu izveo je 1818. godine engleski lekar dr Džejms Blandel. Kako krvne grupe tada nisu bile poznate, ova transfuzija je slučajno uspela. Godine 1901. austrijski lekar dr Karl Landštajner otkrio je sistem ABO krvnih grupa, pa je transfuzija postala bezbednija. Tokom decenija, transfuziološka služba je unapređivana i organizaciono i funkcionalno kako bi se obezbedila što bezbednija krv. Banke krvi 1970-ih se kreću ka sistemu dobrovoljnih davalaca krvi. Prekretnica za organizovanje bolničkih banaka krvi bila je 1987. godina, kada je evropska direktiva omogućila okupljanje država članica vezano za pravnu odgovornost za krvne proizvode, počev od jula 1988. godine. „Strategija bezbedne krvi“ se razvija na osnovu smernica SZO. Na osnovu člana 152. Ugovora iz Amsterdama iz 1999. godine i amandmana na Direktivu 2001/83 / EC - EP i EC, kreirana je Direktiva 2002/98 / EU Evropskog parlamenta i Saveta 2003. godine. Do sada je objavljeno 8 izdanja vodiča „Crvena knjiga“. Oslanjajući se na međunarodne vodiče i standarde, može se reći da se klinička transfuzija Republike Srbije razvijala uporedo sa svetskim trendovima. Evropska komisija deluje kroz preporuke od kojih su u praksi najvažnije: Preporuka br.R (88) 4 koja se odnosi na odgovornosti zdravstvenih vlasti u oblasti transfuzije krvi. Savremene terapijske procedure obuhvataju sistem budnosti zdravstvenih radnika zbog čega je 1998. godine formirana Evropska mreža hemovigilance (EHN), od koje je kasnije 2009. godine formirana Međunarodna mreža hemoovigilance (IHN).

Zaključak: Terapijski pomak ka personalizovanoj terapiji, uključujući terapiju matičnim ćelijama, „patient blood management”, ima budući razvoj u timskom radu i interdisciplinarnoj saradnji sa kliničkim farmakolozima, imunolozima, toksikolozima, hematolozima, akušerima, hirurzima, pedijatrima. Obavezno je upoznavanje svih zdravstvenih profila sa propisima iz kliničke transfuziologije.

Historical Background and the Legislation of Transfusion Medicine

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Introduction: More than 300 years have passed from the first attempts to use blood for therapeutic purposes, to scientifically based postulates of blood use. Each generation of physicians, faced with the need for clinical transfusions to save lives, has contributed to the safety and acceptance of transfusions by tackling the lack of laboratory equipment, legislation and even adequately trained medical staff.

Aim: To indicate the existing regulations for a significant clinical area of Clinical transfusion medicine as a separate entity.

Material and Methods: Online search of the historical and medical development of transfusion and international and domestic regulations in the field of transfusion medicine. A literature search was conducted using PubMed, Cochrane, Embase, and Scopus databases. The search was done on the following keywords: transfusion medicine, regulative, doc - tor's education, history of transfusion.

Topic: The first successful human-to-human transfusion directly from vein to vein was performed in 1818 by the English physician Dr. James Blundell. As blood groups were not known at the time, this transfusion was successful by chance. In 1901, the Austrian doctor Dr. Karl Landsteiner discovered the ABO blod group system, so the transfusion became safer. Over the decades, the blood establishment has been improved both organizationally and functionally in order to ensure the safest possible blood. Blood banks in 1970's move to - ward an all-volunteer blood donor system. The turning point for the organization of hospital blood banks was 1987, when the European directive provided for the gathering of member states on the legal responsibility for blood products, starting in July 1988. A „Safe Blood Strategy" is being developed on the basis of WHO guidelines. On the basis of Article 152 of the Amsterdam Treaty of 1999 and the amendment of Directive 2001/83/ EC - EP and EC, Directive 2002/98/EU of the European Parliament and of the Council 2003 was created. So far, 8 editions of the guidelines „Red Book" have been published. Based on international guides and standards, it can be said that the clinical transfusion of the Republic of Serbia has developed in parallel with world trends. The European Commission operates through recommendations (EC recommendations), of which the most important in practice are: Recommendation No.R (88) 4 concerning the responsibility of health authorities in the field of blood transfusion. Modern therapeutic procedures include vigilance system which is why it was formed European Haemovigilance Network (EHN) in 1998, from which the International Haemovigilance Network was formed later in 2009 (IHN).

Conclusion: The therapeutic shift towards personalized therapy, including therapeutic cells, „patient blood management", has a future development in teamwork and interdisciplinary cooperation with clinical pharmacologists, immunologists, toxicologists, hematologists, obstetricians, surgeons, pediatricians. It is obligatory to acquaint all health profiles with the regulations from clinical transfusion medicine.

Elektrolitni poremećaji izazvani lekovima

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Lekovi mogu uticati na normalan unos, eliminaciju, regulaciju i ukupnu distribuciju elektrolita u organizmu. Abnormalnosti elektrolita uzrokovane lekovima mogu biti dramatične i opasne po život, stvarajući dijagnostičke i terapijske probleme. Disbalans elektrolita se često javlja kod kritično obolelih bolesnika. Lekovi mogu smanjiti apsorpciju elektrolita, promeniti hormonske odgovore koji utiču na homeostazu i direktno uticati na funkciju organa odgovornog za održavanje ravnoteže elektrolita. Koncentracije kalijuma u serumu zavisi od preraspodele kalijuma između tkiva i plazme kao posledica delovanja lekova (agonisti beta2 receptora, ksantini, natrijum bikarbonat). Osim toga, utvrđeno je da lekovi utiču na normalno fiziološko funkcioniranje bubrega, s obzirom na homeostazu kalijuma i sistem renin-aldosteron (ACE inhibitori, inhibitori kalcineurina).

Regulacija nivoa natrijuma u serumu integralno je povezana sa regulacijom ukupne količine vode u organizmu. Lekovi koji dovode do neadekvatnog lučenja antidiuretičkog hormona i njegovog efekta na bubrege mogu izazvati teške hiponatrijemije (SSRI, antipsihotici, karbamazepin, vinkristin, omeprazol). Abnormalni gubici ili unos natrijuma povezani sa upotrebom lekova mogu imati značajne efekte na nivou plazme. Brojni lekovi, prevashodno diuretici i inhibitori protonske pumpe (PPI) mogu uzrokovati gubitak magnezijuma i posledičnu hipomagnezemiju. Osetljive populacije (npr. deca, starije osobe, bolesnici sa dijabetesom, hipertenzijom, srčanom insuficijencijom, pacijenti na politerapiji) i osobe koje su na dugotrajnoj terapiji PPI ili diureticima treba pratiti zbog hipomagnezemije uzrokovane lekovima. Hipo/hiperkalcemija može nastati farmakološkom terapijom na nivou lučenja i delovanja paratireoidnog hormona, metabolizma kostiju ili izlučivanja kalcijuma putem bubrega.

Disbalansi elektrolita izazvani lekovima, kao potencijalna etiologija mogu uzrokovati ozbiljne probleme u kliničkoj praksi, posebno kod kritično obolelih bolesnika. Pažljiv monitoring elektrolita i poznavanje farmakoterapije je posebno značajno kod rizičnih i osetljivih bolesnika.

Drug-induced electrolyte abnormalities

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Drugs can interfere with the normal intake, elimination, regulation and total body distribution of electrolytes. These drug-induced abnormalities may be dramatic and life threatening, posing diagnostic and management problems to the physician. Electrolyte imbalances are common in critically ill patients. Medications can interfere with the absorption of electrolytes, alter hormonal responses affecting homeostasis, as well as directly impact organ function responsible for maintaining electrolyte balance. Serum potassium concentrations can be altered as potassium shifts between the tissue and plasma compartments secondary to drug actions (beta2 receptor agonists, xanthenes, sodium bicarbonate). In addition, drugs have been shown to interfere with the normal physiological functioning of the kidney with respect to potassium homeostasis, as well as the renin-aldosterone axis (ACE inhibitors, calcineurin inhibitors).

The regulation of serum sodium levels is integrally related to the regulation of total body water. Thus, drugs that alter the regulation of antidiuretic hormone secretion and its action on the kidney can result in large changes in serum sodium concentrations (SSRI, antipsychotics, carbamazepine, vincristine, omeprazole). Abnormal losses or intake of sodium related to drug use can also have profound effects in the plasma compartment. Several drugs including diuretics and proton-pump inhibitors can cause magnesium loss and hypomagnesemia. Especially high-risk patients (e.g., children, the elderly, patients with diabetes, patients with hypertension, patients on polypharmacotherapy) and individuals under long-term medication with drugs such as PPIs or diuretics should be monitored for drug-induced magnesium deficiency. The normally fine regulation of serum calcium concentrations can be easily upset by pharmacological therapy at the level of parathyroid hormone secretion and action, bone metabolism or renal calcium excretion.

Through awareness of these drug-induced changes in electrolytes and the mechanisms involved, subtle and often dangerous problems in clinical management can be handled rationally.Clinicians encountering electrolyte disturbances should be vigilant in monitoring the patient's medications as a potential etiology.

Troškovi lečenja ulkusne bolesti

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Uvod: Ulkusna bolest je defekt sluznice koji prodire do mišićnog sloja. Može se javiti na bilo kom mjestu gdje postoji aktivnost HCL i pepsina. Najčešće se javlja na želucu i duodenumu. Ovo je hronična i recidivantna bolest, a *H. pylori* se navodi kao najčešći uzročnik nastanka ove bolesti (90-95%).

Cilj: Cilj ovog istraživanja bio je da se analiziraju troškovi terapije ulkusne bolesti izazvane *H. Pylori* iz perspektive Republičkog fonda za zdravstveno osiguranje (RFZO) u Republici Srbiji.

Materijal i metode: Za protokol liječenja kao osnovnu smjernicu koristili smo Nacionalni vodič dobre kliničke prakse-Racionalna upotreba antibiotika. Troškovi liječenja ulkusne bolesti izračunati su na osnovu cijene antibiotika i inhibitora protonske pumpe koji se nalaze na pozitivnim listama koje su u elektronskoj bazi podataka Republičkog fonda za zdravstveno osiguranje (RFZO).

Rezultati: Najjeftinija terapija za 2020. godinu je bila alternativa terapija za 10 dana sa pantoprazolom, doksiciklinom, metronidazolom i bizmutom (0,06% budžeta), a najskuplja terapija je bila terapija prvog izbora za 14 dana sa omeprazolom, amoksicilinom i metronidazolom (0,13 % budžeta). Budžet za ljekove izdate na recept 2020. godine je bio 32.900.000.000,00 RSD.

Zaključak: Postoji razlika u finansijskom trošku liječenja ulkusne bolesti različitim kombinacijama ljekova. Najveću uštedu imamo kombinacijama sa pantoprazolom kao IPP. Efikasnost terapije zavisi i od rezistencije sojeva *H. pylori* na klaritomicin i metronidazol, zbog toga bi trebalo početi pratiti prevalenciju rezistencije na ove antibiotike.

Ključne riječi: ulkusna bolest, *H. pylori*, antibiotici

Costs of Treatment Peptic Ulcer Disease

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Introduction: Ulcer disease is a defect of the mucosa that penetrates to the muscle layer. It can occur anywhere there is activity of HCL and pepsin. It most often occurs on the stomach and duodenum. This is a chronic and recurrent disease, and *H. pylori* is cited as the most common cause of this disease (90-95%).

Objective: The aim of this study was to analyze the costs of treatment of ulcer disease caused by *H. pylori*, ie its eradication based on the recommendations of the National Guide to Good Clinical Practice-Rational Use of Antibiotics from the perspective of the Republic Health Insurance Fund (RHIF) in Serbia.

Material and methods: For the treatment protocol as a basic guideline we used the National Guide to Good Clinical Practice-Rational Use of Antibiotics. The costs of ulcer treatment were calculated based on the price of antibiotics and proton pump inhibitors on the positive lists in the electronic database of the Republic Health Insurance Fund (RHIF).

Results: The cheapest therapy for 2020 was the alternative 10-day therapy with pantoprazole, doxycycline, metronidazole and bismuth (0.06% of the budget), and the most expensive therapy was the first-choice therapy for 14 days with omeprazole, amoxicillin and metronidazole (0.13 % of the budget). The budget for prescription drugs in 2020 was 32,900,000,000.00 RSD

Conclusion: There is a difference in the financial cost of treating ulcer disease with different drug combinations. We have the greatest savings in combinations with pantoprazole as an IPP. The effectiveness of therapy also depends on the resistance of *H. pylori* strains to clarithomycin and metronidazole, therefore the prevalence of resistance to these antibiotics should be monitored.

Key words: ulcer disease, *H.pylori*, antibiotics

Dugodelujući antipsihotici u lečenju psihoza

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Uvođenje antipsihotika u terapiju shizofrenije i drugih psihotičnih poremećaja (shizoafektivnih psihoza, bipolarnog poremećaja) je znatno poboljšalo tok i ishod ovih bolesti. Međutim, ubrzo posle uvođenja terapije antipsihoticima, od strane kliničara je opservirana loša terapijska adherenca pacijenata.

Terapijska adherence je nedavno definisana kao >80% uzimanja lekova tokom 12 meseci i/ili<1 nedelje propustenih lekova (preko 3 meseca). Slaba adherence je relevantan faktor rizika za recidive kod hronicnih i novih pacijenata.

Dugodelujući injekcioni antipsihotici prve generacije (prvobitno depo antipsihotici) su uvedeni 1966. godine (flufenazin enantat, flufenazin dekanoat), a nesto kasnije haloperidol dekanoat, sa intervalom primene od 2 do 4 nedelje.

Oralni antipsihotici druge generacije su doveli do smanjenja incidence neželjenih efekata (ekstrapiramidnog sindroma), iako njihovu upotrebu može da ometa pojava metabilickog sindroma.

Dugodelujući antipsihotici druge generacije su dugodelujući risperidon (svake 2 nedelje), paliperidon palmitat PP1M (svake 4 nedelje), paliperidon palmitat PP3M (svakih 12 nedelja), olanzapin pamoat (svake 2 ili 4 nedelje), dugodelujući aripiprazol (svake 4 nedelje). Moguće prednosti dugodelujućih injekcionih antipsihotika druge generacije su rano prepoznavanje nepridržavanja terapije, diskriminativnost između nepridržavanja terapije i izostanka terapijskog odgovora, stabilna koncentracija leka u plazmi, bolji odnos između doze i nivoa leka u plazmi.

Mogući nedostaci dugodelujućih injekcionih antipsihotika druge generacije su spora titracija doze, duže vreme za postizanje stabilnog nivoa, manja fleksibilnost prilagođavanja doze, odloženo povlačenje neprijatnih i/ili teških neželjenih efekata, bol na mestu injekcije, postinjekcioni sindrom kod primene olanzapin pamoata koji zahteva praćenje od 3 sata.

Potrebno je dodatno proceniti odnos rizika i koristi dugotrajnog lečenja, kao i efikasnost i podnosljivost ove terapije kod trudnih žena i starijih pacijenata.

Long-acting antipsychotics in the treatment of psychoses

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The introduction of antipsychotics in the treatment of schizophrenia and other psychotic disorders (schizoaffective psychoses, bipolar disorder) has significantly improved course and outcome of these diseases. However, shortly after the introduction of antipsychotic therapy, poor therapeutic adherence of patients has observed by clinicians.

Therapeutic adherence has recently been defined as >80% of medication taken over 12 monts and/or <1 week missed medication (over 3 monts). Poor adherence is a relevant risk factor for relapse in both chronic and new patients.

The first-generation long-acting injectable antipsychotics (originally depot antipsychotics) were introduced in 1966 year (fluphenazine enanthate, fluphenazine decanoate) and a little later haloperidol decanoate, with an interval of application from 2 to 4 weeks.

Oral second-generation antipsychotics (SGA) led to a reduction of incidence of unwanted effects (extrapyramidal syndrome), even though their use may be hindered by occurrence of metabolic syndrome.

Long-acting injectable (LAI) SGA are Risperidone long-acting (every 2 weeks), Paliperidone Palmitate PP1M (every 4 weeks), Paliperidone Palmitate PP3M (every 12 weeks), Olanzapine pamoate (every 2 or 4 weeks), Aripiprazole long-acting (every 4 weeks). Potential advantages of LAI SGA are early identification of therapeutic non-adherence, discriminating between non-adherence or lack of response, more stable plasma concentrations of drug, better relationship between dose and drug plasma level.

Potential disadvantages of LAI SGA are slow dose titration, longer time to achieve steady-state levels, less flexibility of dose adjustment, delayed disappearance of distressing and/or severe unwanted effects, pain at the injection site, post-injection syndrome at the administrating of olanzapine pamoate which requires monitoring of 3 hours.

It is needed to be futher assessed risk-benefit balance of long-term treatment as well as efficacy and tolerability of this therapy in pregnant women and elderly patients.

Ponovljeni pokušaji suicida samotrovanjem u Vojvodini

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Uvod: Ponovljena akutna samotrovanja čine značajan procenat svih prijema u Urgentni Centar, sa samopovređivanjem kao glavnim razlogom.

Cilj: Analiza karakteristika pacijenata koji su zbrinuti zbog ponovljenog samotrovanja sa suicidalnim namerama (Repetitive self-poisoning with suicidal intent (RSP-SI)) u Vojvodini, sa ciljem da se predloži moguća preventivna strategija i bolja kontrola ovakvih slučajeva.

Materijali i metode: Retrospektivno istraživanje je uključivalo podatke koje se tiču pacijenata zbrinutih zbog RSP-SI tokom petogodišnjeg perioda u Vojvodini.

Rezultati: Ponovljeno samotrovanje je uočeno kod 485 pacijenata, od kojih je 35,05% prijavilo pokušaj suicida. Prosečan broj RSP-SI po pacijentu je iznosio 3,61±3,08. Period između dva RSP-SI kod žena je iznosio 9,69±13,60 meseci, a kod muškaraca 6,95±11,02 meseca. Skoro dve trećine pacijenata je bilo nezaposleno (65,29%). Najveći broj pacijenata je imao duševne poremećaje i poremećaje ponašanja uzrokovane upotrebom psihoaktivnih supstanci (MKB F10-19; 51,18%) kao i neuroze, stresne i somatoformne poremećaje (MKB F40-48; 33,53%). Jedna supstanca je identifikovana kao uzrok kod 39,15% RSP-SI. U 58.08% RSP-SI je više od jedne supstance potvrđeno (2,50±0,73 supstanci po RSP-SI). Kombinacija alkohola i benzodijazepina je identifikovana kod 19.41% svih RSP-SI. Psihijatrijska intervencija je bila neophodna kod 70,31% RSP-SI. Pet pacijenata sa RSP-SI je izvršilo samoubistvo (2,94%).

Zaključci: Rano prepoznavanje i lečenje psihijatrijskih poremećaja, kao i bolja kontrola propisivanja psihotropnih lekova mogu predstavljati glavnu preventivnu strategiju za pacijente sa ponovljenim pokušajima suicida.

Repetitive suicide attempts by poisoning in Vojvodina

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Objective: Repetitive acute poisoning takes great part of all the Emergency Department admissions, with self-harming as one of the main reasons.

The aim is to analyze the characteristics of the patients treated for repetitive self-poisoning with suicidal intent (RSP-SI) in Serbia in order to propose preventative strategy and better management of the issue.

Material and Methods: The retrospective study included data regarding patients treated for RSP-SI during a 5-year period in Vojvodina.

Results: Repetitive self-poisoning was determined in 485 patients, of whom 35.05% reported suicidal intention. Mean number of repetitive self-poisoning with suicidal intention (RSP-SI) per patient was 3.61±3.08. Mean period between two RSP-SI in group of females and males was 9.69±13.60 and 6.95±11.02 months, respectively. 65.29% of patients with RSP-SI were unemployed. The most of the patients had mental and behavioral disorders due to psychoactive substance use (F10-19)(51.18%) and anxiety, dissociative, stress-related, somatoform and other nonpsychotic mental disorders (F40-48) (33.53%). The sole etiological agent was identified in 39.15% attempts. In 58.08% of the attempts more than one substance was detected (2.50±0.73) per attempt). The co-ingestion of alcohol and benzodiazepines was the most common combination (19.41%). Psychiatry intervention was needed in 70.31% of the patients. Five (2.94%) patients with RSP-SI committed suicide.

Conclusion: Recognition and treatment of mental disorders as well as the control of psychiatric medications prescribing could represent one of the most important preventive strategies for repetitive suicidal behavior.

Primena antibiotika kod ECMO pacijenata

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Antibiotici spadaju u najvažnije lekove koji se primenjuju kod pacijenata podvrgnutih ECMO proceduri zbog čestih infekcija. Imaju ključni uticaj na preživljavanje pacijenata. Farmakokinetika lekova tokom ECMO procedura menja se na više načina: (1) može doći do gubitka aktivnog leka zbog sekvestracije u ECMO sistemu ili vezivanja za membrane (2) mogu se izmeniti najvažniji farmakokinetički parametri, volumen distribucije, Vd i klirens, CL. Lipofilni antibiotici, vezani u visokom procentu za proteine plazme, sa velikim Vd sekvestriraju se u sistemu gde krv kruži (kanile i pumpa) – npr. fluorohinoloni, klindamicin ili tigeciklin. Hidrofilni antibiotici, sa malim Vd, podložniji su hemodiluciji i direktnoj adsorpciji za membranu za oksigenaciju, npr. aminoglikozidi, beta-laktami, glikopeptidi, linezolid i kolistin. Konkretne preporuke o primeni pojedinih antibiotika biće razmotrene u pojedinostima. Npr. nekada je potrebno povećanje doze, kao kod aminoglikozida ili kolistina, a posebno treba voditi računa o njihovoj stabilnosti (karbapenemi su manje stabilni nego piperacilin sa tazobaktamom).

Use of antibiotics in ECMO patients

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Antibiotics are among the most important drugs used in patients undergoing ECMO procedures due to frequent infections. They have a crucial impact on patients' survival. The pharmacokinetics of drugs during ECMO procedures change in several ways: (1) there may be a loss of the active drug due to sequestration in the ECMO system or binding to membranes (2) the most important pharmacokinetic parameters, volume of distribution, Vd and clearance, CL, may be changed. Lipophilic antibiotics, bound in a high percentage to plasma proteins, with a large Vd, are sequestered in the system where the blood circulates (cannulae and circuit) - e.g., fluoroquinolones, clindamycin, or tigecycline. Hydrophilic antibiotics with low Vd are more susceptible to hemodilution and direct adsorption to the membrane for oxygenation, e.g., aminoglycosides, beta-lactams, glycopeptides, linezolid, and colistin. Specific recommendations on the use of certain antibiotics will be discussed in detail. For example, sometimes it is necessary to increase the dose, as with aminoglycosides or colistin, and special attention should be paid to their stability (carbapenems are less stable than piperacillin with tazobactam).

Paroksetin smanjuje kardiotoksičnost doksorubicina

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Paroksetin (P) je antidepresiv koji inhibira kinazu G protein-spregnutih receptora tip 2 (GRK2), ključnog enzima u nishodnoj regulaciji beta-adrenergičkih receptora (ß-AR), koja karakteriše srčanu dekompenzaciju. U ovoj studiji ispitivali smo efekat P na razvoj srčane dekompenzacije kod pacova tretiranih kardiotoksičnom dozom doksorubicina (DOX). Eksperimenti su rađeni na mužjacima Wistar pacova koji su primali DOX (5 mg/kg i.v., n = 23), DOX+P (10 mg/kg/dan p.o., n = 11) ili rastvarač (0,5 mL/kg, NaCl, i.v., n = 7). Praćeni su parametri opšte toksičnosti i ehokardiografski parametri. Na kraju eksperimenta urađena je histopatološka analiza srca i RT-qPCR analiza ekspresije gena za ß1-AR, ß2-AR, GRK2, GRK3, beta-arestin 1 i beta-arestin 2. DOX pacovi bili su lošeg opšteg stanja, smanjene telesne mase i stope preživljavanja. Ehokardiografijom je utvrđeno postojanje dva fenotipa sa sličnom stopom preživljavanja: hipertorfična kardiomiopatija (DOX-HCM) i dilataciona kardiomiopatija (DOX-DCM). Kod DOX-HCM pacova pokazana je povećana genska ekspresija i sinteza GRK2 i GRK3. DOX+P pacovi bili su dobrog opšteg stanja, povećanog preživljavanja i očuvane srčane morfologije i funkcije. Kod njih je genska ekspresija ß1-AR and ß2-AR bila povećana, a GRK2 i GRK3 smanjena. Ova studija je pokazala po prvi put da P efikasno smanjuje kardiotoksičnost DOX.

Ključne reči: paroksetin, doksorubicin, kardiotoksičnost, ß-AR, GRK2, GRK3

Paroxetine attenuates doxorubicin-induced cardiotoxicity

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Paroxetine (P) is an antidepressant that inhibits G protein-coupled receptor kinase type 2 (GRK2), a key enzyme in the down-regulation of beta-adrenergic receptors (ß-AR) that characterizes cardiac decompensation. Here we examined the protective effect of P on the development of cardiac decompensation in rats treated with a cardiotoxic dose of doxorubicin (DOX). Experiments were performed in male Wistar rats receiving DOX (5 mg/kg i.v., n = 23), DOX+P (10 mg/kg/day p.o., n = 11) or vehicle (0.5 mL/kg, NaCl , i.v., n = 7). General toxicity and echocardiographic parameters were monitored. At the end of experimentation heart histology, ß1-AR, ß2-AR, GRK2, GRK3, beta-arrestin 1 and beta-arrestin 2 gene expression was evaluated. DOX rats exhibited poor general condition, reduced body weight and survival. Echocardiography revealed the existence of two phenotypes with similar survival: hypertrophic cardiomyopathy (DOX-HCM) and dilated cardiomyopathy (DOX-DCM). Increased gene expression and synthesis of GRK2 and GRK3 were demonstrated in DOX-HCM rats. DOX+P rats exhibited good general condition, increased survival, and preserved cardiac morphology and function. In these rats, gene expression and synthesis of ß1-AR and ß2-AR were increased, while GRK2 and GRK3 were decreased. This study shows for the first time that P effectively prevents DOX-induced cardiotoxicity.

Key words: paroxetine, doxorubicin, cardiotoxicity, ß-AR, GRK2, GRK3

Uticaj pola primaoca i davaoca i farmakogenomike na doziranje takrolimusa: pilot studija

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Takrolimus (TAC), imunosupresivni lek koji se široko koristi u transplantaciji bubrega, ima usku terapijsku širinu i veliku interindividualnu farmakokinetsku varijabilnost. Brojni faktori doprinose toj varijabilnosti, među kojima genotip primaoca i pol spadaju u najznačajnije. Zbog toga, sprovođenje terapijskog monitoringa leka (TDM) je od izuzetnog značaja za održavanje adekvatnih koncentracija TAC u krvi, a pokazatelj koji predstavlja odnos izmerene koncentracije leka u krvi pre sledeće doze i doze izražene u mg/kg težine pacijenta (C0/D) je već šire prihvaćena strategija. U pacijenata sa transplantiranim bubregom je ispitivana primena izabranih TDM parametara za procenu uticaja pola (i primaoca i davaoca), kao i *CYP3A5* genskog polimorfizma na njihovo izlaganje TAC. Nakon transplantacije, pacijenti su primali trojnu terapiju, kortikosteroide (metilprednizolom, pa prednizon), mikofenolat mofetil i TAC (Prograf®, Fujisava, Japan). TAC je bio davan u početnoj dozi od 0.1-0.3 mg/kg, podeljenoj u dve, date na 12 sati, počevši sa danom transplantacije. C0 vrednost je bila merena hemiluminescentnim mikročestičnim imunoesejom. Ispitivani primaoci bubrega ženskog pola su bili statistički značajno manje izloženi TAC nego muškarci. U skladu sa tim, primaoci bubrega muškog pola, bez obzira na to da li je davalac bio muškarac ili žena, su imali značajno veći C0/D odnos za TAC, u poređenju sa ženama primaocima.

S druge strane, analiza *CYP3A5 A6986G* polimorfizma je pokazala da funkcionalno stanje CYP3A5 enzima značajno utiče na koncentracije TAC u ranoj fazi nakon transplantacije. Stoga, razmatranje i funkcionalnog stanja ovog enzima i pola i primaoca i davaoca bi mogli doprineti mnogo efikasnijoj i bezbednijoj primeni TAC u pacijenata sa transplantiranim bubregom.

Costs for antibacterial drugs in the treatment of bacteria-caused pneumonia

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Tacrolimus (TAC), immunosuppresive drug widely used in renal transplantation, has narrow therapeutic index and high inter-individual pharmacokinetic variability. Numerous factors have been identified as contributors to the latter one, among which genotype and gender are among most important. Due to that, therapeutic drug monitoring (TDM) is essential in maintaining adequate blood concentrations of drug, and dose-adjusted tacrolimus trough concentrations (C0/D) is already widely accepted strategy. The use of selected TDM parameters for the assesment of the gender (both donor and recipients), as well as *CYP3A5* genetic polymorphism on TAC exposure in renal transplant recipients was studied. After kidney transplantation patients were subjected to the triple-drug therapy, consisting of corticosteroids (methylprednisolone, prednisone), mycophenolate mofetil and TAC (Prograf®, Fujisava, Japan). TAC was introduced in the initial oral dose of 0.1-0.3 mg/kg, divided in 12 hours intervals starting on the day of transplantation. C0 were measured by chemilluminescence microparticles immunoassay (CMIA). According to the results, the renal transplant recipients showed lower TAC exposure in females than in males. In accordance with that, male recipients, regardless of the donor's gender, had a higher TAC C0/D ratio compared to female recipients.

On the other hand, analysis of the *CYP3A5 A6986G* polymorphism showed that the functional state of the CYP3A5 enzyme significantly affects TAC concentrations in the early phase after transplantation. Therefore, consideration of both functional state of this enzyme and gender of both donor and recipient could contribute to a more effective and safer usage of TAC in kidney transplant patients.

Korelacija farmakoloških i psiholoških faktora u psihofarmakološkom procesu lečenja

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Kompleksnost psihofarmakološkog tretmana u psihijatriji upućuje na sagledavanje psiholoških procesa u korelaciji sa strukturama CNS, psihofarmacima i dinamičkim procesima transmitersko – receptorskih interakcija.

Uspešnost lečenja i adekvatan terapiski odgovor u svim oblastima medicine, u psihijatriji posebno, zavise pored adekvatne medikamentozne terapije, od psihološke dimenzije odnosa sa terapeutom, poverenja u terapijski ishod i spremnosti da se poštuju uzusi savremene psihofarmakoterapije.

Uzajamnost uticaja psiholoških, farmakoloških i biohemisjskih procesa na ishod lečenja zasniva se na „feed back" procesima. Evidentno je da je primena lekova čiji su mehanizmi delovanja u određenim strukturama CNS sa željenim terapijskim postignućima, pokazatelj biološke osnove psiholoških simptoma i sledstveno, psihološke nadgradnje kao što je empatija. Bihevioralne manifestacije psihijatrijskih poremećaja, u kontinuumu od prepoznatljive funkcionalnosti do patologije i psihopatološke simptomatologije, imaju osnova u strukturama CNS (reinforsment, pozitivna/negativna uslovljavanja), transmiterskim sistemima, receptorskoj dinamici (stimulacija/blokada) na pre i post sinaptičkoj membrani do delikatnih, kaskadnih intraneuronskih prcesa.

Složenost funkcionisanja ključnih struktura kao što su amigdala, prefrontalni korteks i hipokampus čija se uloga menja zavisno od spoljašnjih impulsa (input) koji se primaju i od impulsa koji se odašilju ka releventnim oblastima predstavlja važan aspekt i biologije i klinike u psihijatriji.

Correlation of pharmacological and psychological factors in the psychopharmacological treatment process

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The complexity of psychopharmacological treatment in psychiatry points to the observation of psychological processes in correlation with CNS structures, psychopharmaceuticals and dynamic processes of transmitter-receptor interactions.

The success of treatment and an adequate therapeutic response in all areas of medicine, especially in psychiatry, depend not only on adequate drug therapy, but also on the psychological dimension of the relationship with the therapist, trust in the therapeutic outcome and the willingness to respect the rules of modern psychopharmacotherapy.

The mutual influence of psychological, pharmacological and biochemical processes on the outcome of treatment is based on „feed back" processes. It is evident that the application of drugs whose mechanisms of action are in certain structures of the CNS with the desired therapeutic achievements is an indicator of the biological basis of psychological symptoms and, consequently, of psychological superstructures such as empathy. Behavioral manifestations of psychiatric disorders, in a continuum from recognizable functionality to pathology and psychopathological symptomatology, have a basis in CNS structures (reinforcement, positive/negative conditioning), transmitter systems, receptor dynamics (stimulation/blockade) on the pre- and post-synaptic membrane to delicate, cascading intraneuronal processes.

The complexity of the functioning of key structures such as the amygdala, prefrontal cortex and hippocampus, whose role changes depending on the external impulses (input) that are received and on the impulses that are sent to the relevant areas, represents an important aspect of both biology and clinic in psychiatry.

Uticaj vitamina D3 na objektivne pokazatelje zdravstvenog stanja kod pacijenata sa sarkoidozom

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Uvod: Ro stadijum i spirometrijski pokazatelji spadaju u objektivne pokazatelje težine bolesti kod pacijenata sa sarkoidozom. Još uvek ne postoje izveštaji o uticaju nivoa vitamina D3 u serumu na Ro stadijum i spirometrijske pokazatelje kod ovih pacijenata.

Ciljevi: Cilj ovog istraživanja bio je utvrđivanje povezanost nivoa vitamina D3 u serumu sa Ro stadijumom i spirometrijskim pokazateljima kod bolesnika sa sarkoidozom.

Metodi: U prospektivnoj studiji na 400 pacijenata sa sarkoidozom, mereni su testovi plućne funkcije (spirometrija i difuzijski kapacitet za ugljenik monoksid), Ro stadijum i vitamin D3 u serumu.

Rezultati: Nije pronađena značajna povezanost serumskog vitamina D3 sa spirometrijskim pokazateljima u ispitivanoj populaciji pacijenata. Pacijenti sa Ro stadijumom III imali su znatno niže ($p = 0.043$) nivoe serumskog vitamina D3 (8.60 ng/L ± 4.89 ng/L v.s. 14.42 ng/L ± 10.26 ng/L).

Zaključak: Niske vrednosti vitamina D3 u serumu značajno utiču na razvoj plućnih infiltrata bez bilateralne hilarne limfadenopatije sa stepenom spontane rezolucije od 10% do 20% kod bolesnika sa sarkoidozom.

The effect of vitamin D3 on objective indicators of health status in patients with sarcoidosis

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Introduction: Ro stage and spirometric indicators are objective indicators of disease severity in sarcoidosis patients. On the other hand, there are still no reports on the influence of serum vitamin D3 levels on Ro stage and spirometric indicators in these patients.

The Aim: The aim of this study was to determine the association of serum vitamin D3 levels with Ro stage and spirometric indicators in sarcoidosis patients.

Methods: In the prospective study of 400 sarcoidosis patients, Pulmonary function tests (spirometry and diffusing capacity for carbon monoxide), Ro stage and serum vitamin D3 were measured.

Results: No significant association of serum vitamin D3 with spirometric indicators was found in the examined patient population. Patients with Ro stage III had significantly lower levels of serum vitamin D3 ($p = 0.043$) compared to patients with Ro stage 0, I or II (8.60 ng/L ± 4.89 ng/L vs. 14.42 ng/L ± 10.26 ng/L).

Conclusion: Low levels of serum vitamin D3 significantly influence the development of pulmonary infiltrates without bilateral hilar lymphadenopathy with a degree of spontaneous resolution of 10% to 20% in sarcoidosis patients.

Nanonosač produžava kliničku upotrebu leka

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Desetak godina nakon uvođenja novog leka u kliničku upotrebu, dolazi do pojave mlađih generacija lekova. Praćenjem neželjenih dejstava lekova postiže se njihovo pravilnije pozicioniranje, ali se i stvara privid da je novi lek bolji. Odlučili smo se za unapredjenje već postojećih lekova jer su dobro proučeni, pa je lakše korigovati njihove poznate nedostatke i unaprediti lek, nego napraviti formulaciju novog leka. Ovo je posebno značajno u grupama lekova koji su najviše upotrebljavani u kliničkoj praksi: antibiotici, NSAIL, hipolipemici, antidijabetici.

U radu su prezentovane mogućnosti prevazilaženja neželjnih dejstava lekova, koji ustvari predstavljaju glavne nedostatke koji skraćuju farmakoterapijski upotrebni život lekova.

Razvoj novih oblika lekova, posebno lekova sa nanonosačem, predstavlja zapravo put ka efikasnijoj terapiji, farmakoekonomskoj uštedi, ali i bezbednijoj farmakoterapiji.

Nanocarrier extends the clinical use of the drug

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Ten years after a new drug has been introduced into clinical use, the most recent generations of drugs appear. By monitoring the side effects of drugs, their correct positioning is achieved, but this creates the impression that the new drug is also better. We decided to improve existing drugs because they have been well studied, so it's easier to improve the drug by correcting its known shortcomings than to create a brand new drug formulation. This is particularly significant in the drugs most commonly used in clinical practice: antibiotics, NSAIDs, hypolipemic drugs, and antidiabetics.

This paper presents possibilities for overcoming the main disadvantages of drugs that induce unwanted effects and shorten their pharmacotherapeutically useful life.

The development of new forms of drugs, especially drugs with nanocarriers, actually represents a path to more effective therapy, pharmacoeconomic savings, but also safer pharmacotherapy.

Uloga budućih propisivača antibiotika u pristupu *Jedno Zdravlje* u vezi sa antibakterijskom rezistencijom – perspektive u Srbiji

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Uvod: Problem antimikrobne rezistencije je kompleksan i skreće pažnju na potrebu za pristupom „Jedno zdravlje" u njegovom rešavanju, što uključuje i humanu i veterinarsku medicinu. Studenti medicinskih nauka, kao budući propisivači antibiotika, mogu u značajnoj meri uticati na pitanja u vezi sa antimikrobnom rezistencijom u budućnosti.

Cilj rada: Cilj ovog istraživanja bio je da ispita znanje, stavove i ponašanje studenata medicine, stomatologije i veterinarske medicine u vezi sa upotrebom antibiotika.

Materijal i metode: Studija preseka obuhvatila je ukupno 400 studenata integrisanih akademskih studija medicine (M), stomatologije (S) i veterinarske medicine (V). Izabrane grupe čine budući zdravstveni radnici koji će propisivati antibiotike. Ispitanici su popunili anonimni upitnik.

Rezultati: Studenti M i S pokazali su u značajnoj meri viši skor znanja u odnosu na studente V ($p<0,001$). Multivarijantnom regresijom identifikovani su prediktori adekvatnog znanja: ženski pol ($B=0,571$; $p=0,02$), viša prosečna ocena ($B=1,204$; $p<0,001$), studenti M ($B=0,802$; $p=0,006$) i studenti S ($B=0,769$; $p=0,026$), studenti koji su koristili antibiotik dok se ne potroši celo pakovanje ($B=0,974$; $p=0,036$) i studenti koji su koristili antibiotike onako kako im je lekar propisao ($B=1,964$; $p<0,001$). Od svih ispitanih studenata samomedikaciju je prijavilo njih 42,8%. Identifikovani prediktori samomedikacije su češća ($B=0,587$; $p<0,001$) i neadekvatna ($B=0,719$; $p<0,007$) upotreba, korišćenje antibiotika do prestanka simptoma ($B=2,142$; $p<0,001$) ili dok se ne potroši pakovanje ($B=1,010$; $p<0,001$).

Zaključak: Ponovna evaluacija nastavnog plana i programa koji se odnosi na upotrebu antibiotika i antimikrobnu rezistenciju, pre svega nastave kliničke farmakologije, mogla bi biti korisna.

Ovaj rad je podržan od strane Ministarstva prosvete i nauke Republike Srbije, projekat broj. III 42012. i Pokrajinskog sekretarijata za visoko obrazovanje i naučnoistraživačku delatnost, Autonomne Pokrajine Vojvodine (projekat broj. 142-451-2621/2021-01)

The role of prospective prescribers of antibiotics in the *One Health* approach to antibacterial resistance - perspectives in Serbia

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Introduction: The complex problem of antimicrobial resistance (AMR) requires actions taken with the One Health approach, involving both human and veterinarian medicine. Health professions students, as the future antibiotic providers, can greatly impact antibiotic-related issues in the future. Goal: The study was conducted to evaluate knowledge, attitudes and behaviour of prospective antibiotic prescribers in relation to prudent use of antibiotics.

Material and methods: This cross-sectional questionnaire-based study was performed on 400 students of health professions allowed to prescribe antibiotics (Medicine (M), Dentistry (D) and Veterinary medicine (V)) of the University of Novi Sad, Serbia.

Results: M and D students showed a significantly higher knowledge score compared to V students ($p<0.001$). Multivariate regression identified the following predictors of adequate antibiotic knowledge: being female student ($B=0.571$; $p=0.02$), higher grade average ($B=1.204$; $p<0.001$), students of M ($B=0.802$; $p=0.006$) and D ($B=0.769$; $p=0.026$), and students who used antibiotics during the last infection until the bottle was finished ($B=0.974$; $p<0.001$) or for the period advised by the doctor ($B=1.964$; $p<0.001$). Out of the total sample, self-medication was reported among 42.8% of students. The identified predictors of of self-medication were: more frequent ($B=0.587$; $p<0.001$) and irregular ($B=0.719$; $p=0.007$) antibiotic use, using antibiotics until symptoms resolved ($B=2.142$; $p<0.001$) or until the bottle was finished ($B=1.01$; $p<0.001$) during the last infection.

Conclusion: It seems prudent to re-evaluate the educational curricula regarding antibiotic use and AMR in Serbia, specifically teaching of clinical pharmacology.

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Bakterije zaboravljaju rezistenciju – da li smo mi to zaboravili?

Branka M. Terzić

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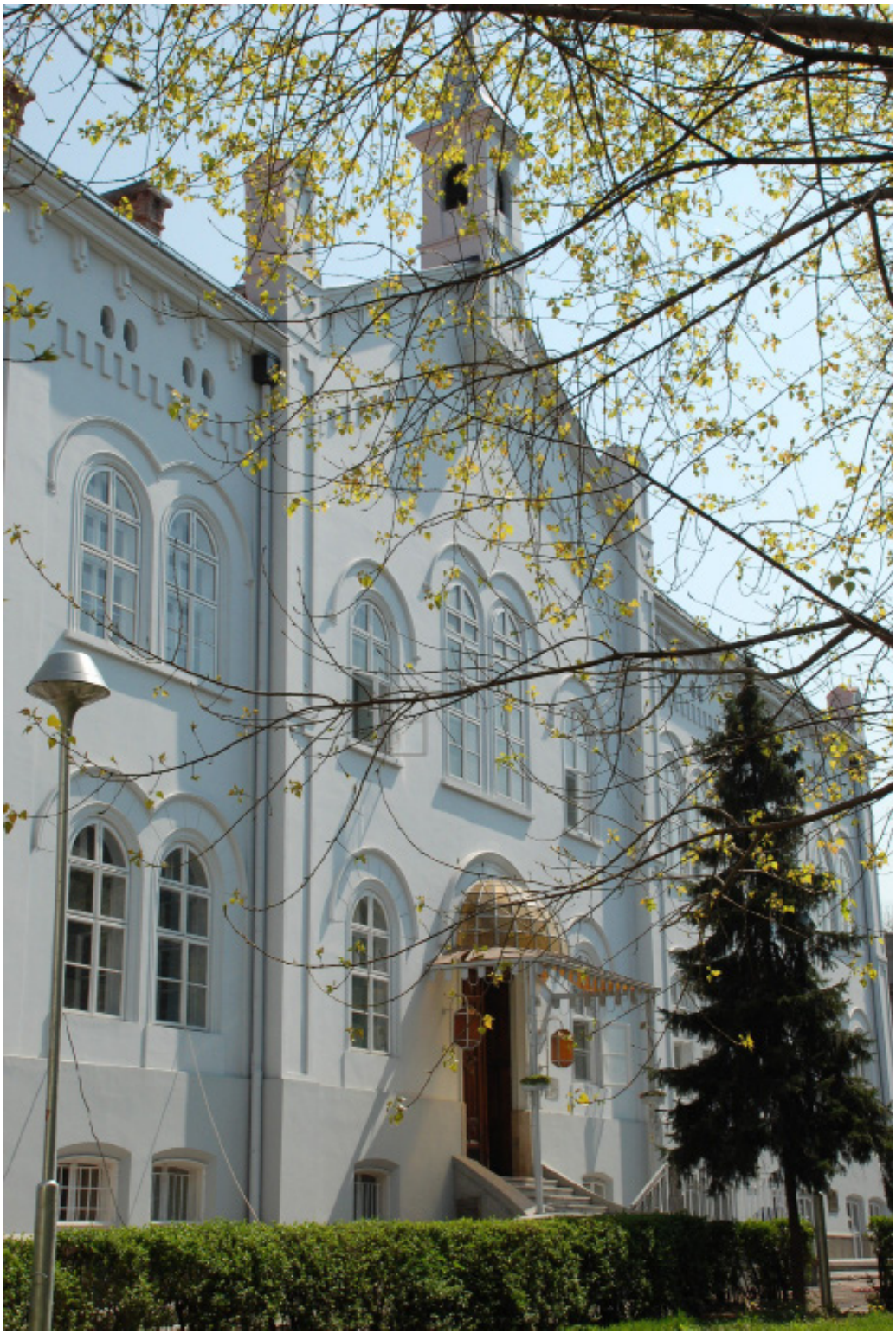

Bacteria forget resistance - have we forgotten it?

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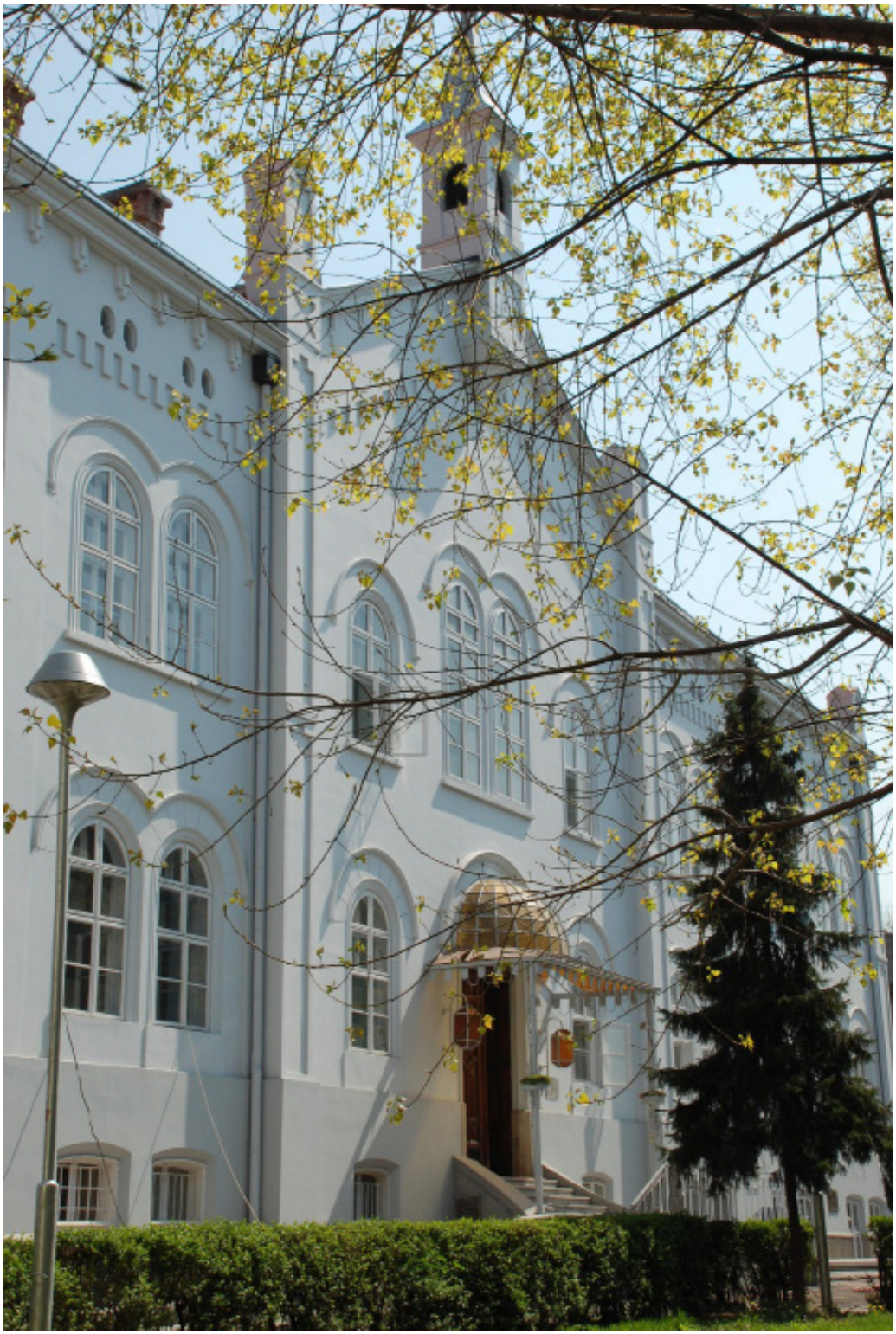

Transmiterski disbalans: put u suicidalni rizik

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Samoubistvo se definiše kao svesno i namerno uništenje svog života, pri čemu postoji svesnost postupka i posledica. Suicidalnost je psihijatrijski termin i definiše se kao sklonost ka samoubitvu, koja se stepenuje u nekoliko nivoa izraženosti. Motivi za samoubistvu su u velikom procentu patološki-proističu iz psihopatologije, ređe racionalni, kulturološki... Do povezivanja suicida sa medicinskim i socijalnim stanjima dolazi tek u XIX veku. Epidemiološke studije navode suicid kao 15-ti po redu uzrok smrti, a 2-gi po redu u adolescentnoj populaciji. Stoga je definisanje faktora rizika za suicid sve značajnije.. Psihijatrijski poremećaji se ističu kao glavni činioci u razvoju suicidalnosti, pri čemu su poremećaji raspoloženja, shizofrenija, adikcije i poremećaji ličnosti najznačajniji. Ostali faktori rizika , naročito biološki su predmet istraživanja i dobijeni podaci ukazuju na genetske poremećaje, strukturne poremećaje CNS, neurotransmiterski disbalans i neuroendokrine poremećaje u kod suicidalnih osoba. U okviru istraživanja upliva neurotransmiterskih poremećaja na suicidalnost,u fokusu je serotonergički sistem, kao bitan deo odgovora na stres u CNS. Rezultati su ukazali na sniženje serotoninske transmisije kao i sniženje nivoa serotoninsog transportera u sinaptičkim pukotinama u regionima prefrontalnog korteksa i raphe nuclei osoba koje su pokušale ili izvršile suicid. Istraživanja dopaminergičkog, GABA i glutamateričkog sistema nisu bila dovoljno opsežna za značajnije zaključke o njihovim poremećajima u suicidalnosti. Ističu se i neuroplastičnost CNS i neuroimunološki faktorikao bitan deo neurobiologije suicida. Značaj poremećaja HPA/hipotalamus-hipofiza-adrenalne žlezde/osovine, se takođe istražuje, sa nalazima poremećanih nivoa cortizola u serumu, CRH/ Corticotropin Realising Hormon/ u CNS, uvećane nadbubrežne žlezde. Rezultati neurobioloških istraživanja se koriste za pronalaženje pouzdanih biomarkera, koji bi kod vulnerabilnih grupa ukazali na suicidalni rizik. U tom smislu su do sada obećavajuće rezultate dale neuroimiging tehnike, dok su neke laboratorijke metode, na pr. merenje nivoa cortizola manje pouzdane. Integrisanje kliničkih podataka i bioloških istraćivanja bi omogućile efikasniju prevenciju i tretman suicidalnog ponašanja.

Transmitter imbalance: the path to suicidal risk

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Suicide is defined as the conscious and intentional destruction of one's life, in which there is awareness of the procedure and consequences. Suicidality is a psychiatric term and is defined as a tendency towards suicide, which is graded in several levels of expression. Motives for suicide are in a large percentage pathological - stemming from psychopathology, less often rational, cultural... The connection of suicide with medical and social conditions occurs in the 19th century. Epidemiological studies list suicide as the 15th leading cause of death, and the 2nd leading cause of death in the adolescent population. Therefore, defining risk factors for suicide is increasingly important. Psychiatric disorders stand out as the main factors in the development of suicidality, with mood disorders, schizophrenia, addictions and personality disorders being the most important. Other risk factors, especially biological ones, are the subject of research and the obtained data indicate genetic disorders, structural disorders of the CNS, neurotransmitter imbalance and neuroendocrine disorders in suicidal individuals. As part of research into the influence of neurotransmitter disorders on suicidality, the focus is on the serotonergic system, as an important part of the response to stress in the CNS. The results indicated a decrease in serotonin transmission as well as a decrease in the level of the serotonin transporter in the synaptic clefts in the regions of the prefrontal cortex and raphe nuclei of persons who attempted or committed suicide. Investigations of the dopaminergic, GABA and glutamatergic systems were not extensive enough for significant conclusions about their disorders in suicidality. Neuroplasticity of the CNS and neuroimmunological factors are highlighted as an important part of the neurobiology of suicide. The importance of HPA/hypothalamus-pituitary-adrenal/axis disorders is also explored, with findings of disturbed serum cortisol levels, CRH/ Corticotropin Realizing Hormone/ in the CNS, enlarged adrenal glands. The results of neurobiological research are used to find reliable biomarkers, which would indicate a suicidal risk in vulnerable groups. In this sense, neuroimaging techniques have so far given promising results, while some laboratory methods, e.g. measurement of cortisol levels is less reliable. Integrating clinical data and biological research would enable more effective prevention and treatment of suicidal behavior.

Bulnexo, nove terapijske mogućnosti u lečenju opijatskih zavisnika

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Opijatska zavisnost je težak i honični psihijatrijski poremećaj, koji u poslednjim dekadama dostiže epidemijske razmere na globalnom nivou. Pored uticaja na mentalno i fizičko zdravlje pojedinaca, adikcija opijata je udružena sa povišenim rizikom širenja transmisionih oboljenja, kao što su HIV, Hepatitis C, TBC, kao i sa visokim procentom kriminala, visokom stoom mortaliteta zbog over-dose, ekonomskim opterećenja društva. Dugotrajnost i zahtevnost terapijskih programa potpune apstinencije kao i visok stepen recidivizma su doveli do preporuke Svetske zdravstvene organizacije za razvoj harm-reduction programa, odnosno substitucione terapije agonistima i parcijalnim agonistima opijatskih receptora. Isti se sprovode na teritoriji Srbije u značajno dugom periodu, što je doprinelo sticanju znanja i iskustva na ovom području terapije opijatskih zavisnika. Pored već poznatih metadona i buprenorfina, najnovija dvokomponentna formulacija leka, koji se koristi u programu supstitucione terapije, jeste Bulnexo, koji sadrži buprenorfin i nalokson u kombinaciji. Buprenorfin je parcijalni agonist M opioidnih receptora, sa visokim afinitetom vezivanja za receptore, kao i antagonist Kapa receptora, što mu omogućuje brzo i dugotrajno delovanje, kao i kontrolu sedacije i disforije. Nalokson, kao druga komponenta leka, je antagonist opijatnih receptora i deluje na osnovni simptom adikcije- na žudnju i antidot je za druge opijate, u slučaju recidiva. Odnos buprenorfina i naloksona u leku je 4:1 i prepručuje se sublingvalna primena, koja povećava bioraspoloživost buprenorfina. Prednost Bulnexa je njegov dobar upliv na kvalitet života zavisnika i dobra adherencija u tretmanu. Pri tom, manja je atraktivan kao primarna supstanca zavisnosti, a time i manje atraktivnosti za zloupotrebu i uličnu preprodaju. S obzirom da je averzivan za i.v. primenu-izaziva apstinencijanu krizu, znatno je manji rizik od predoziranja, kao i smanjen rizik od prenošenja transmisivnih bolesti. Bulnexo se u terapiju uvodi slično buprenorfinu, u malim dozama, dalja korekcija doza se vrši tokom prvih nekoliko dana terapije, uz praćenje stanja pacijenta.

Bulnexo, new therapeutic possibilities in the treatment of opiate addicts

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Opiate addiction is a severe and chronic psychiatric disorder, which in recent decades has reached epidemic proportions on a global scale. In addition to the impact on the mental and physical health of individuals, opiate addiction is associated with an increased risk of spreading communicable diseases, such as HIV, Hepatitis C, TB, as well as with a high percentage of crime, high mortality due to overdose, and economic burden on society. The long duration and demandingness of therapeutic programs of complete abstinence as well as the high degree of recidivism have led to the recommendation of the World Health Organization for the development of harm-reduction programs, that is, substitution therapy with agonists and partial agonists of opiate receptors. The same have been carried out on the territory of Serbia for a significantly long period, which has contributed to the acquisition of knowledge and experience in this area of therapy for opiate addicts. In addition to the already known methadone and buprenorphine, the newest two-component formulation of the drug, which is used in the substitution therapy program, is Bulnexo, which contains buprenorphine and naloxone in combination. Buprenorphine is a partial agonist of M opioid receptors, with a high binding affinity for the receptors, as well as an antagonist of the Kappa receptor, which enables it to have a fast and long-lasting effect, as well as the control of sedation and dysphoria. Naloxone, as the second component of the drug, is an antagonist of opiate receptors and acts on the basic symptom of addiction - craving and is an antidote for other opiates in case of relapse. The ratio of buprenorphine and naloxone in the drug is 4:1 and sublingual administration is recommended, which increases the bioavailability of buprenorphine. The advantage of Bulnex is its good impact on the quality of life of addicts and good adherence to treatment. At the same time, it is less attractive as a primary substance of addiction, and thus less attractive for abuse and street resale. Since it is aversive to i.v. application-causes an abstinence crisis, there is a significantly lower risk of overdose, as well as a reduced risk of transmitting transmissible diseases. Bulnexo is introduced into the therapy similarly to buprenorphine, in small doses, further correction of doses is made during the first few days of therapy, with monitoring of the patient's condition.

Stručni savet kliničkog farmakologa pacijentima o vakcinaciji protiv COVID-19

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Cilj: Pandemija COVID-19 predstavlja veliki izazov za zdravstvene radnike u svim disciplinama. Cilj rada je da predstavi iskustva kliničkih farmakologa u savetovanju pacijenata u vezi primene vakcine protiv kovida 19.

Metode: Sprovedena je studija slučaja sa ospervacionim dizajnom u Univerzitetskom kliničkom centru Kragujevac, Kragujevac, Srbija. Podaci su prikupljeni iz bolničkog informacionog sistema iz kojeg su odabrani izveštaji lekara specijalista ambulante kliničkih farmakologa sačinjeni tokom 2021. godine. Varijable studije su zasnovane na relevatnim podacima o pacijentima, vakcinaciji protiv kovida 19 i radu kliničkog farmakologa.

Rezultati: Analizirani su podaci kod ukupno 14 pacijenata. Najčešći razlog dolaska pacijenta u ambulantu kliničkog farmakologa je mišljenje o mogućnosti primene vakcine protiv kovida 19 kod postojanja lične anamneze prethodne alergijske reakcije na vakcine ili druge lekove, uključujući i anafilaksu. Drugi razlozi su postojanje lične anamneze na druge reakcije u vezi s prethodnom primenom vakcina odnosno drugih lekova i prisustvo hroničnog oboljenja i trudnoće. U svim slučajevima, dato je odgovarajuće stručno mišljenje, koje uključuje i savet o terapijskoj alternativi.

Zaključak: Klinički farmakolozi imaju važnu ulogu u pružanju zdravstvenih usluga tokom pandemije, jer svojim aktivnim zalaganjem bitno doprinose razrešavanju složenih kliničkih slučajeva u vezi vakcinacije protiv kovida 19.

Ključne reči: klinička farmakologija, pružanje zdravstvene zaštite, COVID-19 vakcine

Expert advice of a clinical pharmacologist to patients on vaccination against COVID-19

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Objective: The COVID-19 pandemic poses a major challenge for healthcare professionals in all disciplines. The aim of this paper is to present the experiences of clinical pharmacologists in advising patients regarding the use of the COVID-19 vaccines.

Methods: We conducted a case study with observational design at the University Clinical Center Kragujevac, Kragujevac, Serbia. The data were collected from the hospital information system, from which the reports of the specialists of the outpatient clinic of clinical pharmacologists, done during 2021, were selected. The study variables were based on relevant patient data, vaccination against COVID-19, and the work of clinical pharmacologists.

Results: Data from a total of 14 patients were analyzed. The most common reason for a patient's visit to the clinic of a clinical pharmacologist is the opinion about the possibility of using the vaccine against COVID-19 if there is a personal history of a previous allergic reaction to vaccines or other drugs, including anaphylaxis. Other reasons are the existence of a personal history of other reactions related to previous use of vaccines or other drugs and the presence of chronic disease or pregnancy. In all cases, an appropriate expert opinion was given, which includes advice on a therapeutic alternative.

Conclusion: Clinical pharmacologists play an important role in providing health services during a pandemic, because their active efforts significantly contribute to resolving complex clinical cases related to COVID-19 vaccination.

Key words: clinical pharmacology, delivery of health care, COVID-19 vaccines

Značaj suplementacije oralnim preparatima gvožđa kao vid *Patient Blood Menagement*-a u ginekologiji i akušerstvu

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Nedostatak gvožđa (ID) je najčešći razlog anemije (IDA) kod trudnica pošto su zalihe gvožđa često nedovoljne da zadovolje sve veće zahteve trudnoće. Nivo eritropoetina se povećava tokom trudnoće, samim tim se povećava masa eritrocita što zahteva oko 450 mg gvožđa. Dodatne količine gvožđa su neophodne za rast fetusa (225 mg), placentu (80 mg) i gubitak krvi tokom normalnog vaginalnog porođaja (250 mg). Ukupno oko 1000 mg gvožđa je potrebno tokom normalne trudnoće, u odnosu na period van trudnoće, što je ekvivalentno 6,3 mg/dan. Pored toga, laktacija će zahtevati dodatnu potrebu od 1 mg na dan. Bez suplementacije, 80% žena u terminu neće imati dovoljne zalihe gvožđa, a smatra se da je potrebno 2 godine da gvožđe iz ishrane zameni gvožđe izgubljeno sa svakom trudnoćom. Preporuke u cilju prevencije anemije u trudnoći uključuju suplemente koji sadrže gvožđe i folnu kiselinu, obogaćivanje osnovnih namirnica gvožđem i drugim vitaminima i mineralima, edukacija o zdravlju i ishrani, kontrola parazitskih infekcija i poboljšanje sanitarnih uslova. Preporuka za suplementaciju oralnim gvožđem za blage do umerene slučajeve anemije (Hb 70–105 g/l) tokom prvog i drugog tromesečja je doza u rasponu od 40 do 200 mg dnevno elementarnog gvožđa. Doza gvožđa se prilagođava prema deficitu gvožđa koji se procenjuje na osnovu saturacije transferina i nivoa feritina. Neanemične žene u riziku od ID uključuju one sa prethodnim anemijama, multiparitet, uzastopne trudnoće u razmaku manjem od godinu dana od porođaja i vegetarijanci. Posebnu pažnju treba posvetiti i trudnim tinejdžerkama, ženama sa visokim rizikom od krvarenja ili sa nedavnom istorijom krvarenja. Preporuka je da ove žene treba da primaju dnevno oralno gvožđe (30-60 mg) i bez provere serumskog feritina. Efekat terapije se procenjuje nakon dve nedelje terapije na osnovu porasta hemoglobina i broja retikulocita. Ukoliko porast hemoglobina nije zadovoljavajući povećava se doza a u slučaju slabog podnošenja preporučuje se parenteralna primena gvožđa. Blagovremenu primenu medicinskih i drugih metoda dizajniranih da održe koncentraciju hemoglobina, optimizuju hemostazu i minimiziraju gubitak krvi, kao i nastojanju da se poboljša ishod lečenja pacijenata nazivamo „Patient blood management" (PBM). PBM je vid personalizovane medicine i predstavlja multidisciplinarni pristup koji ima za cilj poboljšanje lečenja pacijenata, posebno onih koji su u riziku od anemije i kod kojih postoji značajna verovatnoća da će doći do gubitka krvi i potrebe za primenom transfuzije.

Significance of iron supplementation as a form of *Patient Blood Management* in gynecology and obstetrics

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Iron deficiency (ID) is the most common cause of anaemia (IDA) in pregnant women, since iron stores are often insufficient to meet the increasing demands of pregnancy. The level of erythropoietin increases during pregnancy, thereby increasing the mass of erythrocytes, which requires about 450 mg of iron. Additional amounts of iron are necessary for fetal growth (225 mg), placenta (80 mg) and blood loss during normal vaginal delivery (250 mg). In total, about 1000 mg of iron is needed during normal pregnancy, compared to the no pregnancy period, which is equivalent to 6.3 mg/day. Next, lactation will require extra 1 mg of iron per day. Without supplementation, 80% of women at term will not have adequate iron stores, and it is thought to take 2 years for dietary iron to replace the iron lost with each pregnancy. Recommendations for the prevention of anaemia in pregnancy include supplements containing iron and folic acid, fortification of basic foods with iron and other vitamins and minerals, education about health and nutrition, control of parasitic infections and improvement of sanitary conditions. The recommendation for oral iron supplementation for mild to moderate cases of anaemia (Hb 70-105 g/l) during the first and second trimester is a dose ranging from 40 to 200 mg per day of elemental iron. The dose of iron is adjusted according to the iron deficit, which is estimated on the basis of transferrin saturation and ferritin level. Non-anemic women at risk for ID include those with previous anaemia, multiparity, consecutive pregnancy less than a year apart and vegetarians. Special attention should also be paid to pregnant teenagers, women with a high risk of bleeding or with a recent history of bleeding. It is recommended that these women should receive daily oral iron (30-60 mg) without checking serum ferritin. The effect of therapy is evaluated after two weeks of therapy based on the increase in hemoglobin and the number of reticulocytes. If the increase in hemoglobin is not satisfactory, the dose is increased, and in case of poor tolerance, parenteral administration of iron is recommended. The timely application of medical and other methods designed to maintain hemoglobin concentration, optimize hemostasis and minimize blood loss, as well as the effort to improve the outcome of patient treatment, is called „Patient blood management" (PBM). PBM is a form of personalized medicine and represents a multidisciplinary approach aimed at improving the treatment of patients, especially those at risk of anaemia and in whom there is a significant likelihood of blood loss and the need for transfusion.

Uloga intravenske primene gvožđa u korekciji sideropenijske anemije

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Uvod: Sideropenijska anemija (SA) je najrasprostanjenija vrsta anemije u svetu. Etiološki gledano, mnogo je uzroka koji mogu dovesti do SA međutim, svi uzroci se svode na nedovoljni unos ili apsorpciju gvožđa, neodgovarajući metabolizam gvožđa u organizmu, povećane potrebe za gvožđem te povećano gubljenje gvožđa. U centru terapije SA osim terapije u okviru osnovnog uzroka anemije, nalazi se primena preparata gvožđa. Gvožđe se u terapiji SA može primeniti oralno, intramuskularno i intravenski.

Cilj: Analizirajući dostupne naučno-istaživačke i pregledne članke ukazati na ulogu intravenske primene gvožđa u korekciji anemije.

Materijal i metode: U ovom preglednom članku koristili smo dostupne podatke istraživača pretraživajući termine: sideropenijska anemija i intravenska primena gvožđa, koristeći se pretraživačem PubMed.

Diskusija: Razvoj preparata gvožđa za intravensku primenu prešao je dug put, od primene prvih preparata koji su bili toksični i nosili su visok rizik za neželjenu reakciju do današnjih preparata koji su sigurni za primenu i nose mali rizik za anafilaktičku reakciju i neželjene reakcije. Prednosti intravenske primene gvožđe su brza i efikasna nadoknada gvožđa i korekcija anemije, osigurana komplijansa, manja potreba za transfuzijom eritrocita u korekciji, kao i bezbedna primena sa malim rizikom od neželjenih reakcija. Intravenska primena preparata gvožđa zahteva konstantan monitoring pacijenta, adekvatnu opremu i obučeno osoblje kako bi se blagovremeno i adekvatno lečio pacijent u slučaju pojave neželjene reakcije.

Zaključak: Procena rizika/koristi od intravenske primene gvožđa u odnosu na primenu per os mora se sagledati iz ugla personalizovane terapije sideropenijske anemije.

The role of intravenous iron administration in the correction of iron deficiency anemia

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Introduction: Sideropenic anemia (SA) is the most common type of anemia in the world. Etiologically, there are many causes that can lead to SA, however, all causes have in common insufficient iron intake or absorption, inadequate iron metabolism in the body, increased iron needs and increased iron loss. At the center of therapy of SA, in addition to therapy for the underlying cause of anemia, is the use of iron which can be administered orally, intramuscularly and intravenously.

Aim: Analyzing the available scientific research and review articles, we aimed to point out the role of intravenous iron administration in the correction of iron deficiency anemia.

Material and methods: In this review article, we used available data by searching for the terms: sideropenic anemia and intravenous iron administration, using the PubMed search engine.

Discussion: The development of iron preparations for intravenous administration has come a long way, from the use of the first preparations that were toxic and carried a high risk for an adverse reaction to today's preparations that are safe for use and carry a low risk of anaphylactic reaction and adverse reactions. The advantages of intravenous iron administration are fast and effective iron replacement and correction of anemia, ensured compliance, less need for erythrocyte transfusion in correction, as well as safe administration with a low risk of adverse reactions. Intravenous administration of iron preparations requires constant monitoring, adequate equipment and trained personnel in order to treat the patient in a timely and adequate manner in case of unwanted reactions.

Conclusion: The risk/benefit assessment of intravenous iron administration versus oral administration must be viewed from the perspective of personalized therapy for iron deficiency anemia.

Značaj premedikacije u transfuziji

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Uvod: Najčešći oblik transfuzijskih reakcija koje se smatraju imunski posredovane su febrilna nehemolizna transfuzijska reakcija i alergijske reakcije. Pacijenti transfundovani sa koncentrovanim trombocitima ili nedeleukocitovanim krvnim komponentama imaju veću stopu reakcija. U ovom preglednom članku koristili smo naučno-istraživačke podatke autora čiji su radovi objavljeni na PubMed-u.

Cilj ovog članka je da se istakne značaj premedikacije u transfuziji kao i smernica za što sigurniju primenu transfuzije.

Tema: Pretransfuzijska medikacija može obuhvatati acetaminofen, sam ili u kombinaciji sa difenhidraminom, ili hidrokortizonom zbog njihovih farmakoloških dejstava. Acetaminofen (paracetamol) je nesteroidni antiinflamatorni lek koji se koristi kao analgetik i antipiretik sa veoma slabim antiinflamatornim efektom. Glavni toksični efekat acetaminofena je oštećenje jetre. Difenhidramin pripada prvoj generaciji antihistaminika koji se koriste za lečenje akutne alergijske reakcije. Prolazi krvno-moždanu barijeru i dovodi do pospanosti i smanjenja kognitivne sposobnosti. Može dovesti do kardiotoksičnosti i aritmija. Hidrokortizon (glukokortikoid) je farmakološko ime za kortizol čija antiinflamatorna I imunosupresivna svojstva se koriste za prevenciju I lečenje ozbiljnih alergijskih reakcija kao što su anafilaksa i alergijski posredovan angioedem. Mehanizam delovanja uključuje inhibiciju funkcije leukocita.

Zaključak: Kombinovani pristup dovodi do redukcije transfuzijskih reakcija, odnosno leukoredukcijom krvnih produkata, upotrebom afereznih trombocita od jednog donora, opravdanom primenom premedikacije kao i hemoterapije.

Ključne reči: transfuzijske reakcije, premedikacija

Significance of pre-transfusion medications in blood transfusion

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Introduction: The most common forms of transfusion reaction which are considered immunological adverse events are febrile non-haemolytic transfusion reactions and allergic reactions. Patients transfused with pooled platelet concentrate or non-leukoreduced blood components had the high rate of reactions. In this review article we used scientific research data of the authors whose articles are published on the PubMed.

The aim of this review article was to highlight the importance of pretransfusion medication and to give guidelines for the safest possible application of blood products.

Topic: Pretransfusion medication can involve acetaminophen, alone or in combination with diphenhydramine, or hydrocortisone due to their pharmacological actions. Acetaminophen (paracetamol) is a non-steroidal anti-inflammatory drug with potent antipyretic and analgesic properties but with very weak anti-inflammatory properties. The main toxicity is liver damage. Diphenhydramine is a first-generation antihistamine drug used for treating acute allergic reactions. Diphenhydramine crosses the blood-brain barrier and cause drowsiness and impairing cognitive performance. Also can cause cardiotoxicity and arrhythmias. Hydrocortisone(glucocorticoid) is the pharmacological name for cortisol whose anti-inflammatory and immunosuppressive properties are used for preventing and treating severe allergic reactions such as anaphylaxis and allergy mediated angiooedema. The mechanism of action involves the inhibition of leukocyte functions.

Conclusion: A combined approache leads to reduction in transfusion reaction, respectively leukoreduction of blood products, use of single-donor apheresis platelet units, justified application of pretransfusion medication and blood transfusion.

Key Words: transfusion reaction, premedication

Tumor markeri i metode određivanja

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Maligne bolesti zauzimaju drugo mesto u strukturi mortaliteta posle KVB. Za određivanje tumor markera (TM) značajne su RIA i IRMA metode kojima se dobija najtačnija i najpreciznija koncentracija TM i kod kojih se ne javljaju interferencije kao kod mnogih metoda. Zbog čega RIA i IRMA predstavljaju referentne metode za određivanje TM. TM su supstance nastale direktnom sintezom TU ćelija ili sintezom izazvanom od TU ćelija u netumoroznom tkivu. Radioimunološkim *in vitro* metodama RIA i IRMA može se otkriti tumor određivanjem TM kada je sadržaj 10^6 ćelija i težina 1mg. Određivanjem TM otkrivamo vezu za određeni tip neoplazme i pružaju nam se informacije o remsiji ili recidivu bolesti kao i ukazivanje na veličinu tumor mase. RIA i IRMA metodama se brzo i pouzdano otkrivaju TM i neki enzimi koji ukazuju na tumore. To su najpouzdanije i najpreciznije metode za određivanje TM, hormona, enzima, vitamina, lekova i dr. Daju veliku tačnost koncentracije TM u cirkulaciji, jako su osetljive, specifične i tačne zbog specifičnosti monoklonskih antitela i obeleživaca J^{125} koji daje stabilan kompleks AT-AG reakcije dok kod IRMA imaju dva AT (sendvič metoda), obeleživač J^{125} sa $t_{1/2}$=60 dana i Eγ=35 KeV. To su najosetljivije kvantitativne i kvalitativne tehnike koje se koriste u svim oblastima, izvode se u svim telesnim tečnostima u veoma malim koncentacijama, reda 10^{-12}mol/l. Afinitet RIA 10^9 do 10^{11}. IRMA je osetljivija 5 x 10^{-14} – 10^{-17} (kocka šećera u olimpijskom bazenu) što govori o preciznosti metode. Metode karakteriše visoka specifičnost i preciznost zbog monklonskih i poliklonskih antitela, meri koncetraciju samo jedne supstance koja se ispituje - princip ključa i nema interferencije kao kod drugih metoda. Tačnost metoda RIA i IRMA daju brz i pouzdan način za uspostavljanje dijagnoze, praćenje mnogih bolesti, kao i praćenje efikasnosti terapije i operacije. RIA i IRMA su *in vitro* dijagnostike, gde pacijent ne dobija dozu JZ već se određuje iz uzorka krvi pacijenta. RIA i IRMA metodama se dobija tačna koncentracija TM jer su monoklonoska specifična antitela samo za taj marker koji se određuje dok kod drugih metoda ,kao što je ICMA, su mišija antitela gde dolazi do interferencija i lažno pozitivnih ili negativnih rezultata.

Tumor markers and methods of determination

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Malignant diseases take the second place in the structure of mortality after CVD. For the determination of tumor markers (TM), RIA and IRMA methods are important, which provide the most accurate and precise concentration of TM and in which no interference occurs as in many other methods. This is why RIA and IRMA are the reference methods for determining TM. TM are substances formed by the direct synthesis of TU cells or by synthesis induced by TU cells in non-tumor tissue. In vitro radioimmunoassay methods RIA and IRMA can detect a tumor by determining TM when the cells content is 10^6 and the weight is 1mg. By determining TM, we discover the connection for a certain type of neoplasm and get information about remission or recurrence of the disease, as well as indication of the size of the tumor mass. RIA and IRMA methods quickly and reliably detect TM and some enzymes that indicate tumors. These are the most reliable and precise methods for determining TM, hormones, enzymes, vitamins, drugs, etc. They give high accuracy of TM concentration in the blood circulation, which is very sensitive, specific and accurate due to the specificity of monoclonal antibodies and markers J^{125} which gives a stable complex of AT-AG reaction while IRMA have two AT (sandwich method), marker J^{125} with $t_{1/2}$=60 days and Eγ=35 KeV. These are the most sensitive quantitative and qualitative techniques used in all areas, performed in all body fluids in very small concentrations, in the range of 10^{-12} mol/l. Affinity RIA 10^9 to 10^{11}. IRMA is more sensitive 5 x 10^{-14}-10^{-17} (sugar cube in the Olympic pool), what indicate the precision of this method. The methods are characterized by high specificity and precision due to monoclonal and polyclonal antibodies, measure the concentration of only one substance being tested - the key principle and there is no interference as with other methods. RIA and IRMA are in vitro diagnostics, where the patient does not receive a dose of IR nor it is determined from a patient's blood sample. RIA and IRMA methods give the correct concentration of TM because of monoclonal specific antibodies that are only for specific marker which is determined, while other methods, such as ICMA, are mouse antibodies where interference occurs as well as false positive or negative results. The choice of method is highly important, therefore RIA and IRMA methods provide a fast and reliable way to establish the diagnosis, monitor many diseases, as well as the effectiveness of therapy and surgery.

Troškovi i potrošnja kontrastnih sredstava u Srbiji od 2011. do 2020. godine

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Pozadina/cilj: Milioni radioloških pregleda se izvode godišnje u različitim zemljama širom sveta pomoću klasične radiografije (rendgensko snimanje), dijagnostičke ultrasonografije (US), kompjuterske tomografije (CT), magnetne rezonance (MRI), fluoroskopije, nuklearne medicine i pregleda pozitronskom emisionom tomografijom (PET) - PET-CT i SPECT skeniranje. Radiološki pregledi (tehnike snimanja) se mogu obaviti sa ili bez upotrebe kontrastnih sredstava. Kontrastni mediji se mogu koristiti sa tehnikama snimanja kako bi se poboljšale razlike koje se vide između telesnih tkiva na slikama. Cilj ove studije je da prikaže desetogodišnju potrošnju i troškove kontrastnih sredstava za radiološku dijagnostiku u Srbiji.

Metode: Ovo je retrospektivna, opservaciona studija upotrebe lekova. U studiji je analizirana potrošnja svih kontrastnih sredstava za radiološku dijagnostiku [jodna sredstva, barijum kontrastna sredstva, MR kontrastna sredstva (paramagnetna kontrastna sredstva i superparamagnetna kontrastna sredstva) i ultrazvučna kontrastna sredstva] tokom desetogodišnjeg perioda (2011-2020. godine) u Srbiji. Podaci su analizirani korišćenjem ukupne količine kontrastnih sredstava izraženih kao ukupna aktivna supstanca u mg ili mg na 1000 stanovnika.

Rezultati: Tokom desetogodišnjeg perioda u Srbiji ukupna izdvajanja za kontrastna sredstva su imala trend rasta, ali sa godišnjim varijacijama (7,4 miliona evra potrošeno je u 2011. godini, dok je u 2019. godini 12 miliona evra, a 2020. manje od 10 miliona evra). S druge strane, potrošnja kontrastnih sredstava pokazuje konstantan pad sa oko 24,479 miliona mg u 2011. na oko 12,541 miliona mg u 2020.

Zaključci: U Srbiji izdvajanja za kontrastna sredstva pokazuju rastući trend tokom posmatranog desetogodišnjeg perioda, iako se stvarna potrošnja izražena u mg smanjuje.

Ključne reči: potrošnja, troškovi, Srbija, kontrastna sredstva

Costs and consumption of contrast agents in Serbia from 2011 to 2020

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Background/Aim: Millions of radiologic examinations are performed each year in different countries worldwide by Plain Radiography (X-ray), Diagnostic Ultrasonography (US), Computed Tomography (CT), Magnetic Resonance Imaging (MRI), Fluoroscopy, Nuclear Medicine, and Positron Emission Tomography (PET) exams- PET-CT and SPECT Scans. Radiologic examinations (imaging techniques) can be performed with or without the use of contrast agents. Contrast media may be used with imaging techniques to enhance the differences seen between the body tissues on the images. The aim of this study is to present ten-year consumption and costs of contrast agents for radiological diagnostics in Serbia.

Methods: This is retrospective, observational, drug utilisation study. Consumption of all contrast agents for radiological diagnostics [Iodine Agents, Barium Contrast Media, MR Contrast Media (Paramagnetic Contrast Agents and Superparamagnetic Contrast Agents), and Ultrasound Contrast Media] has been calculated concerning ten-year period (2011-2020) in Serbia. Data were analysed using total amount of contrast agents expressed as active substance in total mg or mg per 1000 inhabitants.

Results: During the ten-year period in Serbia, the total allocations for contrast agents showed a rising trend, but with annual variations (7.4 million Euros were spent in 2011; in 2019 costs amounted to 12 million Euros, while in 2020 less than 10 million Euros was invested). On the other hand, consumption of contrast agents shows a constant decline from about 24,479 million mg in 2011 to about 12,541 million mg in 2020.

Conclusions: In Serbia, allocations for contrast agents is substantial with a rising trend noted for the ten years of observation, although the actual consumption expressed in mg constantly decrease.

Key words: consumption, costs, Serbia, contrast agents

Izazovi u doziranju vankomicina kod oštećenja mozga izazvanih traumom

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Traumatska povreda mozga je teško stanje koje je često komplikovano infekcijama, koje otežavaju oporavak, produžavaju lečenje i povećavaju mortalitet. Gram pozitivne bakterije su najčešći uzročnici infekcija nakon kraniotomija. Takođe, ovo stanje je često praćeno hipermetabolizmom i povećanim bubrežnim klirensom. Povećan bubrežni klirens je fenomen koji karakteriše povećan klirens kreatinina iznad 130 mL/min/1,73m^2 i povezan je sa smanjenim koncentracijama određenih antibiotika u krvi, kao što je vankomicin. Ovo može biti uzrok neuspeha lečenja. Odgovarajuća metoda merenja koncentracije antibiotika u krvi je posebno važna kod ovih pacijenata.

Prikazan je pacijent sa traumatskom povredom mozga praćenom sekundarnom infekcijom i povećanim bubrežnim klirensom uz subterapijske koncentracije vankomicina u vreme lečenja. Inflamatorni parametri su bili povećani tokom postoperativnog perioda. Empirijska antimikrobna terapija uključivala je meropenem 1g/8 h, vankomicin 1g/12 h i 200 mg/dan flukonazola. Izmerene su najniže koncentracije vankomicina u serumu i dobijena vrednost je bila ispod terapijskih koncentracija (1,33 μg/ml). Urađeno je naknadno prilagođavanje doze vankomicina na 1g/8 h i postignute koncentracije u plazmi bile su oko 2,3 μg/ml. Minimalna ciljna koncentracija od 15–20 mg/mL je potrebna da bi se postigla vrednost odnosa AUC0-24:MIC ≥ 400 za invazivne MRSA infekcije kod odraslih.

Dodatna istraživanja farmakokinetike vankomicina i sprovođenje rutinskog terapijskog monitoringa kod ovih pacijenata mogu doprineti optimizaciji njegovog doziranja.

Challenge in vancomycin dosing in traumatic brain injuries

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Traumatic brain injury is a severe condition frequently complicated with infections, and results in prolonged hospitalizations and intrahospital mortality. Infections caused by gram-positive bacteria are the most common infections after craniotomy. Also, this condition is often accompanied by hypermetabolism and augmented renal clearance. This is a phenomenon characterized by augmented creatinine clearance above 130 mL/min/1.73m^2, which has been associated with decreased blood concentrations of selected antibiotics, like vancomycin. This probably may cause treatment failure. The method of antibiotics blood concentration measurement is especially important in critically ill patients.

A patient with traumatic brain injury accompanied by secondary infection and augmented renal clearance accompanied with subtherapeutic vancomycin concentrations at the time of treatment is presented. Inflammatory parameters were increased during the postoperative period. Empirical antimicrobial therapy included meropenem 1g/8h, vancomycin 1g/12 h, and 200 mg/day fluconazole. Serum trough concentrations of vancomycin were measured, and the obtained value was below therapeutic range concentrations (1.33 μg/ml). Subsequent dose adjustment of vancomycin to 1g/8 h was performed and the achieved plasma concentrations were about 2.3 μg/ml. A minimum target concentration of 15–20 μg/mL would be required to achieve AUC0-24:MIC ≥ 400 for invasive MRSA infections in adults.

Further investigations of the pharmacokinetics of vancomycin in these patients are necessary, as well as the implementation of routine therapeutic drug monitoring in the hospitals since further optimization of its dosing is needed.

Potrošnja rezervnih antibiotika u Vojnomedicinskoj akademiji pre i tokom pandemije Covid-19

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Svetska zdravstvena organizacija (SZO) je 2021. objavila novu listu esencijalnih lekova, gde su navedeni rezervni i antibiotici pod posebnim nadzorom koji se ne nalaze u grupi rezervnih. U Vojnomedicinskoj akademiji (VMA), na listi rezervnih antibiotika nalaze se antimikrobni lekovi iz 7 grupa (polimiksini, glicilciklini, oksazolidinoni, karbapenemi, beta-laktamski antibiotici sa inhibitorom beta-laktamaze, cefalosporini 4. generacije i glikopeptidni antibiotici). Od antibiotika koji se koriste u VMA, rezervni antibiotici sa liste SZO su samo kolistin i linezolid. Međutim, da bi se obezbedilo odgovarajuće praćenje potrošnje i smanjenje mogućnosti rezistencije na ovu grupu lekova, u VMA se još 5 grupa antimikrobnih lekova smatra rezervnim i koriste u specijalnom režimu propisivanja. Praćena je i analizirana njihova potrošnja u periodu pre (od 2009.-2019. god) i tokom pandemije COVID-19 (2020.-2021. god), gde je potrošnja izražena kao broj DDD/100 BD. Najveća potrošnja svih rezervnih antibiotika zabeležena je u 2018. god. (13,92 DDD/100 BD), kao nastavak trenda porasta potrošnje iz prethodnih godina, da bi nastao značajan pad u 2019. godini (9,26 DDD/100 BD). U godinama pandemije, zabeležen je porast potrošnje (11,53 i 12,76 DDD/100 BD, u 2020. i 2021. god., redom). U svim navedenim godinama, najviše su korišćeni meropenem, vankomicin i imipenem sa cilastatinom.

Reserve antibiotics consumption in military medical academy, before and during covid-19 pandemic

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World health organization (WHO) published new 22nd Model List of Essential Medicines in 2021. with Access, Watch and Reserve group antibiotics. In Military Medical Academy (MMA), ten antibiotics are classified within a reserve group (Polymyxines, Glycylcycline, Oxazolidinones, Carbapenems, Beta-lactam / beta-lactamase inhibitor, Fourth-generation-cephalosporines, Glycopeptides). Compared to the WHO list, only two of them (linezolid and colistin) are maching the same Reserve group, while others belong to the Watch group list. We analyzed their consumption in MMA, ten years before COVID-19 pandemic (2009 – 2019 y.) and during first two years (2019 - 2020 y.). Consumption is expressed as a number of DDD/100 BD. Maximum utilization of all reserve antibiotics was recorded in 2018 (13.92 DDD/100 BD). In the very next year there was a drop in the consumption (year 2019, 9.26 DDD/100 BD), but in the pandemic years a slight increase occurred (11,53 i 12,76 DDD/100 BD, in 2020 and 2021, respectively). Antibiotics with highest utilization rate were meropenem, vancomycin and imipenem, cilastatin.

Infliksimab u lečenju toksične epidermalne nekrolize izazvane ko-trimoksazol-om: prikaz slučaja

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Toksična epidermalna nekroliza (TEN), poznata i kao Lajlov sindrom, predstavlja veoma redak, idiosinkratski, životno ugrožavajući, sistemski mukokutani poremećaj, koji se uglavnom javlja kao neželjena reakcija posle primene antibiotika, antiepileptika, nesteroidnih antiinflamatornih lekova, alopurinola i drugih medikamenata. Ova akutna hipersenzitivna reakcija karakteriše se široko rasprostranjenim regijama eritema i nekroze kože sa buloznim odvajanjem i eksfolijacijom epidermisa i mukoznih membrana, što progredira u ozbiljne infektivne i neinfektivne komplikacije, sa mogućim razvojem multiorganske insuficijencije i pojavom smrtnog ishoda kod 10-70% pacijenata. Uzimajući u obzir da terapijske smernice još uvek nisu jasno formulisane lečenje TEN je neizvesno i povezano sa velikim izazovima. Obuhvata promptno prepoznavanje ovog poremećaja i obustavu inkriminisanog leka, uz primenu simptomatske, potporne i imunosupresivne nefarmakološke i farmakološke terapije. Nespecifična i specifična imunosupresivna terapija zasniva se na pretpostavljenim patofiziološkim mehanizmima nastanka TEN, među kojima se izdvaja inflamatorni učinak faktora nekroze tumora alfa (TNF alfa). U radu prikazujemo slučaj pacijentkinje, stare 52 godine, koja je razvila težak oblik TEN nakon upotrebe Bactrim®-a (sulfametokazol, trimetoprim). U lečenju ove pacijentkinje po prvi put u našoj ustanovi primenjen je jednokratno infliksimab, antagonista TNF alfa. Međutim, uprkos primeni ove specifične imunosupresivne terapije pacijentkinja je egzitirala 16 dana nakon postavljanja dijagnoze.

Infliximab in the treatment of co-trimoxazole-induced toxic epidermal necrolysis: a case report

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Toxic epidermal necrolysis (TEN), also known as Lyell's syndrome, is a very rare, idiosyncratic, life-threatening, systemic mucocutaneous disorder, which mainly occurs as an adverse reaction after the administration of antibiotics, antiepileptics, non-steroidal anti-inflammatory drugs, allopurinol and other drugs. This acute hypersensitivity reaction is characterized by widespread areas of erythema and necrosis of the skin with bullous separation and exfoliation of the epidermis and mucous membranes, which progresses to serious infectious and non-infectious complications, with the possible development of multiorgan failure and death in 10-70% of patients. Considering that therapeutic guidelines are still not clearly formulated, the treatment of TEN is uncertain and associated with great challenges. It includes prompt recognition of this disorder and suspension of the incriminated drug, along with the application of symptomatic, supportive and immunosuppressive non-pharmacological and pharmacological therapy. Nonspecific and specific immunosuppressive therapy is based on presumed pathophysiological mechanisms of TEN, among which the inflammatory effect of tumor necrosis factor alpha (TNF alpha) stands out. In this paper, we present the case of a 52-year-old female patient who developed a severe form of TEN after using Bactrim® (sulfamethoxazole, trimethoprim). In the treatment of this patient, for the first time in our institution, infliximab, a TNF alpha antagonist, was used once. However, despite the application of this specific immunosuppressive therapy, the patient died 16 days after the diagnosis.

Antioksidativni efekat CardiofortIN-a u doksorubicinom izazvanoj kardiotoksičnosti

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Doksorubicin, antraciklinski citotoksični antibiotik, koristi se u lečenju različitih malignih oboljenja. Kliničku upotrebu doksorubicina ograničavaju neželjena dejsta, najverovatnije uzrokovana oksidativnim stresom.

Ukupno 36 životinja je podeljeno u 4 grupe. Životinje su dobijale fiziološki rastvor (K), CardiofortIN (CF, 19.25 mg/kg), doksorubicin sam (D, 1.5 mg/kg) ili sa CardiofortIN-om (CFD). Indukovana je akutna kardiotoksičnost jednom, intraperitonealnom dozom doksorubicina 8-og dana eksperimenta, dok su se fiziološki rastvor i CF primenjivali od 1-og do 8-og dana. Srčano tkivo je histološki obrađeno i bojeno hematoksilin-eozinom. Mikroskopskom analizom utvrdjeno je postojanje oštećenja miokarda. Iz homogenata srca određen je intenzitet lipidne peroksidacije (malonilaldehid, MDA) i aktivnost antioksidativnih enzima (AE) (superoksid dismutaza; katalaza, glutation S-transferaza; glutation peroksidaza).

Doksorubicin značajno povećava intenzitet lipidne peroksidacije i smanjuje aktivnost AE ($p<0,05$) u poređenju sa K grupom. Primena CF prevenira porast lipidne peroksidacije ($p<0,01$) i normalizuje aktivnost AE. U grupi D, tkivni indikatori oštećenja miokarda (vakuolizacija, dezorganizacija miofilamenata, perinuklearni halo) bili su češći i izraženiji u poređenju sa CFD grupom.

CardiofortIN antioksidativnim delovanjem ima potencijal sprečavanja doksorubicinom-izazvane kardiotoksičnosti, što se ogleda u redukciji oštećenja miokarda na životinjskom modelu.

Ključne reči: doksorubicin, kardiotoksičnost, CardiofortIN, oksidativni stres, miokard

Ovaj eksperiment je podržan od strane Autonomne Pokrajine Vojvodine (Projekat br. 142-451-2543/2021-02)

Antioxidative effects of CardiofortIN in doxorubicin cardiotoxicity

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Doxorubicin is an anthracycline cytostatic antibiotic. Anthracyclines are commonly used antineoplastic agents in the treatment of a variety of malignancies. Cardiotoxicity remains an irreversible complication of anthracycline-based chemotherapy, which limits the use of doxorubicin. It is believed that doxorubicin cardiotoxicity is caused by DNA and myocardium damage through induction of oxidative stress.

In total, 36 animals, were randomly divided into 4 groups. According to study design, animals were given saline (C), CardiofortIN (CF, 19.25 mg/kg), doxorubicin alone (D, 1.5 mg/kg) or with CardiofortIN (CFD). We induced a model of acute cardiotoxicity, with a single, intraperitoneal dose of doxorybicin, on the 8th experimental day, while saline and CF were given from the 1st-8th experimental day. Heart tissue samples were processed by standard histological technique and stained with the hematoxylin-eosin method. Tissue slides were microscopically analyzed for the presence of indicators of myocardial damage. From the heart tissue homogenate were determined the intensity of lipid peroxidation (determined by the amount of malonyl aldehyde (MDA)) and specific antioxidative enzyme (AOE) activity (superoxide dismutase; catalase; glutathione S-transferase; glutathione peroxidase).

Doxorubicin increases the intensity of lipid peroxidation, while in the CFD group the intensity of lipid peroxidation was significantly lower ($p < 0.01$). Doxorubicin significantly reduces the activity of AOE compared to the K group ($p < 0.05$). CardiofortIN treatment (CFD group) attenuates doxorubicin's prooxidative effect, compared to the D group. In the D group, tissue indicators of myocardial damage (vacuolization, myofilaments disorganization, nuclear changes and perinuclear halo) were more pronounced and frequent, as opposed to group CFD.

CardiofortIN has a high potential for preventing doxorubicin cardiotoxic effects, through lowering lipid peroxidation, inducing AO activity, and leading to reduction of myocardial damage in animal model.

Key words: doxorubicin, cardiotoxicity, oxidative stress, myocardium

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Uticaj statina na prisustvo Bcl2-pozitivnih makrofaga

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Statini imaju više plejotropnih efekata, takođe postoje indicije da utiču na preživljavanje makrofaga.

Analizirano je tkivo zida aorte 50 pacijenata, od kojih neki nisu (nonS, n=25), a neki su imali terapiju statinima (S, n=25). Svaka grupa je imala uzorke zdravog tkiva aorte, blage i teške aterosklerotične promene. Tkivo je obojeno hematoksilin-eozin metodom i imunohistohemijski (anti-Bcl2 antitelo). Prisustvo Bcl2 pozitivnih makrofaga (Bcl2+MF) je određeno semikvantitativno.

Zdrave aorte S-grupe su imale značajno povećano prisustvo Bcl2+MF u odnosu na nonS (80% prema 6,67%). Najčešće je povećan Bcl2+MF pronađen u intimi i mediji zida aorte. Patološki izmenjene aorte S grupe češće su imale izražen porast Bcl2+MF (36,25% prema 25%). Aterosklerotski uzorci S grupe (i blage i teške) imali su značajno povećanje Bcl2+MF češće nego nonS. Izraženo povećanje Bcl2+MF aterosklerotskih plakova grupe S u poređenju sa nonS, statistički se češće nalazi u subintimalnom delu plaka i na granici sa medijom aorte.

Povećan broj Bcl2+MF se pripisuje statinima zbog njihove sposobnosti pojačavanja antiapoptotičkih faktora, kako u zdravom tako i u aterosklerotično izmenjenom tkivu aorte. To može dovesti do potenciranja i produženja zapaljenja, dok ono može izazvati oštećenje zida aorte i pucanje plakova, te se dovodi u pitanje pozitivan efekat statina na zid aorte kod pacijenata sa aterosklerozom.

Impact of statins on presence of Bcl2-positive macrophages

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Statins have many pleiotropic effects. Beside those, there are indications that they affect macrophage survival.

Aortic wall tissue of 50 patients was analysed, some of whom did not (nonS, n=25) and some of whom had statin therapy (S, n=25). Each group had samples of healthy aortic tissue, mild and severe atherosclerotic changes. Tissue was stained with hematoxylin-eosin and immunohistochemically (anti-Bcl2 antibody). Presence of Bcl2-positive macrophages (Bcl2+MP) was determined semiquantitatively.

S-group healthy aortas had significantely increased presence of Bcl2+MP opposite to nonS (80% vs 6,67%). Most frequently, increased Bcl2+MP were found in intima and media of aortic wall. S-group pathologicaly altered aortas more often had marked Bcl2+MP increase (36,25% vs 25%). Atherosclerotic samples of the S-group (both mild and severe) had a marked increase in Bcl2+MP significantly more frequent compared to nonS. Marked Bcl2+MP increase in atherosclerotic plaques of group S, compared to nonS, is statistically more often found in the subintimal part of the plaque and at the border with the media of the aorta.

Statins attributed to greater number of Bcl-2+MP by enhancing antiapoptotic factors, both in healthy and atherosclerotic altered aortic tissue. This can lead to potentiation and prolongation of inflammation. Since inflammation can cause damage to the aortic wall, and rupture of the plaques, it calls into question the positive effect of statins on the aortic wall with atherosclerosis.

Faktori uticaja na znanje o sintetskim kanabinoidima - studija sprovedena među budućim zdravstvenim radnicima

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S obzirom da postojeći nastavni plan pruža minimalan broj informacija cilj je ispitati znanje studenata zdravstvenih zanimanja o SC i istražiti faktore koji utiču na stečeno znanje. Unakrsna studija među 510 studenata medicine, stomatologije i farmacije sprovedena je na Medicinskom fakultetu Univerziteta u Novom Sadu, Srbija, tokom 2017. godine. Četrdeset i devet posto učenika je odgovorilo potvrdno na pitanje da li znaju šta su SC, pri čemu su osobe muškog pola pokazale bolje znanje od pripadnica ženskog pola (p=0,014). Ni profesionalne kvalifikacije roditelja (p=0,953 majka, p=0,500 otac) niti postojanje profila na društvenim mrežama (p=0,057) nisu uticali na prethodno znanje studenata o SC. Studenti farmacije su pokazali bolje znanje o SC u odnosu na studente drugih smerova (p=0.000), kao i studenti završnih godina u odnosu na studente 1. i 2. godine studija (p=0.000). Obnavljanje godine nije uticalo na znanje koje su studenti pokazali prilikom popunjavanja upitnika (p=0,616). Studenti koji su konzumirali alkohol pokazali su bolje znanje o SC u odnosu na one koji nisu konzumirali alkohol (p=0,008). Međutim, većina ispitanika je na najveći broj tvrdnji o SC odgovorila sa „ne znam”.

Factors influencing knowledge of synthetic cannabinoids – study conducted among future healthcare professionals

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Since there is not enough information in the current curriculum the main goal is to assess the level of knowledge of students of health professions about SC and examine the factors that influence that knowledge. A cross-section study was conducted among 510 students of medicine, dentistry and pharmacy at the Faculty of Medicine, University of Novi Sad, Serbia, during 2017 using a structured questionnaire. Forty-nine percent of students answered positively to the question if they knew what SCs were, with male students demonstrating a better knowledge than female ones (p=0.014). There was no correlation between previous knowledge about SCs and professional qualifications of the student's parents (p=0.953 mother, p=0.500 father) or the student's social media profile existence (p=0.057) . Pharmacy students showed better previous knowledge about SCs in comparison with students of other courses (p=0.000) as well as the final year students when compared to those from the 1st and 2nd year of study (p=0.000). The repetition of a year level did not affect student's knowledge (p=0.616). Students with experience in alcohol usage showed better previous knowledge of SCs in comparison with alcohol non-users (p=0.008). However, most of the respondents answered „do not know" on the majority of statements about SCs offered.

Uticaj ekstrakta rogača na lipidni profil kod pacova sa indukovanom hiperlipoproteinemijom

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Hiperlipoproteinemije su najčešći metabolički poremećaji u opštoj populaciji i jedan od glavnih faktora rizika za razvoj kardiovaskularnih oboljenja. Biljka rogača (Ceratonia siliqua L.) predstavlja izvor bioaktivnih jedinjenja, među kojima su najznačajniji polifenolna jedinjenja sa potencijalnim antioksidativnim efektom i uticajem na metabolizam lipida.

Ispitivanje je sprovedeno na belim laboratorijskim pacovima soja Wistar, kod kojih je indukovana hiperlipoproteinemija metodom ishrane životinja hranom fortifikovanom holesterolom (3%) i holnom kiselinom (0,5%). Životinje su tretirane per os tokom 4 nedelje, ekstraktom rogača (400 mg/kg) i simvastatinom (10 mg/kg). Žrtvovanje je sprovedeno metodom kardiopunkcije su uzeti uzorci krvi u kojima je određen lipidni status.

Koncentracije ukupnog, non-HDL i LDL holesterola kod hiperlipoproteinemičnih životinja koje su tretirane ekstraktom rogača su niže, dok je nivo HDL holesterola bio viši u odnosu na životinje tretirane fiziološkim rastvorom. Sinergističkim dejstvom ekstrakt rogača i simvastatin doveli su do smanjenja ukupnog holesterola u odnosu na kontrolnu grupu ($p<0,05$). Kod životinja tretiranih ekstraktom rogača došlo je do statistički značajnog smanjenja telesne mase u odnosu na životinje sa hiperlipoproteinemijom, koje su tretirane fiziološkim rastvorom ($p<0,05$).

Ekstrakt rogača ispoljava uticaj na metabolizam lipida kao i na smanjene telesne mase pacova kod kojih je indukovana hiperlipoproteinemija. Rezultati dobijeni ovom studijom predstavljaju korisnu osnovu za buduća ispitivanja.

Ovaj rad je podržan od strane Pokrajinskog sekretarijata za visoko obrazovanje i naučnoistraživačku delatnost APV (Projekat broj: 142-451-2574/2021).

Effects of carob pods extract on lipid profile in rats with induced hyperlipidemia

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Hyperlipoproteinemia is the most common metabolic disorder and one of the main risk factors for the development of cardiovascular disease. Carob beans are a source of polyphenolic compounds with a potential antioxidant effect and have an impact on metabolism of the lipids.

The research was conducted on white Wistar laboratory rats, in which hyperlipoproteinemia was induced by food enriched with cholesterol (3%) and cholic acid (0.5). During 4 weeks the animals were orally treated with carob extract (400 mg/kg) and simvastatin (10 mg/kg). After sacrificed, samples of blood were collected by using the cardiopunction method and then used in the assessment of lipid profile.

Concentrations of the total, non-HDL and LDL cholesterol in serum hyperlipoproteinemic animals treated with carob extract were lower, while the level of HDL cholesterol is higher in comparison with control group. The synergistic effect of carob extract and simvastatin led to a significant reduction in total cholesterol compared to the group treated with saline ($p < 0.05$). In animals treated with carob extract, there was a decrease in body weight compared to hyperlipidemic animals ($p < 0.05$).

Carob extract effects on the metabolism of lipids and has significant hypocholesterolemic potential. The potential effect of carob extract in the treatment of obesity has been shown. The results obtained by this study in the preclinical environment represent a useful basis for future trials.

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Znanje i učestalost zloupotrebe psihostimulanasa kod studenata Medicinskog fakulteta u Novom Sadu

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Uvod: Primećuje se porast upotrebe psihostimulanasa u nemedicinske svrhe kod studenata različitih univerziteta. Studenti medicinskih fakulteta naročito su skloni njihovoj upotrebi.

Cilj: Ispitati učestalost i razloge upotrebe psihostimulanasa, kao i znanje o psihostimulansima kod studenata Medicinskog fakulteta u Novom Sadu.

Materijal i metode: Istraživanje je bilo prospektivno i sprovodilo se na Medicinskom fakultetu u Novom Sadu, među studentima svih smerova i godina studija. Sprovedena je anonimna anketa u vidu upitnika o obaveštenosti i upotrebi psihostimulanasa.

Rezultati: Učestalost upotrebe psihostimulanasa iznosila je 12%. Najviše studenata je navelo da psihostimulanse koristi najčešće za poboljšanje koncentracije tokom učenja (6,5%). Češće su psihostimulanse koristili studenti muškog (22.6%), nego ženskog pola (7.2%), $p<0.001$. Studenti koji više puta nedeljno konzumiraju alkohol takođe su češće koristili psihostimulanse (57.1%), $p<0.001$. Isto važi i za studente koji su aktivni pušači (36.4%), $p<0.001$. Takođe, 30.1% onih koji su izjavili da su konzumirali marihuanu, probalo je i psihostimulanse, za razliku od onih koji nisu probali marihuanu ($p<0.001$). Prosečan skor znanja iznosio je 8,54 ± 0,43. Veće vrednosti skora znanja ($p<0.05$) su imali studenti koji aktivno puše i oni koji su probali marihuanu, kao i studenti farmacije i studenti završnih godina.

Zaključak: Najčešći razlog upotrebe psihostimulanasa je poboljšanje kognitivnih sposobnosti. Studenti poseduju zadovoljavajući nivo znanja o psihostimulansima.

Ključne reči: studenti, psihostimulansi, znanje, nemedicinska upotreba

Ovaj rad je podržan od strane Ministarstva za nauku I tehnološki razvoj Republike Srbije, Broj projekta 41012.

Knowledge and misuse of psychostimulants among students of Faculty of Medicine in Novi Sad

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Introduction: The increase in the consumption of psychostimulants for non-medical purposes by students from different universities has been noticed. Medical students are more prone to use psychostimulants.

Aim: To examine the frequency of use, reasons for using and knowledge about the psychostimulants among students of the Faculty of Medicine in Novi Sad.

Material and methods: This prospective research included students of all study programs and years of study at the Faculty of Medicine in Novi Sad. Anonymous survey on the knowledge and the use of psychostimulants was used.

Results: The frequency of psychostimulant use was 12%. Most students reported using psychostimulants to increase concentration for the purpose of studying (6.5%). Psychostimulants were more commonly used by male students (22.6%), $p<0.001$. Students who use alcohol several times a week are more likely to also use psychostimulants (57.1%), $p<0.001$. The same was observed for students who are active smokers (36.4%), $p<0.001$. Also, 30.1% of those who stated that they had consumed marijuana in the past also claimed to have tried psychostimulants in comparison to just 1.6% of those who had not, $p<0.001$. The average score of knowledge was 8.54 ± 0.43. Statistically higher values of knowledge score ($p<0.05$) were observed among students who actively smoke and those who had consumed marijuana as well as in pharmacy and final-year students.

Conclusion: The most common reason for psychostimulant use is the increase of cognitive abilities. Students have a satisfactory level of knowledge about psychostimulants.

Key words: students, psychostimulants, knowledge, non-medical use

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Antibiotici u studentskim kućnim apotekama: uvid u upotrebu, čuvanje i odlaganje

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Uvod: Neadekvatna upotreba antibiotika, uključujući samomedikaciju doprinosi bržem razvoju bakterijske rezistencije. Istraživanje lekova koji se čuvaju u domaćinstvima omogućava uvid u navike vezane za antibiotike, njihovo čuvanje, upotrebu i odlaganje.

Cilj: Cilj istraživanja bio je ispitivanje zastupljenosti antibiotika u kućnim apotekama studentskih domova, kao i učestalosti samomedikacije. Pored toga, određeni su i načini njihovog čuvanja i odlaganja.

Materijal i metode: Istraživanje je sprovedeno u periodu od 01.novembra do 20.decembra 2018.godine, obuhvatilo je 70 studentskih smeštaja u Novom Sadu. Podaci su prikupljeni putem standardizovanog upitnika i direktnim uvidom u inventar antibiotika. Zabeležene su vrste lekova, način nabavke leka, indikacije i trajanje upotrebe.

Rezultati: Tokom inspekcije kućnih apoteka, pronađeno je 337 lekova. Antibiotici su pronađeni u 20 studentskih soba (28,57%), što ih čini prisutnim u procentu od 5,93% ukupnih lekova. Od 20 pakovanja antibiotika samoinicijativno je kupljeno 6 (30%). Najučestalije pronađeni antibiotici su amoksicilin i cefaleksin.

Zaključak: Samomedikacija anitibioticima je učestalija kod studenata u odnosu na opštu populaciju. Velik deo lekova iz studentskih domaćinstava se pravilno čuva, ali se zanemarljiv broj istih adekvatno odlaže.

Ključne reči: antibiotici, samomedikacija, studenti, OTC, POM

Ovaj rad je podržan od strane Ministarstva za nauku i tehnološki razvoj Republike Srbije, Broj projekta 41012.

Antibiotics in student home-pharmacies: insight into drug use, storage and disposal

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Introduction: Inappropriate use of antibiotics, including self-medication contributes to the faster development of bacterial resistance. Researching medicines stored in households provides insight into habits related to antibiotics, their storage, use and disposal.

The aim: Examination of the presence of antibiotics in home pharmacies of student dormitories and the frequency of self-medication. Secondary aim was the identification of methods of their storage and disposal.

Material and methods: The research was conducted from November 1 to December 20, 2018. and included 70 student accommodations in Novi Sad. The data were collected through a standardized questionnaire and direct inspection of the antibiotic inventory. Types of drugs, methods of obtaining, indications and duration of use were also recorded.

Results: During the inspection of home pharmacies, 337 medicines were found. Antibiotics were found in 20 student rooms (28.57%), which accounted for 5.93% of the total number. Out of 20 packages of antibiotics, 6 (30%) were purchased self initiatively. The most frequently found antibiotics are amoxicillin and cephalexin.

Conclusion: Self-medication with antibiotics is more common among students compared to general population. A large part of medicines from student households are properly stored, but a negligible number of them are properly disposed of.

Keywords: antibiotics, self-medication, students, OTC, POM

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In vitro antidijabetesna aktivnost vodenog ekstrakta gljive *Coprinus comatus*

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Dokazano je da gljiva *Coprinus comatus* poseduje razna farmakološka dejstva, a jedno od njih je i antidijabetesno. Jedan od mehanizama antidijabetesnog dejstva bi mogao biti i inhibicija enzima zaslužnih za metabolizam ugljenih hidrata, kao što su α-amilaza i α-glukozidaza, kao i dipeptidil peptidaza-4. Stoga je u ovom radu ispitana aktivnost ovih enzima nakon njihove inhibicije ekstraktom gljive. Cilj rada je bio da se ispita *in vitro* aktivnost vodenog ekstrakta gljive *C. comatus* na gorepomenute enzime. Kao uzorak koristio se komercijalni preparat gljive *C. comatus* od koga je pripremljen vodeni ekstrakt, koji je zatim liofiliziran. Inhibitorna aktivnost je ispitivana spektrofotometrijskim metodama u triplikatu. Vodeni ekstrakt gljive *C. comatus* je pokazao doznu zavisnost pri inhibiciji svih ispitivanih enzima. Ekstrakt je bilo potrebno primeniti u višestruko većoj koncentracijiji kako bi se postigla inhibicija 50 % aktivnosti enzima α-amilaze, α-glukozidaza i dipeptidil peptidaze-4 u poređenju sa pozitivnim kontrolama (akarboza i sitagliptin). Na osnovu rezultata istraživanja može se zaključiti da iako je postignuta 50%-inhibicija enzimske aktivnosti sa primenom ekstrakta gljive *C. comatus* ona nije dovoljna da objasni njeno antidijabetesno dejstvo. Stoga, potrebno je da se nastave istraživanja i ispitaju dodatni mehanizmi, kao i druge formulacije da bi se razjasnila *in vivo* svojstva gljive.

In vitro antidiabetic activity of mushroom *Coprinus comatus* water extract

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It is proven that mushroom *Coprinus comatus* has many pharmacological activities, including antidiabetic. One of the mechanisms of antidiabetic activity may be the inhibition of enzymes responsible for carbohydrates metabolism, such as α-amylase and α-glucosidase and dipeptidyl peptidase-4. Therefore, in this study the activity of these enzymes after their inhibition with *C. comatus* extract was examined. The aim of this study was to examine *in vitro* activity of aqueous extract of mushroom *C. comatus* on previously mentioned enzymes. As a sample it was used. The sample of the commercial preparation of mushroom was used for making of an aqueous extract, which is then lyophilised. Inhibitory activity was measured in triplicate by spectrophotometric methods. Examined water extract of *C. comatus* mushroom showed dose-dependent inhibition of all tested enzymes. Compared to positive controls (acarbose and sitagliptin) the extract was used in much higher concentrations in order to achieve 50% inhibition of enzymes α-amylase, α-glucosidase and dipeptidyl peptidase-4. Based on the results of study it can be concluded that although it was achieved 50% inhibition of enzyme activity with use of *C. comatus* mushroom extract, it is not sufficient to explain its antidiabetic activity. Therefore, it is necessary to examine additional mechanisms, or to make other extract formulations in order to confirm *in vivo* mushroom activity.

Slučaj akutnog kardiogenog edema pluća udruženog sa hipertenzijom i postojećom miokardiopatijom

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Akutni kardiogeni edem pluća je jedno od najurgentnijih stanja u internoj medicini. Hipertenzija kod već postojeće miokardiopatije usled neadekvatnog lečenja je jedan od najčešćih uzroka nastanka akutnog kardiogenog edema pluća.

Predstavljamo slučaj 75 god starog pacijenta, muškog pola, kome SHMP izlazi na teren zbog prijavljenog gušenja. Pacijent od ranije ima identifikovanu hipertenziju koju leči beta blokatorima, ACE inhibitorima i diureticima, uz ultrazvučno dokazanu kardiomiopatiju sa EF 42%. Klinički se prezentuje somnolencijom, pepeljasto sivom kožom oblivenom znojem, dispnejom praćenom kašljem sa iskašljavanjem penušavog sadržaja. Objektivno Glazgov koma skor 14, tenzija 200/120 mmHg, SpO2 91%, EKG u sedećem položaju: frekvencija 140/min, hipertrofija leve komore uz flater pretkomora, bez znakova ishemije i lezije miokarda. Auskultatorno obilje rano i kasno inspirijumskih pukota u donjim i srednjim plućnim poljima. Po postavljenoj dijagnozi akutnog kardiogenog edema pluća odmah aplikujemo intravenski: morfin-hlorid 0,1 mg/kg telesne mase, nitropreparat Nirmin 1 mg, diuretik furosemid 80 mg, bronhodilatator aminofilin 250 mg i kardiotonik digoksin 0,25 mg. Pacijent je u sedećem položaju uz aplikovanu intravensku liniju i urinarni kateter. Aplikujemo mu i kiseonik 5 l/min i venepunkcijom vadimo 300 ml krvi.

Pacijenata sa stabilnim vitalnim parametrima nakon primenjene farmakoterapije hospitalizujemo radi daljeg posmatranja i tretmana. Akutni kardiogeni edem pluća je stanje koje veoma često nastaje usled neadekvatne upotrebe antihipertenzivne terapije pa je imperativ edukovati pacijenta na značaj redovnog uzimanja propisane terapije. Ovi kritični pacijenti se veoma uspešno predstavljenim farmakoterapijskim pristupom stabilizuju na terenu i medikamentozni postupci su usmereni ka redukciji pretnodnog i naknadnog opterećenja miokarda uz monitoring vitalnih parametara i u zavisnosti od stadijuma akutnog kardiogenog edema pluća.

A case of acute cardiogenic pulmonary edema associated with hypertension and existing myocardiopathy

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Acute cardiogenic pulmonary edema is one of the most urgent conditions in internal medicine. Hypertension in pre-existing myocardiopathy due to inadequate treatment is one of the most common causes of acute cardiogenic pulmonary edema.

We present the case of a 75-year-old male patient, to whom Emergency medical service goes to place of happening due to reported suffocation. The patient has previously identified with hypertension, which is treated with beta blockers, ACE inhibitors and diuretics, and ultrasound-proven cardiomyopathy with an EF of 42%. Clinically, we found somnolence, ashy gray skin covered in sweat, dyspnea followed by cough with expectoration of frothy contents. Objectively Glasgow coma score was 14, blood pressure 200/120 mmHg, SpO2 91%, ECG in sitting position: frequency 140/min, left ventricular hypertrophy with atrial flutter, without signs of ischemia and myocardial lesions. Auscultatory presence of early and late inspiratory crackles in the lower and middle lung fields. After the diagnosis of acute cardiogenic pulmonary edema, we immediately administer intravenously: morphine chloride 0.1 mg/kg of body weight, nitropreparation Nirmin 1 mg, diuretic furosemide 80 mg, bronchodilator aminophylline 250 mg and cardiotonic digoxin 0.25 mg. The patient is in a sitting position with an applied intravenous line and urinary catheter. We also applied oxygen 5 l/min and took 300 ml of blood by venipuncture.

Patients with stable vital parameters after administered pharmacotherapy are hospitalized for further observation and treatment. Acute cardiogenic pulmonary edema is a condition that very often occurs due to the inadequate use of antihypertensive therapy, so it is very important to educate the patient on the importance of regularly taking the prescribed therapy. These critical patients are stabilized in the place of happening with a previosly presented pharmacotherapeutic approach, and medical procedures are aimed to reduce the pre- and post-load of the myocardium with monitoring of vital parameters and depending on the stage of acute cardiogenic pulmonary edema.

Jedinica za informacije o lekovima – u službi zdravstvenih radnika i opšte poplacije

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Uvod: Informacije o lekovima u Srbiji se dobijaju na više različitih načina. Nacionalna agencija za lekove i medicinska sredstva ili međunarodne baze podataka su glavni izvor informacija i za medicinske i za farmaceutske radnike. S druge strane, opšta populacija dobija podatke od lekara opšte prakse i farmaceuta. Jedinica za informacije o lekovima (JIL) na Medicinskom fakultetu Univerziteta u Novom Sadu je regionalni centar za informacije o lekovima koji pruža informacije kako profesionalcima tako i za opštoj populaciji Vojvodine od oko 2 miliona stanovnika.

Ciljevi: Cilj studije je bio da se analiziraju vrste zahteva poslatih JIL.

Metode: Prikupljeni su i analizirani zahtevi za informacije o lekovima koji su poslati JIL od 2011. do 2021. (vrsta klijenta i tražene informacije).

Rezultati: Tokom posmatranog perioda bilo je 2216 zahteva za informacijama o lekovima. Oko 17,5% zahteva stiglo je od opšte populacije (obično pitanja o interakcijama, neželjenim efektima, upotrebi lekova u trudnoći i laktaciji, doziranju i primeni lekova); 76,8% zahteva stiglo je od zdravstvenih radnika (najčešće u vezi sa izborom antibakterijskih lekova kod bakterijskih infekcija, interakcijama lekova, upotrebom lekova u trudnoći i laktaciji) i 5,7% zahteva od strane farmaceutskih radnika (najčešće zainteresovani za upotrebu lekova nakon isteka roka upotrebe).

Zaključak: Jedinica za informacije o lekovima koristan je izvor informacija kako za profesionalce tako i za opštu populaciju kojima nudi različite informacije o lekovima.

Drug Information Unit – serving medical practitioners and general public

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Introduction: Information on drugs in Serbia is obtained via several different ways. National Agency of Drugs and Medical Devices or international databases are main source of information for both medical and pharmaceutical professionals. On the other hand general population obtains data from general practitioners and pharmacists. Drug Information Unit (DIU) at the Medical Faculty, University of Novi Sad, is a regional drug info centre providing information on drugs for both professionals and general population in Vojvodina of about 2 million inhabitants.

Objecitves: The aim of the study was to analyse the type of requests sent to DIU.

Methods: Requests on drug information sent to DIU from 2011 to 2021 were collected and analysed (client type and information requested).

Results: During the observed period there were 2216 requests on drug information. About 17,5% requests were generated by general population (usually questions on interactions, side effects, use of drugs in pregnancy and lactation, dosing and administration); 76,8% from health care professionals (most frequently related to treatment of choice in bacterial infections, drug interactions, drug use in pregnancy and lactation) and 5,7% pharmaceutical professionals (most frequently interest in drug use after expiration date).

Conclusion: It can be concluded that DIU is a useful source of information for both professionals and the general population offering various information on drugs.

Analiza upotrebe analgetika u Republici Srbiji i nordijskim zemljama u periodu 2015.–2018. godine

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Uvod: Lekovi koji se koriste u terapiji bola zovu se analgetici. Analgetici se tradicionalno dele na neopioidne, opioidne i adjuvantne analgetike.

Cilj: Cilj rada bio je da se analizira potrošnja lekova koji se koriste u terapiji bola u Republici Srbiji, u period od 2015. do 2018. godine i da dobijene rezultate uporedimo sa potrošnjom istih lekova u Kraljevini Norveškoj i Republici Finskoj.

Materijal i metode: Podaci o potrošnji lekova za period od 2015. do 2018. godine u Republici Srbiji preuzeti su sa sajta Agencije za lekove i medicinska sredstva Srbije, za Norvešku su preuzeti sa zvaničnog sajta Norveškog instituta za javno zdravlje, a za Finsku sa zvaničnog sajta Finske agencije za lekove.

Rezultati: Potrošnja paracetamola bila je 13 do čak 20 puta manja u Republici Srbiji u poređenju sa Kraljevinom Norveškom i 10 do 15 puta manja u poređenju sa Republikom Finskom. Prosečna potrošnja diklofenaka tokom 4 posmatrane godine iznosila je u Republici Srbiji oko 30, u Kraljevini Norveškoj oko 7 i u Republici Finskoj oko 4 DDD/1000 stanovnika/dan.

Zaključak: U terapiji bola u Republici Srbiji dominira potrošnja antinflamatornih i antireumatskih lekova na prvom mestu diklofenaka. U Kraljevini Norveškoj i Republici Finskoj u terapiji bola dominira potrošnja analgetika na prvom mestu paracetamola.

Ključne reči: terapija bola, analgetici, antinflamatorni i antireumatski lekovi, potrošnja lekova

Analysis of the use of analgesics in the Republic of Serbia and the nordic countries in the period 2015-2018

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Introduction: Drugs used in pain therapy are called analgesics. Analgesics are traditionally divided into non-opioid, opioid and adjuvant analgesics.

Aim: The aim of the study was to analyze the consumption of drugs used in pain therapy in the Serbia, in the period from 2015 to 2018 and to compare our results with the consumption of the same drugs in the two countries, Norway and Finland.

Materials and Methods: Data on drug consumption for the period from 2015 to 2018 in the Republic of Serbia were taken from the website of the Agency for Medicines and Medical Devices of Serbia, for Norway they were taken from the official website of the Norwegian Institute of Public Health, and for Finland from the official website website of the Finnish Medicines Agency.

Results: Paracetamol consumption was 13 to even 20 times lower in the Republic of Serbia compared to the Kingdom of Norway and 10 to 15 times lower compared to the Republic of Finland. The average consumption of diclofenac during the 4 observed years was about 30 in the Republic of Serbia, about 7 in the Kingdom of Norway and about 4 DDD/1000 inhabitants/day in the Republic of Finland.

Conclusion: In the treatment of pain in the Republic of Serbia, consumption of anti-inflammatory and anti-rheumatic drugs dominates, with diclofenac in first place. In the Kingdom of Norway and the Republic of Finland, pain therapy is dominated by the consumption of analgesics, with paracetamol in first place.

Key words: pain therapy, analgesics, anti-inflammatory and antirheumatic drugs, drug consumption

Inkorporacija ibuprofena u PVA filament za 3D štampu metodom natapanja

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Jedna od novijih tehnologija za razvoj farmaceutskih formulacija, koja privlači sve veće interesovanje je 3D štampa. *Fused deposition modeling* (FDM) je tehnologija 3D štampe, koja se često koristi u farmaciji. Metoda natapanjem omogućava inkorporaciju farmaceutski aktivnog sastojka u filamente za FDM 3D štampu. Cilj ove studije je bio ispitivanje uticaja rastvarača na inkorporaciju ibuprofena u polivinilalkoholni (PVA) filament natapanjem.

Određena je rastvorljivost ibuprofena u metanolu, etanolu, acetonu i izopropanolu na 25˚C i na 40˚C, u cilju dobijanja zasićenih rastvora. Inkorporacija ibuprofena u komercijalni PVA filament rađena je metodom natapanja u zasićene rastvore ibuprofena u pomenutim rastvaračima. Inkorporacija je vršena na 25˚C i na 40˚C. Merenje udela ibuprofena u PVA filamentima vršeno je nakon 24h, 48h i 72h inkubacije. Filamenti su rastvarani u forsfatnom puferu pH=6,8, potom je merena apsorbanca tih rastvora UV/Vis spektrofotometrijskom metodom i određene su koncentracije ibuprofena. Na osnovu dobijenih podataka izračunat je udeo ibuprofena u ispitivanim filamentima.

Najveća rastvorljivost uočena je u acetonu (21,67 ± 1,38 mg/ml na 25˚C i 27,35 ± 7,92 mg/ml na 40˚C). U svim rastvaračima rastvorljivost ibuprofena je veća na 40˚C. PVA filamenti potopljeni u metanolni rastvor ibuprofena imali su statistički značajno veći udeo ibuprofena u odnosu na filamente potapane u rastvore drugih rastvarača u svim ispitivanim uslovima. Uticaj povišene temperature na povećanje udela ibuprofena u PVA filamentima uočava se za sve ispitivane rastvarače. Uticaj dužine inkubacije na povećanje inkorporacije ibuprofena u PVA filament uočen je u svim rastvorima na 40˚C, dok na 25˚C duža inkubacija može dovesti do smanjenja udela ibuprofena u filamentu. Najbolju inkorporaciju ibuprofena u PVA filament uočavamo nakon inkubacije u metanolnim rastvorima, gde je srednja vrednost dobijenih udela nakon 72h inkubacije na 40˚C čak 54,42%, ali uz pojavu strukturnih promena filamenta.

Odabir rastvarača, dužina inkubacije i temperatura znatno mogu uticati na efikasnost inkorporacije ibuprofena u PVA filamente metodom natapanja. Važno je odabrati najbolju kombinaciju navedenih faktora, kako bi se dobili filamenti pogodni za 3D štampu.

Ključne reči: polivinilalkohol, rastvarači, *fused deposition modelling*

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Soaking as a method for incorporation of ibuprofen into PVA filament for 3D printing

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One of the newer technologies for the development of pharmaceutical formulations that is attracting increasing interest is 3D printing. Fused deposition modeling (FDM) is a 3D printing technology often used in pharmaceutical field. The soaking method allows the incorporation of active pharmaceutical ingredient into commercially available filaments for FDM 3D printing. The aim of this study was to investigate the influence of an organic solvent on the incorporation of ibuprofen into polyvinyl alcohol (PVA) filament by soaking.

The solubility of ibuprofen in methanol, ethanol, acetone and isopropanol was determined at 25˚C and 40˚C, in order to obtain saturated solutions. Incorporation of ibuprofen into commercial PVA filament was done by soaking filaments in saturated solutions of ibuprofen in the abovementioned solvents. Incorporation was performed at 25˚C and 40˚C. The measurement of the proportion of ibuprofen in PVA filaments was performed after 24h, 48h and 72h of incubation. The filaments were dissolved in phosphate buffer pH=6.8 and the concentrations of ibuprofen were determined by UV/Vis spectrophotometric method. Based on the obtained data, the proportion of ibuprofen in the examined filaments was calculated.

The highest solubility of ibuprofen was observed in acetone (21.67 ± 1.38 mg/ml at 25˚C and 27.35 ± 7.92 mg/ml at 40˚C). The effect of elevated temperature on the increase in the proportion of ibuprofen in PVA filaments is observed for all investigated solvents. The influence of the length of incubation on the increase of incorporation of ibuprofen into the PVA filament was observed in all solutions at 40˚C, while at 25˚C a longer incubation can lead to a decrease in the proportion of ibuprofen in the filaments. The best incorporation of ibuprofen into the PVA filament is observed after incubation in methanol solution, where the mean value of the proportions obtained after 72 hours of incubation at 40˚C is 54.42%.

Solvent selection, incubation length, and temperature can significantly affect the efficiency of ibuprofen incorporation into PVA filaments by the soaking method. It is important to choose the best combination of the above factors, in order to obtain filaments suitable for 3D printing.

Keywords: polyvinyl alcohol, solvents, fused deposition modeling

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Uticaj savetovanja farmaceuta na korisnike prilikom odabira dijetetskog suplementa koji doprinose normalnoj funkciji imunog sistema

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Pandemija korona virusom je povećala potrošnju brojnih lekova i dijetetskih supelemenata za prevenciju i unapređenje zdravlja. Intezivan marketing, velika dostupnost i savetovanje zdravstvenih radnika imali su značajan uticaj na porast potrošnje dijetetskih suplemenata koji deluju na imuni sistem. Kako bi se sprečila nepravilna i prekomerna upotreba ovih preparata, savetovanje od strane farmaceuta prilkom njihovog izdavanja dobija još više na značaju. Cilj ove studije bio je da se odredi koliki uticaj farmaceuti imaju na korisnike prilikom odabira adekvatnog preparata koji doprinosi normalnoj funkciji imunog sistema.

U cilju prikupljanja informacija o tome na šta se najviše korisnici oslanjaju prilikom odabira preparata koji doprinose normalnoj funkciji imunog sistema u Republici Srbiji, osmišljena je anketa u vidu kratkih pitanja sa ponuđenim odgovorima. Anketirano je 100 korisnika apotekarske ustanove „Benu" u Novom Sadu.

Rezultati ankete su pokazali da se 13% korisnika prilikom odabira preparata koji doprinose normalnoj funkciji imunog sistema odlučuje za onaj preparat koji im je preporučen od strane poznanika, kod 19% njih je cena preparata odlučujući faktor, 5% njih bira preparate koje su videli na reklami, dok 63% korisnika donosi odluku na osnovu saveta farmaceuta u apoteci. Takođe, jedan broj korisnika kod kojih je cena uticala na odabir odgovarajućeg preparata, je napomenula da nekada nisu u mogućnosti da poslušaju savet farmaceuta, jer taj preparat ne mogu da priušte.

Zbog potencijalnih interakcija sa drugim lekovima i mogućnosti ispoljavanja toksičnih efekata, preparati koji doprinose normalnoj funkciji imunog sistema treba da se primenjuju uz preporuku farmaceuta, koji je obučen da pruži potrebne informacije za odabir adekvatnog preparata. Rezultati ankete nam pokazuju da najveći broj korisnika ima poverenje u farmaceuta i da na osnovu njegovog saveta donosi odluku. Farmaceut treba da posveti vreme i pažnju da preporuči odgovarajući preparat i pruži sve informacije neophodne za njegovu pravilnu upotrebu.

Ključne reči: savetovanje pacijenata, dijetetski suplementi, imuni sistem.

Ovu studiju je podržalo Ministarstvo prosvete, nauke i tehnološkog razvoja Republike Srbije, broj ugovora 451-03-68/2022-14/200114.

The influence of pharmacist counseling on users when choosing dietary supplements that contribute to the normal function of the immune system

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The corona virus pandemic has led to an increase in the consumption of numerous medicines and dietary supplements. Intensive marketing, great availability and counseling by health workers contribute to the increase in the consumption of dietary supplements that affect the immune system. The goal of this study was to determine how much influence pharmacists have on users when choosing a supplement that contributes to the normal function of the immune system.

In order to collect information on what users rely on the most when choosing dietary supplements that affect the immune system, a survey was designed in the form of short questionnaire. One hundred users of the „Benu" pharmacy in Novi Sad were surveyed.

The results of the survey showed that 13% of users, when choosing dietary supplement that affects the immune system, decide on the supplement that was recommended to them by an acquaintance, in 19% of them the price is a decisive factor, 5% of them choose the supplement that they have seen on an advertisement, while 63% of users make their decision based on the pharmacist's advice. A number of users mentioned that sometimes they were unable to follow the pharmacist's advice, because they couldn't afford the recommended dietary supplement.

Due to potential interactions with medicines, as well as the possibility of manifestation of toxic effects, supplements that affect the immune system should only be applied when their use is indicated, with the recommendation of pharmacists, who are trained to provide the users with all the necessary information on how to choose the right supplement. The results of the survey have shown that the largest number of users trust the pharmacists and make a decision based on their advice. Therefore, the pharmacist should make an effort to recommend the appropriate supplement and provide necessary information for its proper use.

Keywords: patient counseling, dietary supplements, immune system.

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Praksa prepisivanja antibiotika prilikom terapije endodontskih infekcija

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Cilj ove studije je prikazivanje prakse prepisivanja antibiotika stomatologa u Srbiji prilikom lečenja endodontskih infekcija i prenošenje aktuelnih preporuka ESE (Evropskog udruženja endodontologa). Link online upitnika je poslat na 628 e-mail adresa koje su bile javno dostupne na internetu, od kojih je 158 odgovorilo na anketu i rezultiralo da stopa odgovora bude 25,16%. Prema nalazima studije, 55,7% ispitanika je propisivalo antibiotik koji se pije 5 dana. Amoksicilin od 500 mg je bio antibiotik prvog izbora za 55,1% ispitanika, a zatim Klindamicin od 600 mg (18,4%). Za pacijente koji su prijavili alergiju na penicilinske preparate, 61,4% ispitanika je prepisalo Klindamicin. Statistički značajne razlike su se pojavile samo u slučajvima akutnih apikalnih apscesa sa pojavom pogoršanja opšteg stanja pacijenta, pri čemu su stomatolozi, godina starosti od 46-55, najmanje pribegavali ordiniranju antibiotika. Analize su dalje pokazale da se preporuke za bezbedno propisivanje antibiotika nisu uvek poštovale jer su pacijentima ordinirani antibiotici čak i kada nisu bili neophodni. Ovi podaci nam ukazuju na potrebu za dodatnom edukacijom o odgovornoj i adekvatnoj upotrebi antibiotika kako bi se sprečila rezistencija na iste.

Ključne reči: amoksicilin, klindamicin, anketa

Antibiotic Prescribing Practices in Endodontic Infections

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The study goal was to provide an overview of antibiotic prescribing practices of Serbian dentists when treating endodontic infections and to disseminate the current ESE (European Society of Endodontology) recommendations to the study participants. A link to an online questionnaire was sent to 628 Serbian dentists whose email addresses were publicly available on the Internet, 158 of whom responded to the survey, resulting in a 25.16% response rate. According to the study findings, 55.7% of respondents prescribed a 5-day antibiotic course. Moreover, Amoxicillin 500 mg was the first-choice antibiotic for 55.1% of the respondents, followed by Clindamycin 600 mg (18.4%). For patients allergic to penicillin, 61.4% of respondents prescribed Clindamycin. Statistically significant differences emerged only in relation to acute apical abscess with systemic involvement, whereby dentists aged 46-55 were least likely to prescribe antibiotics in these clinical situations ($p = 0.04$). Analyses further revealed that recommendations for safe antibiotic prescribing practices were not always followed, as in certain cases, patients were given antibiotics even when this was not indicated. These findings highlight the need for additional education on responsible antibiotic use to prevent bacterial resistance.

Key words: amoxicillin, clindamycin, survey

Prikaz slučaja aplikovanja MTA na mesto jatrogene perforacije, endodontskog retretmana i apikotomije: Praćenje u trajanju od 18 meseci

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U toku endodontskog tretmana može doći do perforacije kanala korena, a samim tim i negativnog uticaja na integritet korena i ishod lečenja. Pacijent je upućen radi sanacije perforacije kanala korena gorenjeg levog lateralnog sekutića (zuba 22), koja je nastala prilikom prethodnog tretmana. Kada je postavljena dijagnoza simptomatskog apikalnog parodontitisa, doneta je odluka o endodontskom retretmanu, nakon kog će uslediti apikotomija uz zaptivanje perforacije mineral trioksid agregatom (MTA). Celokupan tretman je obavljen u tri posete i kontrolisan dva puta (nakon 12 i 18 meseci). Na poslednjoj kontroli uočeno je ponovno formiranje kosti u periapikalnoj regiji tretiranog zuba. Postignut uspeh u ovom slučaju zavisio je od adekvatno posatavljene dijagnoze, dezinfekcije kanala korena i hirurškog mesta kao i zaptivanja perforacije kanala korena radi sprečavanja rekontaminacije.

Ključne reči: prikaz slučaja, MTA, mineral trioksid agregat

A case report of root canal retreatment through endodontic surgery and MTA repair of iatrogenic perforation with an 18-month follow-up

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Root perforations may occur following endodontic treatment, thus compromising the root integrity and treatment outcome. A patient presented with root perforation following an earlier treatment of the upper left lateral incisor (tooth 22). Once symptomatic periapical periodontitis was diagnosed, a decision was made to retreat the root canal using mineral trioxide aggregate (MTA) and perform apicoectomy. The planned procedures were performed in three sessions and two follow-up visits, after 12 and 18 months, respectively, were arranged. At the last follow-up, bone neoformation was observed at the periapical area of the treated tooth. The successful outcome in this case depended on appropriate diagnosis, root canal and surgical site disinfection, as well as sealing root canal perforation to prevent recontamination.

Key words: case report, MTA, mineral trioxide aggregate

Povećanje rastvorljivosti nifedipina pomoću formulacije čvrstih disperzija

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Nifedipin je predstavnik lekova koji pripadaju drugoj grupi biofarmaceutskog sistema klasifikacije. Odlikuje ga niska rastvorljivost i visoka permeabilnost. Tehnologija čvrstih disperzija se pokazala kao dobar pristup za povećanja rastvorljivosti, brzine rastvaranja i posledično biološke raspoloživosti.

Cilj ovog rada bio je da se izrade čvrste disperzije nifedipina sa dva različita polimera, u tri različita odnosa i ispita da li dolazi do povećanja rastvorljivosti u in vitro uslovima.

Čvrste disperzije nifedipina su izrađene sa polivinilpirolidonom K30 (PVP) i polietilenglikolom 4000 (PEG) u po tri masena odnosa: 1:1, 1:3 i 1:5. Primenjena je niding metoda dobijanja disperzija uz korišćenje koncentrovanog etanola kao medijuma za izradu. Nakon sušenja čvrste disperzije su čuvane zaštićene od svetla (kao i tokom svih narednih eksperimenata) i u eksikatoru. Ispitivanje rastvorljivosti je urađeno u termostatnom vodenom kupatilu, spektrofotometrijskim merenjem koncentracije nifedipina iz zasićenih rastvora. Posmatrana je rastvorljivost u vodi i biorelevantnom medijumu (izotonični fosfatni pufer pH 6,8 sa dodatkom natrijum-laurilsulfata), na 25°C i 37°C, nakon 2h i 24h. Rezultati su dobijeni u triplikatu i poređeni sa fizičkim smešama i samim nifedipinom.

Ispitane čvrste disperzije povećavaju rastvorljivost nifedipina, uključujući i rastvorljivost koja se beleži u samim fizičkim smešama. Razlika u rastvorljivosti izraženija je kod čvrstih disperzija sa različitim polimerima, nego god disperzija kod kojih je variran udeo upotrebljenog polimera. Nakon 24 h u biorelevantnom medijumu, rastvorljivost nifedipina iz čvrstih disperzija sa PVP iznosi: 130,23 ± 3,08 μg/ml, 131,94 ± 10,83 μg/ml i 128,64 ± 9,59 μg/ml (odnosi 1:1, 1:2 i 1:3). Pod istim uslovima rastvorljivost nifedipina iz čvrstih disperzija sa PEG je: 74,45 ± 6,49 μg/ml, 79,12 ± 10,42 μg/ml i 72,11 ± 16,70 μg/ml (odnosi 1:1, 1:3 i 1:5).

Metoda nidinga se pokazala kao pogodna za forulisanje čvrstih disperzija nifedipina. Ove čvrste disperzije imaju veću rastvorljivost zbog čega se može očekivati i veća brzina rastvaranja i bioraspoloživost, ali za konačnu potvrdu je potrebno sprovesti dalja ispitivanja.

Ključne reči: rastvorljivost, PVP, PEG, niding metod, biorelevantni medijum

Enhancement of nifedipine solubility by solid dispersion formulation

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Nifedipine is a representative of drugs that belong to the second group of the biopharmaceutical classification system. It is characterized by low solubility and high permeability. Solid dispersion technology has proven to be a good approach to increase solubility, dissolution rate and consequently bioavailability.

The objective of this paper was to prepare solid dispersions of nifedipine with two different polymers, in three different ratios, and examine potentialy increasing of solubility in in vitro conditions.

Solid dispersions of nifedipine were made with polyvinylpyrrolidone K30 (PVP) and polyethylene glycol 4000 (PEG) in three mass ratios: 1:1, 1:3 and 1:5. The kneading method of obtaining dispersions was applied using concentrated ethanol as a production medium. After drying, the solid dispersions were stored protected from light (as during all subsequent experiments) and in a desiccator. The solubility test was performed in a thermostatic water bath with a shaker, by spectrophotometric measurement of nifedipine concentration from saturated solutions. Solubility in water and biorelevant medium (isotonic phosphate buffer pH 6.8 with addition of sodium lauryl sulfate) was observed at 25°C and 37°C, after 2 h and 24 h. The results were obtained in triplicate and compared with physical mixtures and nifedipine alone.

The tested solid dispersions increase the solubility of nifedipine, including the solubility recorded in the physical mixtures. The difference in solubility is more pronounced in solid dispersions with different polymers than in any dispersion in which the proportion of used polymer is varied. After 24 h in a biorelevant medium, the solubility of nifedipine from solid dispersions with PVP is: 130.23 ± 3.08 μg/ml, 131.94 ± 10.83 μg/ml and 128.64 ± 9.59 μg/ml (ratio 1 :1, 1:2 and 1:3). Under the same conditions, the solubility of nifedipine from solid dispersions with PEG is: 74.45 ± 6.49 μg/ml, 79.12 ± 10.42 μg/ml and 72.11 ± 16.70 μg/ml (ratio 1:1, 1:3 and 1:5).

The kneading method proved to be suitable for formulating nifedipine solid dispersions. These solid dispersions have a higher solubility, which is why a higher dissolution rate and bioavailability can be expected, but further tests are needed for final confirmation.

Key words: solubility, PVP, PEG, kneading method, biorelevant medium

Stabilnost magistralno izrađenih sirupa pantoprazola kao prikladnih farmaceutskih oblika doziranja za primenu u pedijatrijskoj populaciji

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Na tržištu lekova Republike Srbije ne postoje autorizovane formulacije pantoprazola pogodne za sve pedijatrijske populacije. Rešenje u ovakvim situacijama je magistralna izrada lekova, koje je potrebno konstantno unapređivati i sprovoditi studije stabilnosti.

Cilj ovog rada bio je da se izrade sirupi pantoprazola u različitim vehikulumima i ispita njihova stabilnost tokom 28 dana, pri različitim uslovima čuvanja.

Vehikulumi za izradu su odabrani na osnovu podataka iz Američke farmakopeje (USP) i Nemačkog kodeksa lekova (DAC). Takođe je korišćena komercijalno dostupna podloga za sirupe. Sadržaj je određen visokoefikasnom tečnom hromatografijom (HPLC). Dodatno je praćena promena organoleptičkih svojstava i pH vrednosti. Sirupi su čuvani na sobnoj temperaturi i u frižideru.

Hemijska stabilnost magistralno izrađenih sirupa je u direktnoj korelaciji sa pH vrednošću preparata. Pri niskim vrednostima pH dolazi do najveće promene tokom vremena, kako u pogledu organoleptičkih svojstava, tako i u pogledu sadržaja. Prisustvo karbonata u formulaciji dovodi do manje degradacije pantoprazola. Takođe, čuvanje na temperaturi frižidera dovodi do manje degradacije aktivnog principa. Upotreba konzervansa povezana je sa manjom promenom boje preparata, ali istovremeno i sa većim smanjenjem sadržaja.

Od svih ispitanih magistralno izrađenih sirupa pantoprazola, najbolja svojstva hemijske stabilnosti je pokazala formulacija koja je u svom sastavu imala: bikarbonate za podešavanje pH vrednosti, ksantan gumu i hidroksietil celulozu za poboljšanje viskoziteta i nije sadržala konzervans. Poželjna temperatura čuvanja je 2-8°C.

Ključne reči: IPP, uzrastu prikladne formulacije, vehikulumi, podloge

Stability of magistral prepared pantoprazole syrups as appropriate pharmaceutical dosage forms for use in the pediatric population

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There are no authorized pantoprazole formulations suitable for all pediatric populations on the drug market of the Republic of Serbia. The solution in such situations is magistral preparation of medicines, which need to be constantly improved and stability studies carried out.

The aim of this work is to make pantoprazole syrups in different vehicles and to examine their stability during 28 days, under different storage conditions.

Formulation vehicles were selected based on data from the USP Pharmacopoeia and the German Drug Codex (DAC). A commercially available syrup base was also used. The content was determined by high performance liquid chromatography (HPLC). Additionally, changes in organoleptic properties and pH values were noticed. The syrups were stored at room temperature and in the refrigerator.

The chemical stability of magistral prepared syrups is in direct correlation with the pH value of the preparation. At low pH values, the greatest change occurs over time, both in terms of organoleptic properties and in terms of content. The presence of carbonate in the formulation leads to less degradation of pantoprazole. Additionally, storage at refrigerator temperature leads to less degradation of the active supstance. The use of preservatives is associated with a smaller change in the color of the preparation, but at the same time with a greater reduction in content.

Of all the magistral prepared pantoprazole syrups tested, the best properties of chemical stability were shown by the formulation that had in composition: bicarbonates for adjusting the pH value, xanthan gum and hydroxyethyl cellulose to improve viscosity and did not contain a preservative. The preferred storage temperature is 2-8°C.

Key words: IPP, age-appropriate formulation, vehicles, bases

Karakteristike lekova za terapiju dermatofitoza u Srbiji

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Dermatofitoze imaju visoku prevalenciju (20-25%) u većini zemalja u razvoju. Pravi izbor u lečenju nije uvek lako napraviti zbog dostupnosti odgovarajućih lekova, potencijalnih interakcija lekova i neželjenih efekata. U ovoj studiji analiziran je praktičan pristup najčešće korišćenih lokalnih i sistemskh lekova.

Cilj ove studije bio je da se predstave aktuelne terapijske mogućnosti površinskih gljivičnih infekcija kože u Srbiji i da se proceni potrošnja antimikotika.

Pretražene su baze podataka PubMed i Google Scholar da bi se identifikovale aktuelne smernice za lečenje dermatofitnih infekcija u Evropi. Podaci o potrošnji lekova u Republici Srbiji prikupljeni su iz publikacija Agencije za lekove i medicinska sredstva Srbije (ALIMS) o prometu i potrošnji humanih lekova za svaku godinu posmatranog perioda od 2017. do 2019. godine.

U Srbiji je odobreno sedam lokalnih antimikotika za dermatološku primenu i šest za sistemsku primenu. Najviše konzumirani lokalni antifungici za dermatološku upotrebu bili su klotrimazol i mikonazol, za svaku posmatranu godinu. U 2019. godini, izdato je 420991 lekova koji sadrže klotrimazol i 258165 lekova koji sadrže mikonazol. Među sistemskim antimikoticima najviše su se konzumirali itrakonazol i flukonazol. Potrošnja itrakonazola je bila 0,0904 DDD/1000 stanovnika/dan, a flukonazola 0,0744 DDD/1000 stanovnika/dan. Za lečenje najčešće dermatofitoze, tinea pedis, smernice preporučuju upotrebu derivata imidazola. Stoga se očekivala najveća upotreba lokalnih antimikotika, klotrimazola i mikonazola. Oralni terbinafin i itrakonazol se preporučuju za lečenje različitih dermatofitoza. Velika upotreba itrakonazola je u skladu sa smernicama, dok se velika upotreba flukonazola objašnjava njegovom upotrebom za druge indikacije. Lokalne fiksne kombinacije antigljivični lek-kortikosteroida preporučuju se u međunarodnim smernicama za lečenje različitih vrsta inflamatornih dermatomikoza. U Srbiji postoji samo jedna lokalna kombinacija kortikosteroid-antibiotik-antifungalni lek, ali nijedna odobrena lokalna fiksna kombinacija antifungalni lek-kortikosteroidna.

Tip lečenja dermatomikoze zavisi od vrste infekcije tinea, težine infekcije i karakteristika i preferencija svakog pacijenta. U Srbiji ne postoje nacionalne smernice za lečenje dermatofitoza. Stoga lekari opšte prakse, kao i specijalisti koji leče pacijente sa gljivičnim oboljenjima, najčešće odlučuju koji lek da prepišu na osnovu sopstvenog iskustva ili pod uticajem lokalnog farmaceutskog marketinga.

Ključne reči: klotrimazol, mikonazol, itrakonazol, flukonazol

Characteristics of drugs for the treatment of dermatophytosis in Serbia

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Dermatophytosis is common worldwide, with a high prevalence (20-25%) in most developing countries. Choosing the right treatment is not always easy due to the availability of appropriate drugs, potential drug interactions, and side effects. In this study, a practical approach to the most commonly used topical and systemic drugs is analysed.

The aim of this study was to present the current therapeutic options for superficial fungal infections of the skin in Serbia and to evaluate the consumption of antifungals.

PubMed and Google Scholar databases were searched to identify current guidelines for the treatment of dermatophytic infections in Europe. Data on drug consumption in the Republic of Serbia were collected from the publications of the Serbian Agency for Medicines and Medical Devices (ALIMS) on trade and consumption of human drugs for each year of the observation period from 2017 to 2019.

In Serbia, seven topical antifungals were approved for dermatological use and six for systemic use. The most consumed topical antifungals for dermatological use were clotrimazole and miconazole, for each observed year. In 2019, the number of topical antifungals dispensed was 420991 for clotrimazole and 258165 for miconazole. For systemic antifungals, itraconazole and fluconazole were the most consumed. Consumption of itraconazole was 0.0904 DDD/1000 inhabitants/day and that of fluconazole was 0.0744 DDD/1000 inhabitants/day. For the treatment of the most common dermatophytosis, tinea pedis, the guidelines recommend the use of imidazole derivatives. Therefore, the highest usage of topical antifungals, clotrimazole and miconazole was expected. Oral terbinafine and itraconazole are recommended for the treatment of various dermatophytoses. The high use of itraconazole is consistent with the guidelines, whereas the high use of fluconazole is explained by its use for other indications. Topical antifungal-corticosteroid fixed combinations are recommended in international guidelines for the treatment of various types of inflammatory dermatomycoses. In Serbia, there is only one topical corticosteroid-antibiotic-antifungal combination, but no approved topical antifungal-corticosteroid fixed combinations.

The type of treatment for dermatomycosis depends on the type of tinea infection, the severity of the infection, and the characteristics and preferences of each patient. In Serbia, there are no national guidelines for the treatment of dermatophytosis. Therefore, general practitioners, as well as specialists treating patients with fungal diseases, usually decide which drug to prescribe based on their own experience or under the influence of local pharmaceutical marketing.

Key words: clotrimazole, miconazole, itraconazole, fliconazole

Povezanost androgene alopecije sa prognozom COVID-19: opservaciona studija

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Individualna sklonost ka razvoju akutnog respiratornog distres sindroma povezana je sa uzrastom i najčešćim komorbiditetima. Teški akutni respiratorni sindrom koronavirus 2 (SARS-CoV-2) prvenstveno inficira pneumocite tipa II kod ljudi, uz pomoć transmembranske serinske proteaze tipa 2 (TMPRSS2). Jedini poznati promoteri transkripcije gena koji kodiraju TMPRSS2 su androgeni. Teoretski, povišen nivo androgena ili androgenih receptora može dovesti do veće ekspresije TMPRSS2 i višeg nivoa viremije kao posledice.

Cilj ovog istraživanja bio je da se indirektno ispita da li težina infekcije SARS-CoV-2 zavisi od ekspresije androgenih receptora.

Ova opservaciona studija analizirala je pacijente muškog pola, hospitalizovane zbog infekcije SARS-CoV-2 u odnosu na dužinu hospitalizacije, ishod bolesti, vrstu neophodne podrške kiseonikom i prisustvo komorbiditeta i alopecije. Za procenu stanja kose koristili smo prilagođenu verziju Hamilton-Norvudove skale i prisustvo Gabrinovog znaka. U studiji je ukupno učestvovalo 208 pacijenata. Postojale su statistički značajne razlike u poređenju prosečne starosti pacijenata sa različitim tipovima alopecije kada su grupe podeljene prema prisustvu Gabrinovog znaka ($t = 4{,}958$, $p > 0{,}01$). Ishodi i vrsta potrebne minimalne podrške kiseonikom, u poređenju sa tipom alopecije u slučaju Gabrin +/− klasifikacije, pokazali su statistički značajnu razliku u ishodu bolesti ($p = 0{,}027$). Nije bilo statistički značajnih razlika u distribuciji komorbiditeta među grupama sa alopecijom, ali je hipertenzija bila povezana sa lošom prognozom COVID-19.

Naši nalazi sugerišu da su Gabrinov znak i hipertenzija povezani sa lošom prognozom COVID-19.

Ključne reči: alopecija, korona virus, Gabrinov znak

Androgenic alopecia relation to COVID-19 prognosis: observational study

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Individual susceptibility to developing acute respiratory distress syndrome is related to age and most frequent comorbidities. Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) primarily infects the type II pneumocytes in humans, with the help of transmembrane serine protease type 2 (TMPRSS2). The only known transcriptional promoters of genes coding TMPRSS2 are androgenic. Theoretically, the elevated level of androgens or androgen receptors could lead to a higher expression of TMPRSS2 and a higher level of viremia as a consequence.

The aim of this research was to indirectly investigate whether the severity of SARS-CoV-2 infection depends on the expression of androgen receptors.

This observational study analysed male patients hospitalized for SARS-CoV-2 infection with respect to the length of hospitalisation, the outcome of the disease, the type of necessary oxygen support and the presence of comorbidities and hairiness. In hairiness estimation, we used an adapted version of the Hamilton–Norwood scale and the presence of the Gabrin sign.

In total, 208 patients participated in the study. There were statistically significant differences comparing the average age of patients with the different types of alopecia when groups were divided according to the presence of the Gabrin sign ($t = 4.958$, $p > 0.01$). The outcomes and the type of needed minimal oxygen support, compared with the type of alopecia in the case of Gabrin + / − classification showed a statistically significant difference in the outcome of the disease ($p = 0.027$). There were no statistically significant differences in the distribution of comorbidities among alopecia groups, but hypertension was related to poor COVID-19 prognosis.

Our findings suggest that the Gabrin sign and hypertension are related to a poor COVID-19 prognosis.

Key words: alopecia, corona virus, Gabrin sign

Poređenje potrošnje analoga glukagonu sličnog peptida 1 (GLP-1) u Srbiji i Finskoj, u periodu od 2018. do 2020. godine

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Analozi glukagonu sličnog peptida-1 (GLP-1) ili mimetici inkretina su antidijabetički lekovi koji se primenjuju parenteralno, u obliku injekcionih penova.

Podaci o potrošnji pet analoga GLP-1 (liraglutida, dulaglutida, liksisenatida, semaglutida i eksenatida) preuzeti su od Agencije za lekove i medicinska sredstva Srbije – ALIMS i Finske agencije za lekove – Fimea. Rezultati su izraženi u DDD (definisanim dnevnim dozama) na 1000 stanovnika/dan.

Tokom posmatranog perioda (od 2018. do 2020. godine) potrošnja analoga GLP-1 bila je znatno veća u Finskoj u odnosu na Srbiju. U Srbiji se od svih lekova iz grupe koristio samo liraglutid (0,02, 0,01 i 0,01 DDD/1000 stanovnika/dan tokom 2018, 2019 i 2020. godine redom). U Finskoj je tokom tri posmatrane godine zabeležena potrošnja liraglutida od 1,92, 2,08 i 1,77 DDD/1000 stanovnika/dan. U poslednjoj godini došlo je do pada potrošnje liraglutide, ali je zabeležena potrošnja semiglutida od 2,49 DDD/1000 stanovnika/dan. U Finskoj su takođe korišćeni dulaglutid, liksisenatid i eksenatid.

Finska kao zemlja sa razvijenom farmakoterapijskom praksom ima značajno veću potrošnju lekova iz ispitane grupe u odnosu na Srbiju. Potrebno je razmotriti faktore koji su doveli do razlike u potrošnji i kreirati nove smernice u skladu sa savremenom farmakoterapijom koje bi dovele do izjednačavanja potrošnje.

Ključne reči: dijabetes melitus, dijabetes, potrošnja lekova

Comparison of glucagon-like peptide-1 analogues consumption between Serbia and Finland, in the period 2018-2020

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Glucagon-like peptide-1 (GLP-1) analogues or incretin mimetics are antidiabetic drugs administered parenterally, in form of the injectable pen devices.

The information about the consumption of five GLP-1 analogues (liraglutide, dulaglutide, lixisenatide, semaglutide and exenatide) was taken from the Medicines and Medical Devices Agency of Serbia - ALIMS, and Finnish Medicines Agency - Fimea. The results are expressed in DDDs (defined daily doses) per 1000 inhabitants/day.

During the observed period (2018-2020) the consumption of GLP-1 analogues was much higher in Finland compared to Serbia. In Serbia, of all drugs from the group, only liraglutide was used (0.02, 0.01 and 0.01 DDD/1000 inhabitants/day during 2018, 2019 and 2020, respectively). In Finland, liraglutide consumption of 1.92, 2.08 and 1.77 DDD/1000 inhabitants/day was recorded during the three observed years. In the last year, there was a decrease in the consumption of liraglutide, but the consumption of semiglutide was recorded at 2.49 DDD/1000 inhabitants/day. Dulaglutide, lixisenatide and exenatide have also been used in Finland.

Finland, as a country with a developed pharmacotherapeutic practice, has a significantly higher consumption of drugs from the examined group compared to Serbia. It is necessary to consider the factors that led to the difference in consumption and create new guidelines in accordance with modern pharmacotherapy that would lead to an equalization of consumption.

Key words: diabetes mellitus, diabetes, drug consumption

Vrednosti HbA1c kod pacijenata sa dijabetes melitusom u Srbiji: studija preseka, anketa

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Dijabetes je hronična nezarazna bolest sa porastom broja obolelih svake godine, kako u svetu tako i u Srbiji.

Kako bi se procenilai informisanost i stavovi prema dijabetesu, u februaru 2022. sprovedena je onlajn anketa poprečnog preseka. U njoj su učestvovala 422 punoletna ispitanika sa dijagnozom dijabetesa melitusa (DM) koji su živeli u Srbiji.

Ispitanici su označili svoje nivoe HbA1c. Prijavljene vrednosti HbA1c od 6,5% ili niže smatrane su optimalnim. Procenat ispitanika koji su prijavili optimalne vrednosti HbA1c nije se razlikovao u zavisnosti od tipa dijabetesa ($p \geq 0.05$). Samo oko trećine (35,2% tip 1 i 31,4% DM tipa 2) ispitanika je prijavilo HbA1c 6,5% ili niže. 54,6% pacijenata tipa 1 i 38,35% pacijenata sa dijabetesom tipa 2 prijavilo je nivoe HbA1c više od 6,5%. Skoro jedna trećina pacijenata tipa 2 (31,4%) nije znala vrednost HbA1c.

Dobra kontrola dijabetesa povezana je sa manjim rizikom od akutnih i hroničnih komplikacija. Edukativni programi zdravstvenog sistema i savetodavna uloga zdravstvenih radnika su veoma važni kako bi pacijenti sa dijabetesom bolje regulisali bolest.

Ključne reči: dijabetes melitus, dijabetes, glikozilirani hemoglobin

Values of HbA1c in patients with diabetes mellitus in Serbia: a cross-sectional survey

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Diabetes is a chronic, non-communicable disease with an annually increasing number of patients worldwide and in Serbia.

In order to evaluate knowledge and attitudes toward diabetes, an online cross-sectional survey was conducted in February 2022. It included 422 adults with diagnosed diabetes mellitus (DM) living in Serbia.

Respondents were asked to report their HbA1c levels. Self-reported values of HbA1c 6.5% or less were considered optimal. The proportion of respondents who reported optimal HbA1c values did not differ by diabetes type ($p \geq 0.05$). Only about a third (35.2% of type 1 and 31.4% of type 2 DM) respondents reported HbA1c 6.5% or less. 54.6% of type 1 and 38.35% of type 2 diabetic patients reported HbA1c levels of more than 6.5%. Almost one-third of type 2 patients (31.4%) did not know the value of HbA1c.

Good diabetes control is associated with lower acute and chronic complications risk. The health system's educational programs for patients with type 2 DM and health professionals' advisory role are very important in order to help patients with diabetes better regulate the disease.

Key words: diabetes mellitus, diabetes, glycated hemoglobin

Faktori povezani sa neodgovarajućim propisivanjem lekova kod starijih pacijenata sa različitim stepenima bubrežne insuficijencije

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Ciljevi ovog istraživanja bili su da se uporedi prevalencija potencijalno neadekvatno propisanih lekova (PIP) kod pacijenata na hemodijalizi i pacijenata sa različitim stepenom bubrežne insuficijencije, kao i da se ispitaju veze između neadekvatnog propisivanja i određenih kliničkih ili demografskih karakteristika pacijenata. Studija je osmišljena kao studija preseka sprovedena na odeljenju za nefrologiju Kliničkog centra u Nišu, Srbija. Pacijenti su podeljeni u dve grupe: (1) pacijenti na hemodijalizi i (2) pacijenti sa različitim stepenom hronične bubrežne insuficijencije. Prisustvo ili odsustvo potencijalno neodgovarajućeg propisivanja lekova utvrđeno je korišćenjem Beersovih kriterijuma. Studija je obuhvatila ukupno 218 pacijenata starosti 65 i više godina. Od 83 pacijenta u prvoj grupi, prema Beers kriterijumima, neadekvatno propisivanje je utvrđeno kod 27 (32,5%) pacijenata, a od ukupno 135 pacijenata u drugoj grupi, 44 pacijenta (32,6%) sa potencijalno neodgovarajuće propisanim lekovima su bila otkrivena. U obe studijske grupe (pacijenti na hemodijalizi / pacijenti sa različitim stepenom hronične bubrežne insuficijencije) PIP je češći kod pacijenata koji su uzimali više lekova ($t=5,612$, $p<0,001$)/($t=5,748$), $p<0,001$) i imali veći broj komorbiditeta ($t=3,504$, $p<0,001$)/ ($t=2,094$, $p<0,001$). Zaključno, naša studija je pokazala da je potencijalno neodgovarajuće propisivanje lekova česta pojava i kod pacijenata na hemodijalizi i kod pacijenata sa različitim stepenom bubrežne insuficijencije. Najvažniji faktori vezani za stopu PIP-a u obe grupe bili su broj propisanih lekova i broj komorbiditeta.

Factors related to inadequate prescribing of drugs in elderly patients with various degrees of kidney failure

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The aims of this study were to compare the prevalence of potentiall inappropriate drug prescribing (PIP) in hemodialysis patients and patients with kidney failure who did not require renal replacement therapy, as well as to explore relationships between inappropriate prescribing and certain clinical or demographic characteristics of the patients. The study was designed as a cross-sectional study conducted at the Department of Nephrology, Clinical Center in Nis, Serbia. The patients were divided into two groups: (1) patients on hemodialysis treatment and (2) patients with various degrees of chronic renal failure and without renal replacement therapy. The presence or absence of inappropriate drug prescribing was determined using Beers criteria. The study included a total of 218 patients aged 65 years and over. Out of 83 patients in the first group, according to the Beers criteria, inadequate prescribing was found in 27 (32.5%) patients and from a total of 135 patients in the second group, 44 patients (32.6%) with potentially inappropriately prescribed drugs were detected. In both group studies (patients on hemodialysis treatment / patients with various degrees of chronic renal failure and without renal replacement therapy) PIP was more common in patients who took more drugs ($t=5.612$, $p<0.001$)/($t=5.748$, $p<0.001$) and had more comorbidities ($t=3.504$, $p<0.001$)/ ($t=2.094$, $p<0.001$). In conclusion, our study showed that potentially inappropriate prescribing of drugs was frequent phenomenon in both hemodialysis patients and those without RRT. The most important factors associated with rate of PIPs in both groups were number of prescribed drugs and number of comorbidities.

Upotreba cefalosporina u Univerzitetskom Kliničkom centru Niš

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Uvod: Racionalna upotreba antibiotika je jedan od primarnih ciljeva farmakoterapije. Upotreba antibiotika značajno utiče na nastanak bakterijske rezistencije. Cefalosporini su najčešće korišćeni antibiotici u bolničkim uslovima u našoj zemlji. Cilj ovog istraživanja je analiza njihove potrošnje u tercijarnoj zdravstvenoj ustanovi.

Materijal i metode: Potrošnja cefalosporina je praćena kod pacijenata lečenih u Univerzitetskom Kliničkom centru Niš, u periodu od 2012. do 2020. godine, sa akcentom na cefuroksim i ceftriakson. Upotreba je izražena kao broj definisanisanih dnevnih doza na 100 bolesničkih dana (DBD).

Rezultati: Dobijeni rezultati pokazuju konstantno veliku potrošnju, pri čemu je njihova prosečna potrošnja 16,73 ± 3,63 DBD tokom posmatranog perioda. Ukupna potrošnja cefalosporinskih antibiotika je uvećana za 60,6%, na kraju ispitivanog perioda. Utvrđen je veliki porast potrošnje ceftriaksona od 11,68 DBD na 21,65 DBD, što predstavlja porast od 85,3% od 2012. do 2020. godine, sa prosekom 13,34 ± 3,37 DBD. Za razliku od ceftriaksona, upotreba cefuroksima je značajno manja (4,62 DBD do 4,53 DBD), prosečno 3,4 ± 1,38 DBD u navedenom periodu. Porast potrošnje cefalosporina, posebno ceftriaksona je najveći u 2020. godini.

Zaključak: Utvrđen je značajan porast ukupne potrošnje cefalosporina, posebno ceftriaksona, što se može objasniti epidemiološkom situacijom izazvanom virusom SARS-CoV-2. Neracionalna upotreba cefalosporina može imati značajan uticaj na porast bakterijske rezistencije u bolničkim uslovima.

Use of cephalosporins at the University Clinical Center Niš

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Introduction: Rational use of antibiotics is one of the goals to be pursued in the treatment of patients. Cephalosporins are the most commonly used antibiotics in clinical conditions. The aim of this research is to estimate the consumption of cephalosporins in a tertiary healthcare facility in the period from 2012 to 2020.

Material and methods: Cephalosporins consumption was monitored at the University Clinical Centre Niš, from 2012 to 2020. Cefuroxime and ceftriaxone were chosen as the main representatives of cephalosporins, the usage was monitored in the stated period of time in patients. The utilization of cephalosporins was obtained and expressed as a defined daily dose per 100 bed days (DBD).

Results: The obtained results show constant high consumption of cephalosporins during the observed period of time. The use of ceftriaxone had a significantly high increase in consumption with 11.68 DBD to 21.65 DBD, which is an increase of 85.3% from 2012 to 2020, with an average of 13.34 ± 3.37 DBD. Unlike ceftriaxone, cefuroxime use follows a negative but stable trend, from 4.62 DBD to 4.53 DBD, representing a negative trend in the use of 0.019%, with an average of 3.4 ± 1.38 DBD. However, the total consumption of cephalosporins in this period of time is accompanied by a significant increase of 60.6%, with an average of 16.73 ± 3.63 DBD.

Conclusion: As the most commonly used antibiotic, the use of cephalosporins is accompanied by constant growth, which is more significant in the last year of our research, and can be explained by epidemiological situation caused by the SARS-CoV-2 virus.

Potrošnja fluorohinolona u Univerzitetskom kliničkom centru Niš

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Uvod: Suština racionalne antibiotske terapije podrazumeva propisivanje odgovarajućeg antibiotika na način, u dozi i trajanju terapije individualno prilagođene za svakog pacijenta. Jedna od najčešće propisivanih grupa antibiotika u bolničkim uslovima su fluorohinoloni. Cilj rada bio je praćenje bolničke potrošnje fluorohinolona, sa posebnim osvrtom na propisivanje ciprofloksacina (CIP) i levofloksacina (LEV).

Materijali i metode: Upotreba antibiotika je praćena kod pacijenata lečenih u Univerzitetskom kliničkom centru (UKC) u Nišu, u periodu od 2012. do 2020. godine. Potrošnja antibiotika kod hospitalizovanih pacijenata izražena je kao broj definisanih dnevnih doza/100 bolesničkih dana (DBD).

Rezultati: Tokom perioda praćenja potrošnje antibiotika propisano je od 4,54 DBD do 12,12 DBD flurolohinolona, prosečno 6,42 DBD godišnje u UKC Niš. Najviše propisivani fluorohinolon je CIP sa 61% u navedenom periodu ispitivanja. Najveća potrošnja CIP je bila tokom 2017. godine, kada je propisano 10,51 DBD. Nakon toga registrovana je smanjena porošnja CIP na 2,81 DBD u 2020. kada je zabeležena potrošnja moxifloksana od 2,52 DBD i LEV 6,41 DBD. Utvrđen je trend porasta potrošnje LEV od 0,38 DBD u 2012. do 6,41 DBD u 2020. Najveća potrošnja fluorohinolona zabeležena je u 2017. godini, kada je ukupno propisano 12,12 DBD, od toga 86% CIP.

Zaključak: CIP je najviše korišćen fluorohinolon u UKC, sa tendencijom smanjenja potrošnje na kraju ispitivanog perioda. Utvrđen je značajan porast potrošnje levofloksacina, što može biti posledica epidemiološke situacije izazvane virusom SARS-CoV-2. Neracionalna upotreba fluorohinolona može uticati na porast bakterijske rezistencije u hospitalnim uslovima.

Consumption of fluoroquinolones in University clinical center Niš

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Introduction: The essence of rational antibiotic therapy implies prescribing the appropriate antibiotic in a way, in the dose and duration of therapy individually adjusted for each patient. One of the most commonly prescribed groups of antibiotics in hospital conditions is fluoroquinolones. The aim of this study was to monitor hospital consumption of fluoroquinolones, with special emphasis on prescribing ciprofloxacin (CIP) and levofloxacin (LEV).

Materials and methods: The use of antibiotics was monitored in patients treated at the University Clinical Center (UCC) in Nis, in the period from 2012 to 2020. Antibiotic consumption in hospitalized patients is expressed as the number of defined daily doses / 100 patient days (DBD).

Results: During the period of monitoring the consumption of antibiotics, from 4.54 DBD to 12.12 DBD of fluroloquinolones were prescribed, on average 6.42 DBD per year in UCC Nis. The most prescribed fluoroquinolone is CIP with 61% in the stated study period. The highest consumption of CIP was during 2017, when 10.51 DBD was prescribed. After that, reductions in CIP consumption to 2.81 DBD were registered in 2020, when moxifloxane consumption of 2.52 DBD and LEV 6.41 DBD were recorded. The trend of increase in LEV consumption was determined from 0.38 DBD in 2012. to 6.41 DBD in 2020. The highest consumption of fluoroquinolones was recorded in 2017, when a total of 12.12 DBD was prescribed, of which 86% was CIP.

Conclusion: CIP is the most commonly used fluoroquinolone in UKC, with a tendency to decrease consumption at the end of the study period. A significant increase in levofloxacin consumption was found, which may be a consequence of the epidemiological situation caused by the SARS-CoV-2 virus. Irrational use of fluoroquinolones can lead to an increase in bacterial resistance in hospital conditions.