Srpsko lekarsko društvo
Serbian Medical Society

Sekcija za kliničku farmakologiju i Akademija medicinskih nauka
Section of Clinical Pharmacology and Academy of Medical Sciences

Organizuju simpozijum
Organize the Symposium

X NEDELJA BOLNIČKE KLINIČKE FARMAKOLOGIJE

X WEEK OF THE HOSPITAL CLINICAL PHARMACOLOGY

24 - 25. novembar 2018.
November 24th - 25th, 2018

ZBORNIK SAŽETAKA
BOOK OF ABSTRACTS
Beograd
24 - 25. novembar 2018.

Izdavač
Sekcija za kliničku farmakologiju Srpskog lekarskog društva
Beograd, Džordža Vašingtona 19, 2018

Za izdavača
Doc. dr Boris Milijašević

Glavni i odgovorni urednik
Prim. dr Dragana Maca Kastratović

Grafičko-tehničko uređenje
Doc. dr Boris Milijašević

Štampa
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Džordža Vašlngtona 19, Beograd

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Република Србија
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PROGRAM
PROGRAMME

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

SUBOTA, 24. novembar 2018. / SATURDAY, 24th November 2018

10:00-11:00 **Registracija učesnika simpozijuma**
Registration of the participants

INTEGRACIJA NAUKE I STRUKE - I
INTEGRATION OF SCIENCE AND PROFESSION - I

Moderatori: **Dragana Maca Kastratović,** *predsednik Sekcije za kliničku farmakologiju SLD /*
Moderators: *President of Section for Clinical Pharmacology of Serbian Medical Assotiation*
Slobodan Janković, *predsednik naučnog odbora Sekcije za kliničku farmakologiju SLD / President of Scientific Board of Section for Clinical Pharmacology of Serbian Medical Assotiation*
Viktorija Dragojević Simić, *član Predsedništva Sekcije za kliničku farmakologiju SLD / Member of presidency of Scientific Board of Section for Clinical Pharmacology of Serbian Medical Assotiation*

11:00-11:30 **SVEČANO OTVARANJE / OPENING CEREMONY**

Pozdravne reči - Welcome address:
Radoje Čolović, *Predsednik Srpskog lekarskog društva / President of the Serbian Medical Assotiation*

Ministarstvo prosvete, nauke i tehnološkog razvoja Republike Srbije

Ministarstvo zdravlja Republike Srbije

11:30-11:45 **Deset godina rada Sekcije za kliničku farmakologiju Srpskog lekarskog društva**
Report on the ten-year's work of the Section for Clinical Pharmacology of the Serbian Medical Assotiation
Dragana Maca A. Kastratović, Momir Mikov, Branka Terzić, Slobodan Janković, Boris Milijašević, Srdjan Z.Marković, Radmila Veličković, Mira Vuković, Viktorija Dragojević Simić, Biljana Radojević, Biljana Savić, Ivana Timotijević, Aleksandar Rašković, Ivana Miličević, Snežana Panić, Mihajlo Jakovljević

11:45-12:00 **Trendovi u terapijskom monitoringu imunosupresivnih lekova: da li lc-ms/ms rešenje?**
Trends in therapeutic monitoring of immunosuppressive drugs: is the lc-ms/ms right solution?
Viktorija M. Dragojević-Simić, Vesna M. Jaćević

12:00-12:20 **Da li izbor psihofarmaka u terapiji psihoza bazirati na kliničkoj slici ili biološkim korelatima?**
Does pharmacotherapy choice is based on symptoms or biological correlations in psychotic disorders therapy?
Ivana P. Timotijević, Katarina B. Crnić, Mirjana M. Todorović, Srdjan Z. Marković, Dragana A. Kastratović

12:20-12:40 **Spazam u vaskularnim oboljenjima mozga**
Vasospasm in brain diseases
Tanja Lj. Stričević

12:40-13:00 **Depresija izazvana lekovima**
Drug-induced depression
Slobodan M. Janković

13:00-13:20 **Specificnosti farmakoterapije kod žena**
Specifications of pharmacotherapy in women
Radmila M. Veličković Radovanović

13:20-13:40 **Originalni i generički lekovi**
Original and Generic drugs
Dragana A. Kastratović, Srđan Z. Marković, GlaxoSmithKline Export Ltd

13:40-14:00 **PAUZA / COFFEE BREAK**

14:00-14:20 **Evolucija u dijagnostici i lečenju nesitnoćelijskog karcinoma pluća**
Evolution in the diagnostics and treatment of non-small cell lung cancer
Branka M. Terzić, Violeta Vučinić Mihailović, Roche d.o.o.

14:20-14:40 **Specifičnosti farmakoterapije gerijatrijskih depresija**
Specificity of pharmacotherapy of geriatric depressions
Žana B. Stanković

14:40-15:00 **Informisani pristanak u kritično obolelih**
Informed consent in critically ill
Zoran M. Todorović, Dragana D. Protić

15:00-15:20 **Uticaj pesticida na reproduktivnu sposobnost muškaraca**
The impact of pesticides on the reproductive capacity of men
Saša N. Vukmirović, Ivana Fratrić, Nebojša P. Stilinović, Dragana Živković, Ana J. Sabo

15:20-15:40 **Potrošnja antibiotika u Srbiji**
Consumption of antibiotics in Serbia
Vesela B. Radonjić

15:40-16:30 **KOKTEL / COCKTAIL**

NEDELJA, 25. novembar 2018. / SUNDAY, 25th November 2018

9:30-10:00 **POSTAVLJANJE POSTERA / PLACING POSTERS**

INTEGRACIJA NAUKE I STRUKE - II
INTEGRATION OF SCIENCE AND PROFESSION – II

Moderatori: **Dragana Maca Kastratović,** *predsednik Sekcije za kliničku farmakologiju SLD /*
Moderators: *President of Section for Clinical Pharmacology of Serbian Medical Assotiation*
Aleksandar L. Rašković, *član predsedništva Sekcije za kliničku farmakologiju SLD / member of presidency of Section for Clinical Pharmacology of Serbian Medical Assotiation*
Radmila M. Veličković – Radovanović, *član predsedništva Sekcije za kliničku farmakologiju SLD / member of presidency of Section for Clinical Pharmacology of Serbian Medical Assotiation*

10:00-10:20 **Uticaj hrane na farmakokinetiku**
The influence of food on pharmacokinetics
Momir M. Mikov, Svetlana Goločorbin-Kon, Maja Đanić, Saša N. Vukmirović, Boris Ž. Milijašević, Karmen M. Stankov

10:20-10:40 **Karakteristike farmakoterapije urgentne kardiologije**
Characteristics of pharmacotherapy of urgent cardiology
Branka M. Terzić

10:40-11:00 **Strukturna i diskriminaciona validnost mernih skala rizika za tešku koronarnu arterijsku bolest kod žena u menopauzi**
Structural and discriminatory validity of measuring risk scales for severe coronary arterial disease in women in menopause
Mira H. Vuković, Dušan P. Ružičić

11:00-11:20 **Psihofarmakoterapija poremećaja povezanih sa stresom**
Psychopharmacotherapy in stress induced dissorders
Mirjana M. Todorović, Katarina B. Crnić

11:20-11:40 **Supstituciona terapija opijatskih zavisnika- indikacije i dileme**
Supstitution in opiate addicts- indications and dilemas
Katarina B. Crnić , Mirjana M. Todorović

11:40-12:00 **Pružanje kliničko-farmakoloških informacija u Kliničkom centru Vojvodine**
Providing of clinical pharmacology information in Clinical Center of Vojvodina
Aleksandar L. Rašković, Nebojša P. Stilinović, Nikola B. Martić, Boris Ž. Milijašević

12:00-12:20 **Korelacija između rezistencije i potrošnje antibiotika u Srbiji i pojedinim zemljama Evropske unije**
The correlation between resistance and antimicrobial consumption in Serbia and certain countries of the European Union
Nebojša P. Stilinović, Christina N. Pateli, Saša N. Vukmirović, Olga J. Horvat, Boris Ž. Milijašević, Aleksandar L. Rašković

12:20-13:00 **PAUZA / COFFEE BREAK**

13:00-13:20 **Finansijski menadžment u anesteziologiji i reanimatologiji u Kliničkom centru Srbije**
Financial Management in Anesthesiology and Reanimatology at the Clinical Center of Serbia
Branislava M. Majstorović

13:20-13:40 **RIA i IRMA tehnike u laboratorijskoj medicini**
Application of RIA and IRMA techniques in medicine
Mirjana M. Petrović, Drina Lj. Janković, Isidora Dj. Tasić, Aleksandar A. Vukadinović

13:40-14:00 **Specifičnosti transfuzije kod trudnica sa autoimunim bolestima**
Specific features of transfusion in pregnant women with autoimmune diseases
Ljubinka I. Nikolić

14:00-14:20 **Neadherencija kod vanbolničkih pacijenata sa dijabetes melitusom tip 2**
Non-adherence among type 2 diabetic patients in primary care setting in eastern Bosnia and Herzegovina
Olga J. Horvat, Jelena D. Popržen, Ana D. Tomas, Milica M. Paut Kusturica, Zdenko S. Tomić, Ana J. Sabo

14:20-14:40 **Analiza upotrebe lekova u terapiji respiratornih oboljenja u republici Srbiji u periodu 2011-2016.**
Analysis of the use of drugs in therapy of respiratory diseases in the republic of serbia in the period 2011-2016
Boris Ž. Milijašević, Stanislav J. Sabo, Aleksandar L. Rašković, Nataša Z. Tomić, Nikola B. Martić

14:40-15:00 **Znanje, stavovi i odnos pacijenata prema analgeticima u Srbiji**
Public knowledge, beliefs and behavior regarding the use of antibiotics in Serbia
Tinde I. Halgato, Milica M. Paut Kusturica, Ana D. Tomas, Olga J. Horvat

15:00-15:20 **Stavovi i ponašanja studenata medicine i farmacije o samomedikaciji**
Self-Medication Attitudes and Behaviour Among Medicine and Pharmacy Students
Ana D. Tomas, Nebojša M. Pavlović, Milica N. Paut Kusturica, Zdenko S. Tomić, Olga J. Horvat, Ana J. Sabo

15:20-15:40 **Timski rad - osnova uspeha bolničke farmakologije**
Team work - the base of the success of hospital pharmacology
Dragana A. Kastratović, Srđan Z. Marković

POSTERI
POSTER SESSION

Moderatori: **Radmila Veličković,** *član predsedništva Sekcije za kliničku farmakologiju SLD /*
Moderators: *member of presidency of Section for Clinical Pharmacology of Serbian Medical Assotiation*
Boris Milijašević, *sekretar Sekcije za kliničku farmakologiju SLD / secretary of the Section for Clinical Pharmacology of Serbian Medical Assotiation*

15:40-16:00 **POSTERI / POSTER SESSION**

Poster 1 **Bezbedna primena metamizola: aktuelno stanje**
Safety of metamizole utilization: current views
Milijana N. Miljković, Nemanja K. Rančić, Viktorija M. Dragojević-Simić, Tanja Pekez-Pavlisko, Dušica M. Stamenković

Poster 2	**Faktori koji doprinose pojavi narkomanije** **Contributing factors of substance abuse** *Srđan Z. Marković, Ivan Dimitrijević*
Poster 3	**Antimikrobna svojstva industrijske konoplje: pretklinička ispitivanja** **Antimicrobial properties of industrial hemp: preclinical evidence** *Ana D. Tomas, Milica N. Paut Kusturica, Zdenko S. Tomić, Olga J. Horvat, Ivona M. Tadić, Ana J. Sabo*
Poster 4	**12-MKH: novi pristup u terapiji metaboličkog sindroma** **12-MKC: a novel approach for metabolic syndrome treatment** *Slavica Lazarević, Maja Đanić, Ana D. Tomas, Nebojša M. Pavlović, Svetlana Goločorbin-Kon, Momir M. Mikov*
Poster 5	**Interakcije između gliklazida i probiotskih bakterija u *in vitro* uslovima** **In vitro study of gliclazide-probiotic bacteria interactions** *Maja Đanić, Bojan Stanimirov, Nebojša Pavlović, Slavica Lazarević, Svetlana Goločorbin-Kon, Momir M. Mikov*
Poster 6	**Znanje studenata medicine o upotrebi kanabisa u terapijske svrhe** **Medical school students' knowledge about the use of cannabis in medical purposes** *Milica N. Paut Kusturica, Olga J. Horvat, Ana D. Tomas, Zdenko S. Tomić, Ana J. Sabo*
Poster 7	**Povećanje potrošnje biljnih lekova u Srbiju u periodu od 2006. do 2016.** **The growth rate of consumption of herbal medicines in Serbia in the period from 2006 to 2016** *Katarina Jeremić, Nemanja Todorović, Svetlana Goločorbin-Kon, Nebojša Pavlović, Nataša Milošević, Neda Gavarić, Mladena Lalić-Popović*
Poster 8	**Ispitivanje profila brzine rastvaranja paracetamola iz različito formulisanih tableta sa trenutnim oslobađanjem** **Investigation of dissolution profiles of paracetamol from various immediate release tablet formulations** *Nemanja Todorović, Mladena Lalić-Popović, Svetlana Goločorbin-Kon, Kristina Kermeci, Boris Milijašević, Jelena Jovićić Bata, Nebojša Pavlović*
Poster 9	**Antioksidativna aktivnost rtanjskog čaja (Satureja montana, L.)** **Antioxidant activity of Winter savory extract (Satureja montana, L.)** *Maja Vujović, Marija Vukomanović, Nikola Martić, Milan Ubavić, Boris Milijašević, Aleksandar Rašković*
Poster 10	**Isplativost primene preparata gvožđe (II)-glukonat, mangan-glukonat, bakar-glukonata u odnosu na preparat gvožđe (III) hidroksid polimaltozni kompleks u uslovima u Srbiji** **The cost-effectiveness of the iron (II)-gluconate, manganese-gluconate, copper-based preparations for iron (III) hydroxide polymaltose complex in Serbia** *Boris Ž. Milijašević, Zdenko S. Tomić, Ana J. Sabo*
16:00-16:30	**Diskusija i zaključci** Discussion and Conclusions *Dragana Maca Kastratović, Branka Terzić, Slobodan Janković, Aleksandar Rašković, Radmila Veličković, Mira Vuković, Viktorija Dragojević Simić*

ZBORNIK SAŽETAKA

BOOK OF ABSTRACTS

HOSPITAL PHARMACOLOGY
International Multidisciplinary Journal

Deset godina rada Sekcije za kliničku farmakologiju Srpskog lekarskog društva

Dragana Maca A. Kastratović[1a], Boris Milijašević[1b], Srdjan Z. Marković[1a], Branka Terzić[1a], Slobodan Janković[1c], Radmila Veličković[1d], Momir Mikov[1b], Mira Vuković[1e], Viktorija Dragojević Simić[1a], Biljana Radojević[1a], Biljana Savić[1f], Ivana Timotijević[1a], Aleksandar Rašković[1b], Ivana Miličević[1g], Snežana Panić[1h], Mihajlo Jakovljević[1c]

[1] Sekcija za Kliničku farmakologiju Srpskog lekarskog društva: [a]Beograd, [b]Novi Sad, [c]Kragujevac, [d]Niš, [e]Valjevo, [f]Leskovac, [g]Užice, [h]Kruševac

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. Tokom ovih 10 godina članovi SKFSLD radili su veoma vredno kroz:

1.Kontinuiranu medicinsku edukaciju – kursevi su akreditvani kao Prva kategorija kod Zdravstvenog saveta Srbije, sto je slusaocima donelo maksimalan broj poena u Lekarskoj komori Srbije za licencu za rad. Kursevi su namenjeni lekarima, farmaceutima, ekolozima, biohemicarima, tehnicarima. Tokom 2018 godine najpopularniji kursevi bili su: Serotonin – crvena nit u kliničkoj farmakologiji III, rukovodilac Prof. dr Ivana Timotijevic; Dobra klinička praksa u kliničkim ispitivanjima, rukovodilac Prim. dr Dragana Maca Kastratović.

2. Simpozijume Nedelja Bolnićke kliničke farmakologije I-X, koji se održavaju tradicionalno poslednjeg vikenda novembra tekuće godine. Tema Simpozijuma je Integracija nauke i prakse, učesnici izlažu svoje radove kroz usmene prezentacije, postere, okrugle stolove, komercijalna predavanja. Svake godine učestvuje oko 100 lekara svih medicinskih specijalnosti. 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 2018 nije bilo predavanja po pozivu.

4. Naučno-stručni časopis SKFSLD pokrenula je 2014, kao on line, open access, free full text Hospital Pharmacology International Multidisciplinary Journal, dostupan na http://www.hophonline.org.

5. Priznanja. Tokom ovih 10 godina svi lekari SKFSLD postizali su značajne uspehe na radnim mestima, kroz doktorske disertacije, akademske/profesionalne pozicije.

Ostvarenje razvoja kliničke farmakologije i dalje će ići kroz KME, podršku mlađim lekarima da specijaliziraju kliničku farmakologiju i primene znanja u bolnicama. Starije kolege razvijaće i nadalje nacionalnu i međunarodnu saradnju u oblasti primenjene nauke, sa naglaskom na uključivanje mlađih kolega u multidisciplinarne timove.

Veoma smo ponosni na saradnju i usmerenje najmoćnijih asocijacija kliničke farmakologije: evropske EACPT i međunarodne IUPHAR.

Report on the ten-year's Work of the Section for Clinical Pharmacology of the Serbian Medical Assotiation

Dragana Maca A. Kastratović[1a], Boris Milijašević[1b], Srdjan Z. Marković[1a], Branka Terzić[1a], Slobodan Janković[1c], Radmila Veličković[1d], Momir Mikov[1b], Mira Vuković[1e], Viktorija Dragojević Simić[1a], Biljana Radojević[1a], Biljana Savić[1f], Ivana Timotijević[1a], Aleksandar Rašković[1b], Ivana Miličević[1g], Snežana Panić[1h], Mihajlo Jakovljević[1c]

[1] Section for Clinical Pharmacology Serbian Medical Society: [a]Belgrade, [b]Novi Sad, [c]Kragujevac, [d]Niš, [e]Valjevo, [f]Leskovac, [g]Užice, [h]Kruševac

In 2009, 19th February, Section for Clinical Pharmacology Serbian Medical Society (SCPSMS) has been established in order to implement the clinical pharmacology approach within all medical areas. During the last 10 years, SCPSMS members have worked hard through the:

1. Continuous Medical Education (CME), and received the highest number of points by the Heath Council of Serbia for its extraordinary quality, and these points are required for granting and extending the license. CME is held regularly in SMS premises for clinical pharmacologists and all other doctors. During 2018th the most popular CME courses were: Serotonin – The red thread in clinical pharmacology III, course leader - Prof. dr sci Ivana Timotijevic; Good clinical practice in clinical trials, course leader - Prim dr sci. Dragana Maca Kastratovic;
2. Workshops. In addition, the work of SCPSMS is carried out through annual workshops Weeks of Hospital-Clinical Pharmacology I-X, traditionally at the end of November every year. The topic of the Conferences is "Integration of Science and Profession" and included a two-day workshop, social functions and poster competition. Approximately, there are one hundred clinical pharmacologists and medical specialists, including guests from USA, France, Germany, Greece, Austria, Bulgaria.
3. Invited lecturers. A huge success was made the Scientific Meetings organized by the Academy of Medical Sciences and SCP of the Serbian Medical Society. Invited lecturers were: 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), ect. During 2018 there were no invited lecturers.
4. Scientific-professional Journal. SCPSMS created in 2014 an online, on line, open access, free full text journal specializing in hospital-related pharmacology: Hospital Pharmacology - International Multidisciplinary Journal (http://www.hophonline.org).
5. Acknowledgement. All SCPSMS members made success on their working places, a lot of PhDs, academic/professional positions.

Advancing the interests and training of clinical pharmacologists and medical specialists are the missions of SCPSMS. The incoming years promises to bring to SCPSMS members additional opportunities for first-rate continuing medical education, national and regional research collaborations, and the latest information on advances in the discipline.

In the past and future activities, it means a lot to us and we are extremely proud of collaboration and guidelines of the most powerful international association of clinical pharmacology – IUPHAR and europian EACPT.

Trendovi u terapijskom monitoringu imunosupresivnih lekova: da li je LC-MS/MS pravo rešenje?

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Ciklosporin, takrolimus, sirolimus i everolimus su najznačajniji imunosupresivni lekovi (IL) koji se uspešno primenuju u transplantaciji solidnih organa. Međutim, pošto pokazuju visok stepen interindividualne i intraindividualne farmakokinetske (FK) varijabilnosti, pa nivo ovih lekova u krvi pacijenata nije lako predvideti, stalan terapijski monitoring lekova (TML) je obavezan. Još uvek nije opšteprihvaćeno koji FK parameter najbolje odražava površinu ispod krive koja prikazuje promenu koncentracije leka u plazmi u funkciji vremena (PIK), kao marker zamene za izlaganje organizma leku. Koncentracija leka izmerena neposredno pre davanja naredne doze (C0) se rutinski koristi, kao i druge strategije uzimanja krvi u pojedinim vremenskim tačkama, naročito u vreme resorpcije leka. Međutim, uzimanje uzoraka "nasumično", koristeći 2 do 5 vremenskih tačaka se takođe koristi kako bi se poboljšala korelacija sa izlaganjem leku. Drugo važno pitanje čije bi bolje rešenje doprinelo uspešnijem sprovođenju TM IL kod transplantiranih pacijenata je primena odgovarajuće metodologije pri merenjima. Još uvek se široko koriste visoko automatizovani imunoeseji (IE), koji su laki za izvođenje, ali sa dosta nedostataka. Međutim, metod tečne hromatografije sa tandem masenom spektrometrijom (LC-MS/MS) je praktična alternative IE i danas se čak smatra tehnikom izbora zbog svoje selektivnosti, osetljivosti i fleksibilnosti. Šta više razvijena je brza, selektivna i pouzdana LC-MS/MS metoda za istovremeno određivanje ciklosporina, takrolimusa, sirolimusa i everolimusa u punoj krvi za uspešan TM IL. Sve to obezbeđuje brži i bolji tretman pacijenata uz niže troškove, čineći ovaj metod idealnim za TML.

Trends in therapeutic monitoring of immunosuppressive drugs: is the LC-MS/MS right solution?

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Cyclosporine, tacrolimus, sirolimus, and everolimus are most important immunosuppressive drugs (IDs) successfully applied in solid organ transplantation. However, since they exhibit a great degree of interindividual and intraindividual pharmacokinetic (PK) variability, and patient blood levels are unpredictable, constant therapeutic drug monitoring (TDM) is mandatory. It is still controversial which PK parameters are best suited to estimate the area under the concentration time curve (AUC) as a surrogate marker for drug exposure. The predose drug concentration (C0) is routinely used, as well as other single point sample strategies, especially during the drug absorption phase. However, different sparse samplings, using two to five sampling time points have also been used to improve the correlation with drug exposure. The other important issue contributing successful TM of IDs is the appropriately used methodology. Currently, still widely used are highly automated immunoassays (IAs), easily operated, but with a number of disadvantages. However, specific liquid chromatography tandem mass spectrometry (LC-MS/MS) method are practical alternatives to the IAs, even generally accepted nowadays as the technique of choice because of its selectivity, sensitivity, and flexibility. Moreover, fast, selective and stable LC-MS/MS method for the simultaneous determination of cyclosporine, tacrolimus, sirolimus, and everolimus in whole blood as a tool for TM is newly developed. All of this provides better and faster patient care at lower costs, making the method ideal for TDM.

Da li izbor psihofarmaka u terapiji psihoza bazirati na kliničkoj slici ili biološkim korelatima?

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Veliki skok u razumevanju i lečenju shizofrenije nastao je polovinom 20. veka kada su se pojavili prvi psihofarmaci. Ta otkrića su pokrenula dinamičan odnos saznanja o biološkim osnovama Sch bolesti koja su uticala na usavršavanje psihofarmaka koji su opet proširili i objasnili mnoge etiopatogenetske faktore. Novi atipični antipsihotici su evidentno omogućili da veliki broj bolesnika uspostavi duže remisije i da se omogući njihovo stabilnije funkcionisanje u socijalnom miljeu. Razumevanje etiologije Sch a time i mehanizam delovanja antipsihotika usložnjava se i pomera sa prepoznavanja receprora i transmiterske dinamike. Osnova je svakako u jasnoj povezanosti transmitera, DA, NA, 5-HT, Acetilholina i Histamina sa presinapričkim i postsinapričkim receptorima, ali postaje evidentno da se ne radi o jednostavnim nivoima koncentracija aktivnih supstanci već simptomi, klinička slika i tok bolesti zavisi od promenljivosti odgovornih struktura CNS i funkcionalnih petlji podložnih različitim uticajima. Antipsihotici sa poznatim mehanizmima delovanja menjaju ali i doprinose prepoznavanju dinamike shizofrene simptomatologije. Efikasna terapija Sch psihoze uključuje više novoa. Algoritmi za primenu psihofarmaka su jedna linija, druga bi bila mapiranje CNS sa identifikacijom odgovornih struktura, i treća, možda najvažnija je prepoznavanje ključnih simptoma i identifikovanje njihove transmitersko biloške osnove a zatim primena, pre svega, adekvatnih antipsihotika sa poznatim mehanizmom dejstva. Samo eklektičkim pristupom kliničkoj slici, toku bolesti, i psihofarmakoterapiji može se izbeći pogrešna dijanostika i terapija. Neophodno je da psihofarmakoterapija shizofrenije teži ciljanom uspostavljanju transmitersko receptorskog balansa i personalizovanoj primeni psihofarmaka.

Does pharmacotherapy choice is based on symptoms or biological correlations in psychotic disorders therapy?

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A great improvement in understanding and treating schizophrenia arose in the mid-20th century when the first psychopharmaceuticals appeared. These discoveries have turned a dynamic relationship of knowledge about the biological basics of Sch that influenced the development of new psychopharmaceuticals and explaining many etiopathogenetic factors of disease. New atypical antipsychotics have evidently enabled a large number of patients to establish longer remissions and their more stable functioning in the social milieu. Understanding the etiology of Sch and thus the mechanism of the action of antipsychotics is more complex and shifted from the recognition of the receptor and transmitter dynamics. The basis is certainly in the clear correlation between transmitters, DA, NA, 5-HT, Acetylcholine and Histamine with presynaptic and postsynaptic receptors, but it becomes clear that these are not simple levels of active substance concentrations but symptoms and the course of the disease depend on the variability of the responsible structure and networks of CNS changes under different circumstances. Antipsychotics with known mechanisms of action change but also contribute to the recognition of the dynamics of schizophrenic symptomatology. The effective therapy of Sch psychosis involves more novelty. The algorithms for the application of psychopharmaceuticals are the first line. The other would be the mapping of the CNS with the identification of responsible structures, and the third, perhaps the most important is the identification of key symptoms and their transmitter's and then the application of adequate antipsychotics with known mechanism of action. Only the eclectic approach to the clinical symptoms and psychopharmacotherapy can avoid the wrong diagnosis and therapy. It is necessary that psychopharmacotherapy of schizophrenia strives to establish transmitter-receptor balance and personalized approach to treatment.

Spazam u vaskularnim oboljenjima mozga

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Šta je cerebralni vazospazam?
U kojim bolestima se može pojaviti cerebrovaskularni spazam (CVS)?
Šta je uzrok CVS?
Na kojim krvnim sudovima se javlja CVS?
Znaci i simptomi CVS.
Šta povećava rizik za pojavu VS?
Zašto je CVS problem?
Kako se može CVS detektovati?
Prevencija i tretman.

Vasospasm in brain diseases

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What is cerebral vasospasm?
In which diseases can cerebrovascular spasm (CVS) occur?
What is the cause of CVS?
Which blood vessels can CVS appear on?
Signs and symptoms of CVS.
What increases the risk of occurrence of VS?
Why is CVS a problem?
How can CVS be detected?
Prevention and treatment.

Depresija izazvana lekovima

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Depresija izazvana lekom može biti klasifikovana kao psihoorganski poremećaj, depresivnog tipa. Pacijenti koji su podvrgnuti terapiji lekovima obično dožive značajan psihosocijalni stres zbog patnje i invaliditeta koji su posledica same bolesti, kao i zbog nemogućnosti obavljanja nekih ili svih socijalnih funkcija, tako da je jako teško odrediti da li su lekovi doprineli tome ili ne.
Trenutno se prevalencija depresije izazvane lekovima ne može utvrditi, ali je sigurno da čini značajan deo ukupne prevalencije depresija koja se kreće i do 7%. Najčešći mehanizam nastanka depresije izazvane lekom je smanjenje količine kateholaminskih neurotransmitera u mozgu, a zatim sledi supresija funkcije štitaste žlezde ili poremećaj sekrecije kortikosteroida.
Lekovi do sada povezani sa depresijom su: N2 antagonisti (Cimetidin, Ranitidin), NSAIL, opioidi, kardiovaskularni lekovi (alfa metildopa, hidralazin, propranolol, prazosin, klonidin, digoksin, blokatori kanala za kalcijum, tiazidni diuretici, kortikosteroidi, anabolički steroidi, antiparkinsonici (levodopa), sedativi-hipnotici (barbiturati, hloral hidrat), baklofen, finasterid, interferon alfa i druge vrste interferona. Od kliničara se često zahteva da procene da li je depresija uzrokovana lekom, tako da je u toj situaciji od velike koristi poznavanje iskustava sa depresijom i lekovima objavljenih u medicinskim časopisima.
Kada se depresija otkrije, prvi korak u lečenju je povlačenje dalje primene leka, i praćenje promene stanja pacijenta po danima posle prekida primene. Potrebno je sačekati nekoliko nedelja da se vidi da li će se simptomi depresije povući; za to vreme pacijent mora biti pod striktnim nadzorom, kako bi se izbegla mogućnost pokuša samoubistvo. Ukoliko ne dođe do kompletnog povlaženja simptomatologije depresije, pribegava se primeni antidepresiva.

Drug-induced depression

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Drug-induced depression could be classified as psych organic disorder of depressive type. The patients on drug therapy usually experience significant psychosocial stress due to suffering and incapacity caused by the disorder itself, and it is very difficult to differentiate whether the drugs prescribed contributed to the depression, or not.

Currently, prevalence of drug-induced depression could not be established with certainty, but it contributes largely to overall prevalence of depression of 7%. The most frequent mechanism of drug-induced depression is decrease of catecholamine neurotransmitters in the brain, followed by suppression of thyroid function and increased secretion of corticosteroids.

Drugs known to induce depression are: H2 antagonists (cimetidine, ranitidine), NSAIDs, opioids, cardiovascular drugs (alpha methyldopa, hydralazine, propranolol, prazosine, clonidine, digoxin, calcium channel blockers, thiazide diuretics, corticosteroids, anabolic steroids, antiparkinsonian drugs (levodopa), sedative-hypnotics (barbiturates, chloral hydrate), baclofen, finasteride, interferon alpha and other interferon types. Clinicians are expected to judge whether a depression case was drug-induced or not, and knowing potential of main drug groups to induce depression is important for both psychiatrists and other specialties.

When drug-induced depression is diagnosed, the main step is cessation of the drug use, and careful follow-up of the patient. Several weeks should elapse before we are certain that no further symptom withdrawal could be expected, and during that time the patient has to be under close observation, as the risk of suicide is high. If symptoms of depression do not withdraw completely, an antidepressant should be prescribed.

Specificnosti farmakoterapije kod žena

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Farmakokinetske i farmakodinamske razlike brojnih lekova kod žena u odnosu na muškarce potiču od specifičnosti ženske anatomije, fiziologije i hormonskih fluktuacija za koje se pretpostavlja da mogu biti primarni uzrok farmakoterapijskih razlika uslovljenih polom. Međutim, još uvek je malo kontrolisanih kliničkih ispitivanja koja otkrivaju teorijski postojeće, značajne razlike u farmakokinetici lekova kod žena i pokazuju da pol može da predstavlja značajan faktor varijabilnosti u farmakokinetičkim procesima lekova. Moguća objašnjenja su razlike u sastavu tela žena i / ili fiziološke promene tokom menstrualnog ciklusa, kao i razlike u vezivanju za proteine plazme i hormonski status. Česte i ponekad klinički relevantne rodne razlike su identifikovane za procese eliminacije leka, što je povezano sa ekspresijom enzimskih sistema, specifičnih za pol, npr. CYP3A4 i CYP1A2. Razlike u farmakokinetici i farmakodinamici lekova naročito je važno poznavati tokom različitih faza menstrualnog ciklusa, trudnoće, menopauze, laktacije, upotrebe oralnih kontraceptiva. Rizik od pojave neželjenih reakcija na lekove značajno je veći kod žena nego kod muškaraca. Pri tome treba uzeti u obzir sve osobine organizma žene, osobine leka, starosno doba, varijabilnosti farmakokinetskih parametara leka, kao i mogućnosti ispoljavanja neželjenih reakcija lekova. Međutim, potrebne su dodatne studije koje bi istražile uticaj pola na optimalan izbor i prilagođeno doziranje lekova kod žena.

Ključne reči: žene, farmakoterapija, specifičnost, farmakokinetika, farmakodinamika

Specifications of pharmacotherapy in women

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The pharmacokinetics and pharmacodynamics in women are different from that in men because of women's unique anatomy and physiology. Recently, gender-related studies in clinical pharmacology have been emerging, supporting the observation of gender-induced variations in drug response. The hormonal fluctuations during a woman's life span may influence pharmacotherapy. Possible explanations are differences in body composition between men and women and/or physiological changes during the menstrual cycle as well as differences in plasma protein binding secondary to hormonal characteristics. Frequent and sometimes clinically relevant gender differences could be identified for drug elimination processes and were predominantly linked to the sex-specific expression of metabolic enzyme systems, e.g. CYP3A4 and CYP1A2. Therefore, gender-related pharmacology should be taken into consideration when prescribing medication for a woman. Although gender differences have been described both in pharmacodynamics and pharmacokinetics, their role in clinical practice is not yet completely elucidated. The evidence that women have been less enrolled in clinical trials and that a gender-specific analysis usually is not included in the evaluation of results, contributes largely to this uncertainty. Consequently,adverse drug reactions are still higher in females than in males. Since sex is a fundamental biological variable that cannot be discounted, gender differences in pharmacology have to be considered in order to improve drug safety efficacy and to optimize medical therapy both in men and women. However, further studies are needed to explore the impact of sex and gender on reaching the most appropriate and tailored prescription for each patient, regardless of sex and gende.

Key words: women, pharmacotherapy, differences, pharmacokinetics, pharmacodynamics

Originalni i generički lekovi

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Originalni lek je:
- lek koji je sintetisala, pretklinički i klinički ispitala na velikom broju pacijenata jedna farmaceutska kompanija
- lek koji je godinama kontrolisala i pratila njegova dejstva, farmaceutska kompanija čiji je izum.
- lek koji je ta kompanija zaštitila kao patent pa se još zove brendirani (brand name), inovativni ili pionirski lek.

Generički lek je lek koji je razvijen u potpunosti po uzoru na neki inovativni ili originalni lek.
Nakon isteka perioda patentne zaštite za kompaniju koja je otkrila supstancu i proizvela gotov lek, otvara se mogućnost da i druge farmaceutske kompanije koje nisu otkrile originalnu supstancu počnu da proizvode gotov lek koji sadrži datu supstancu.
Da bi neki generički lek bio pušten u promet, za njega se mora dokazati farmaceutska i terapijska ekvivalencija u odnosu na originalni lek.
U slučaju originalnog leka, reč je o farmakološki aktivnoj supstanci za koju ne postoje prethodna iskustva u primeni kod ljudi. Stoga, takav lek prolazi ekstenzivna (i skupa) pretklinička i klinička ispitivanja, koja dokazuju njegovu efikasnost i bezbednost.
U slučaju generičkog leka, reč je o kopiji već postojećeg leka i u tom slučaju nema potrebe da se takav, generički proizvod ispituje u onom obimu u kojem je pre toga ispitivan originalni (referentni) lek.
U radu se navode rezultati kliničkih ispitivanja IV faze objavljeni u vodećim međunarodnim naučnim časopisima.
Istraživači treba sami da pokreću komparativne farmakodinamske studije brand&generics. Značajno je i potrebno pratiti prijavu neželjenih dejstava lekova, prema zaštićenom imenu, serijskom broju i doznom režimu. Neophodna saradnja bolničkih jedinica za praćenje neželjenih dejstava lekova i medicinskih sredstava sa agencijama, ali i brand proizvođačima.
Najbolja odluka lekara kliničara o tome koji će lek preporučiti svom pacijentu mora biti sinteza iskustva lekara i realnih mogućnosti u datom momentu. Borba za najkvalitetnije lekove mora biti u rukama stručnjaka.

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Original and generic drugs

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Original drug is:
- drug that synthesized, pre-clinically and clinically tested in a large number of patients, by a pharmaceutical company
- drug that has been controlling and monitoring its effects for years, by a pharmaceutical company whose invention is.
- drug that this company protected as a patent and is also called brand name, an innovative or pioneering drug.

A generic drug is a drug developed entirely as an example of an innovative or original drug.
After the expiry of the patent protection period for the company that discovered the substance and produced the finished drug, opens the possibility for other pharmaceutical companies (that did not discovered the original substance and produced original drug) to begin producing a finished drug containing the same substance. In order for a generic drug to be released into the market it is necessary to prove the pharmaceutical and therapeutic equivalence relative to original drug.
In the case of the original drug, it is a pharmacologically active substance for which there are no prior experience in human application. Therefore, such a drug is undergoing extensive (and expensive) preclinical and clinical trials, which prove its effectiveness and safety. In the case of a generic drug, it is a copy of an already existing medicine, and in that case there is no need for such a generic product to be tested in the extent as the original (reference) drug.
The authors of this paper present the results of the IV phase clinical trials published in the leading international scientific journals. The authors of this paper present the results of the IV phase clinical trials published in the leading international scientific journals.
Researchers should themselves run comparative pharmacodynamic studies of brand & generics. It is important to monitor and report drug adverse reactions, according to the protected name, serial number and dosage regimen. Cooperation of hospital units for monitoring of drugs and medical devices adverse effects with agencies and brand manufacturers is necessary,
The best decision of the clinician's doctor about what the drug will recommend to his patient must be a synthesis of the doctor's experience and real possibilities at a given moment. Fighting for the best drugs must be in the hands of an medical specialist.

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Rulebook on the manner of advertising of a medicinal product or medical device, Articles 37 and 38 (Official Gazette 79/2010).

Evolucija u dijagnostici i lečenju nesitnoćelijskog karcinoma pluća

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Karcinom pluća ima ogroman medicinski značaj. Na globalnom nivou karcinom pluća je tokom svake godine razlog smrtnog ishoda više nego karcinom dojke, kolona i prostate zajedno, odnosno jedan od pet obolelih od kancera širom sveta, umire zbog karcinoma pluća. Nesitnoćelijski karcinom pluća (NSCLC) čini oko 85% svih karcinoma pluća. NSCLC je uglavnom slabo osetljiv na hemioterapiju, kada god je to moguće sprovdi se hiruška resekcija tumora u kombinaciji sa hemioterapijom.
Intenzivna ispitivanja biologije kancerskih ćelija i mogućnost analize kancerskog genoma i njegovih izmena, stvorile su nove mogućnosti za otkrivanje novih i vrlo različitih i kancer specifičnih targeta za lekove. To omogućuje pronalaženje novih lekova, specifičnih za kancerske targete.
Alecetinib je visoko selektivan i potentan inhibitor protein kinaze, koji ciljano inhibiše ALK u NSCLCs ćelijama, i značajno usporava progresiju bolesti i popravlja ishod obolelih, mnogo bolje nego standardna hemioterapija. U prekliničkim studijama je pokazano da inhibicija aktivnosti ALK tirozin kinaze dovodi do blokade signalnih puteva uključujući STAT 3 i PI3K/ALK što dovodi do indukcije smrti kancerskih ćelija (apoptoze).
Današnje vreme donosi velike promene u lečenju kancera i novi lekovi predstavljaju veliki napredak u lečenju malignoma, uključujući i imuno-onkologiju i personalizovanu medicinu. Imuno-onkologija se zasniva na novom konceptu korišćenja imunološkog sistema organizma domaćina u borbi protiv kancera. Dalje, primenjuju se i nove antikancerske vakcine, koje mogu biti preventivne za zdrave ljude, ili terapijske, zasnovane na jačanju prirodnog imunog odgovora organizma protiv kancera. Tako da imuno-onkologija danas otvara novo polje u terapiji karcinoma.

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Evolution in diagnostics and treatment of non-small-cell lung carcinoma

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The impact of lung cancer is enormous. Globally, lung cancer causes more deaths each year than breast, colon and prostate cancers together. It is estimated that nearly one in five cancer deaths across the world is caused by lung cancer. Non-small-cell lung carcinoma (NSCLC) presents about 85% of all lung cancers. NSCLCs are mostly insensitive to chemotherapy, and therefore when possible, treated by surgical resection with curative intent, although using of chemotherapy has been increasing. Rapid investigations of cancer biology and ability to analyze cancer genome alterations, give us new opportunity to discover different cancer specific drug targets, and new drugs for these targets.
Alectinib, a highly selective and potent protein kinase inhibitor, targeting mutant ALK in NSCLCs cells, stops disease progression and improves outcomes, much better than conventional chemotherapy. In preclinical studies, inhibition of ALK tyrosine kinase activity led to blockage of downstream signaling pathways including STAT 3 and PI3K/AKT and induction of tumor cell death (apoptosis).
We are at a time of significant change in cancer care, and new drugs represent significant advances in cancer treatment, including immuno-oncology and personalized medicines. Immuno-oncology is based on the concept of harnessing the body's own immune system to fight cancer. Further, new anticancer vaccines can be either preventive, which are intended to prevent cancer from developing in healthy people, or therapeutic, which are meant to treat cancer by strengthening the body's natural immune response against the cancer. Immuno-oncology opens a new field of a cancer therapy today.

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Specifičnosti farmakoterapije gerijatrijskih depresija

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Depresija kod starih (≥65 god.) je čest poremećaj koji dovodi do značajne funkcionalne nesposobnosti i smanjenja kvaliteta života, kao i povećanja stope nesuicidalnog i suicidalnog mortaliteta. Depresija je nepovoljan faktor koji utiče na nastanak, tok i ishod mnogih hroničnih bolesti. Dijagnoza GD uključuje iste kriterijume kao i kod mlađe populacije. Kod starijih depresivnih pacijenata su prisutniji somatski simptomi, pseudodemencija, veća stopa komorbiditeta, mortaliteta, relapsa, opadanja kognitivnih funkcija, manja učestalost depresije u porodičnoj istoriji i osećanja krivice, kao i lošija prognoza.
Kardiovaskularni lekovi, kortikosteroidi, analgetici, antiparkinsonici, antimikrobni lekovi (antibiotici-fluorokinoloni i antivirusni lekovi-citokini), antacidi, inhibitori protonske pumpe, kao i psihofarmaci mogu da indukuju depresiju. Farmakodinamske i farmakokinetske promene u starosti povećavaju rizik za akumulaciju leka u organizmu.
Značajan uticaj na izbor farmakoterapije GD ima komorbiditet, polifarmacija (učestaliji kod starih) i interakcija lekova. Lekove treba uvoditi u nižim dozama, a potom postepeno povećavati ("Start low, go slow"). U gerijatrijskoj populaciji se češće javlajaju neželjeni efekti antidepresiva (AD), kao što su kardiotoksičnost, hiponatremija, pogoršanje kognicije, osteoporoza, posturalna hipotenzija i padovi. Kod starijih osoba je prisutniji sporiji odgovor na terapiju, kao i rezistencija na tretman.
Selektivni inhibitori ponovnog preuuzimanja serotonina (SSRI) i novi AD buproprion (DRI), mirtazapin (NaSSA), moklobemid (RIMA) i venlafaksin (SNRI) su relativno bezbedni kod starijih osoba. Oni imaju manju incidencu antiholinergičkih meželjenih efekata nego stariji antidepresivi (triciklični antidepresivi, koji se koriste kao terapija treće linije; smrtonosni kod predoziranja) i na taj način dobro podnose bolesnici sa kardiovaskularnim oboljenjima.
Velafaksin, mirtazapin i bupropion imaju takođe dobar bezbednosni profil u smislu interakcija lekova. SSRI-i kao što su fluoksetin, paroksetin i fluvoksamin imaju veći rizik od interakcija lekova.
Nagli prekid terapije nekim AD (posebno venlafaksinom i paroksetinom) može dovesti do "sindroma povlačenja" koji uključuje anksioznost, nesanicu i simptome slične gripu. Ovo se može sprečiti postepenim ukidanjem, pa se preporučuje period od 7 do 10 dana.

Specificity of pharmacotherapy of geriatric depressions

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Depression in the elderly (≥65 years) is a common disorder that leads to significant functional disability and a decrease in quality of life, as well as an increase in the rate of non-suicidal and suicidal mortality. Depression is an unfavorable factor that affects the origin, current and outcome of many chronic diseases. Diagnosis of GD includes the same criteria as in the younger population. In elderly depressed patients, somatic symptoms, pseudodementia, higher incidence of comorbidity, mortality, relapse, cognitive function decline, lower incidence of depression in family history and feelings of guilt, as well as poor prognosis are more common.

Cardiovascular drugs, corticosteroids, analgesics, antiparkinsonics, antimicrobial drugs (antibiotics-fluoroquinolones and antiviral drugs-cytokines), antacids, proton pump inhibitors, and psychopharmaceuticals can induce depression. Pharmacodynamic and pharmacokinetic changes in age increase the risk of accumulation of the drug in the body.

Significant influence on the selection of pharmacotherapy of GD has comorbidity and polypharmacy (more common in the old), and drug-drug interactions. Drugs should be introduced at lower doses, and then gradually increased ("Start low, go slow"). Adverse effects of antidepressants (AD), such as cardiotoxicity, hyponatraemia, cognitive impairment, osteoporosis, postural hypotension, and falls are more common in the geriatric population. In the elderly there is a slower response to treatment , as well as resistance to treatment.

The selective serotonin reuptake inhibitors (SSRIs) and the newer AD buproprion (DRI), mirtazapine (NaSSA), moclobemide (RIMA), and venlafaxine (SNRI) are all relatively safe in the elderly. They have less incidence of anticholinergic unwanted effects than older antidepressants (tricyclic antidepressants used as third-line therapy, lethal in overdose) and are thus well tolerated by patients with cardiovascular disease.

SSRIs considered to have the best safety profile in the elderly are citalopram, scitalopram, and sertraline. These have the lowest potential for drug-drug interactions based on their cytochrome P-450 interactions. Venlafaxine , mirtazapine, and bupropion are also considered to have a good safety profile in terms of drug-drug interactions. SSRIs such as fluoxetine, paroxetine, and fluvoxamine have higher risks of drug-drug interactions.

Abrupt discontinuation of therapy with some antidepressants (especially venlafaxine and paroxetine) can lead to a "withdrawal syndrome" that includes anxiety, insomnia and flu-like symptoms. This can be prevented by gradual abolition, so it is recommended for a period of 7 to 10 days.

Informisani pristanak u kritično obolelih

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Autonomija pacijenta je temeljni princip savremene kliničke etike još od Nirnberškog procesa, posebno u Američkoj školi bioetike. Ona je definisana je u Nirnberškom kodeksu i redefinisana u Helsinškoj deklaraciji, Izveštaju iz Belmonta i Deklaraciji iz Barcelone. Osnivači i sledbenici bioetike zasnovane na pravima (npr., Hellegers, Beauchamp i Childers) utemeljili su i promovisali autonomiju pacijenta kao glavni princip bio(medicinske) etike od sedamdesetih godina prošlog veka. Međutim, dosta je kontroverzi vezano za ovaj princip, posebno kod vulnerabilnih pacijenata. Cilj nam je da procenimo stvarno značenje i vrednost autonomije kod kritično obolelih u komunikaciji između zdravstvenih radnika i pacijenata kao i članova njihovih porodica. Može se zaključiti da je zaštita autonomije kritično obolelih pacijenata složeno pitanje. Potrebna je pažljiva procena odnosa koristi i rizika kako bi se našao optimalan način dobijanja informativnog pristanka, odnosno saglasnosti rodbine, ili eventualno primenili terapijski postupci uz naknadni pristanak ili i bez toga.

Informed consent in critically ill

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Patient autonomy has been a cornerstone of contemporary clinical ethics since the Nuremberg trial, especially in American school of bioethics. Patient autonomy has been defined in the Nuremberg Code, and redefined in the Declaration of Helsinki, Belmont Report and Barcelona Declaration. Founders and followers of the rights-oriented bioethics (for example, Hellegers, Beauchamp and Childers) have established and promoted the patient autonomy as the main principle of bio(medical) ethics since 1970s. However, there is a lot of controversy surrounding such a principle, especially in vulnerable patients. We aimed at evaluating the real meaning and value of patient autonomy in critical care settings regarding the communication between health workers and their patients and families. In conclusion, protection of patients autonomy in critically ill is a complex issue. Careful benefit-risk assessment is needed in order to find the most appropriate way of obtaining the informed consent, proxy consent or to omit or delay it.

Uticaj pesticida na reproduktivnu sposobnost muškaraca

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Kvalitet sperme opada na globalnom nivou manifestujući se padom prosečne koncentracije sperme i srednje zapremine. Jedan od mogućih razloga može biti povećana izloženost hemikalijama u životnoj sredini sadržanim u pesticidima, plastici, elektronici i ostalim sintetičkim materijalima. Na tržištu postoji više od 1800 komercijalno korišćenih jedinjenja pesticida. Inhalatorno, dermalno, oralno i transplacentalno izlaganje može: dovesti do smanjenja broja spermatozoida u ejakulatu; uticati na integritet DNK - morfologiju sperme (OP pesticidi); uticati na koncentraciju spermatozoida (paration i metil paration); uticati na pokretljivost spermatozoida utičući na proizvodnju ATP (glavni izvor energije za spermatozoe) (fenvalerat). Direktni efekti pesticida na plodnost muškaraca uključuju efekat endokrine disrupcije (strukturna sličnost pesticida sa reproduktivnim steroidnim hormonima - vezivanje za endokrine receptore i delovanje kao hormonski ligandi (paration i metilparation su strukturno slični estrogenima) i apoptoza germinativnih ćelija - (metilparation, diazinon). Indirektni efekti uključuju uticaj na neuroendokrinu kontrolu na nivou testisa (ometanje proizvodnje i oslobađanja testosterona) i na nivou centralnog nervnog sistema (ometanje efekata gonadotropina), oksidativni stres - pesticidi mogu proizvoditi slobodne radikale i promeniti antioksidativni kapacitet. Na stepen izloženosti pesticidima utiče: broj godina izloženosti, vreme provedeno u prskanju pesticida, učestalost i količina pesticida i stanje pod kojim je došlo do izlaganja. Preventivne mere za smanjenje uticaja izloženosti pesticidima između ostalog uključuju: korišćenje zaštitne opreme, dodatak vitamina (Vit C i E - antioksidansi) i kontrolisana upotreba pesticida.

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Influence Of Pesticides On Male Reproductive Capacity

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Global semen quality is declining with drop in both average sperm concentration and mean seminal volume. One of the reasons for such condition might be the enhanced exposure to environmental chemicals contained in pesticides, food sources, plastics, electronics and other synthetic materials. There are more than 1800 commercially used pesticide compounds available in the market. Exposure by different routes (inhalational, dermal, oral, and placental) can result in decreased sperm count per ejaculate; affect DNA integrity – sperm morphology (OP pesticides); can affect sperm concentration (parathion and methyl parathion); can affect motility by affecting the production of ATP (main source of energy for spermatozoa) (fenvalerate). Direct effects of pesticides on male fertility include endocrine disrupting effect (structural similarity of pesticides with reproductive steroid hormones – binding to endocrine receptors and act as hormonal ligands (parathion and methylparathion are structurally similar to estrogens) and apoptosis of the germ cells - (methylparathion, diazinon...). Indirect effects include impact on neuroendocrine control at testicular level (by interfering the production and release of testosterone) and central nervous system (by interfering gonadotropins), oxidative stress - pesticides can produce free radicals and change antioxidant capacity. Severity of pesticide exposure is determined by: number of years of exposure, time spent for cropping or spraying the pesticide, frequency and quantity of pesticide spraying, and condition under which exposure has occurred. Preventive measures to decrease pesticide exposure amog other things include: use of protective equipment, vitamin supplementation (Vit C and E - antioxidants) and appropriate and controled use of pesticides.

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Potrošnja antibiotika u Srbiji

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Prekomerna,nedovoljna i zloupotreba antibiotika predstavlja vodeći faktor rizika za razvoj otpornosti bakterija na antibiotike i ima uzročno-posledičnu vezu u povećanoj učestalosti rezistencije i multirezistencije. Srbija spada u zemlje sa visokom potrošnjom antibiotika i visokom stopom rezistencije.
Praćenje potrošnje lekova jedan je od poslova Agencije za lekove i medicinska sredstva Srbije, koje se sprovodi od 2004. godine. Upotreba jedinstvene ATC/DDD metodologije i praćenje preporučenih indikatora omogućila je poređenje potrošnje antibiotika u Srbiji sa drugim zemljama.
Ukupna potrošnja (vanbolnička i bolnička) antibakterijskih lekova za sistemsku primenu u 2016. godini bila je 30,1 DDD/1000 stanovnika na dan dok je prosek potrošnje u zemljama članicama EU bio 21,9 DDD/1000 stanovnika na dan. U poređenju sa zemljama EU u 2016. Srbija se nalazi na drugom mestu po potrošnji cefalosporina i karbapenema, na trećem mestu po potrošnji makrolida , na drugom mestu po potrošnji hinolona.
Rezultati ukazuju na potrebu za kvalitativno unapređenje upotrebe antibiotika: potrebno je smanjiti ukupnu potrošnju antibiotika; smanjiti potrošnju pojedinih grupa lekova(hinoloni, makrolidi); povećati potrošnju penicilina osetljivih na beta laktamazu-uskog spektra delovanja (fenoksimetilpenicilin).

Consumption of antibiotics in Serbia

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The overuse, underuse and misuse of antibiotics are a major factor in creating AMR. Serbia is among the European countries with high consumption of antibiotics, and among countries with high resistance rates.
The monitoring of drug consumption is one of the activities of the Agency for Medicines and Medical Devices of Serbia, which has been implemented since 2004. A unique ATC / DDD methodology has made it possible to compare the consumption of antibiotics in Serbia with other countries.
In Serbia during the 2016. year total consumption (community and hospital sector) of antibacterials for systemic use was 30,10 DDD per 1000 inhabitans per day, while average community consumption antibacterials for systemic use was 21,9 DDD per 1000 inhabitans per day in the countries, EU Member States. Serbia has the second highest utilization for cephalosporins, third highest for macrolides, and second highest for quinolones vs. EU Member State in 2016.
The results indicate good antibiotic prescription practices (such as high amoxicillin consumption), but also the need for qualitative improvement in the use of antibiotics: it is necessary to reduce the overall consumption of antibiotics; reduce the consumption of certain groups of drugs (macrolides, quinolones, amoxiclav); Increase the consumption of penicillin-sensitive beta-lactamase-narrow spectrum (phenoxymethylpenicillin).

Утицај хране на фармакокинетику

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Храна може да промени фармакокинетику лекова мењајући њихову ресорпцију, биотрансформацију и екскрецију, а тиме и њихово дејство, односно да доведе до различитих интеракција хране и лекова. Последице интеракција могу бити: појачан или слабији ефект, брже или спорије наступање ефекта; токсичност, нови ефекти или појачане нежељене реакције; синергизам, побољшана биолошка расположивост, смањена токсичност, смањени или повећани трошкови лечења.

Да би се идентификовале могуће интеракција хране и лекова и превенирала нежељена дејства, неопходна је детаљна анамнеза о храни, додацима хране и лековима које пацијенти узимају.

Након утврђивања да је клинички значајна промена код пацијента резултат интеракције лекова и хране, постоји дилема шта учинити? Прекинути узимање лека или хране? Променити лек? Променити дозу?

Због тога је менаџмент интеракција хране и лекова веома важан у раду савременог фармацеута и лекара. Да би то постигли, требада знају где да нађу потребну информацију о клинички значајним интеракцијама, да ли је и када потребно мерити концентрације лекова, који лекови могу да имају токсичне метаболите, да посумњају на интеракције када је терапијски ефект слабији или јачи од очекиваног или када се јавило токсично дејство, при чему треба одабрати лекове и препоручити исхрану за које је мало вероватно да ће ступити у интеракцију.

Лекари и фармацеути треба да занављају своја знања у области интеракција лекова да би на основу најновијих сазнања могли да едукују и препоруче пацијенту најбоље решење.

The influence of food on pharmacokinetics

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Food can change the pharmacokinetics of drugs by alteration of their absorption, biotransformation and excretion, and thus their effect, leading to different food and drug interactions. The consequences of interactions can be: an increased decreased effect, a faster or slower effect occurrence, toxicity, new effects, more frequent side effects, synergism, increased bioavailability, reduced toxicitz, reduced or increased costs of the treatment.
In order to identify the possible interaction of food and medication and to prevent side effects, a detailed history taking of food, food supplements and medicines taken by patients is required.
After determining that a clinically significant change in the patient is the result of the interaction between medicines and food, there is a dilemma about what to do? Stop taking medicine or food? Change the medicne? Change the dose?
The management of food and drug interactions is very important in the as a part of the work of a modern pharmacist and physician. To achieve this, they need to know where to find the necessary information on clinically significant interactions, whether and when to measure drug concentrations, which drugs can have toxic metabolites, they should suspect interactions when the therapeutic effect is weaker or stronger than expected or when there is a toxic effect, whereby medication and food should be selected and recommended if it is unlikely that thez will interact.
Physicians and pharmacists should upgrade their knowledge in the field of interactions in order to learn from the latest knowledge and recommend the best solution to the patient.

Karakteristike farmakoterapije u urgentnoj kardiologiji

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Akutna embolija pluća (EP) je i dalje značajan razlog morbiditeta i mortalite u koronarnoj jedinici. Prema najnovijim vodičima potrebna je brza dijagnoza EP i primena fibrinolitičke i/ili antikoagulantne terapije. Standardna terapija EP je primena LMWH, koji se preklapa sa varfarinom, do postizanja terapijskog INR (2 do 3), za šta je potrebno najkraće 5 dana. Posle toga, potrebna je redovna kontrola INR-a do god traje antiko -agulantna terapija varfarinom.
Do otkrića direktnih oralnih antikoagulantnih lekokova (DOAKs), produžena oralna antikoaguilantna terapije je bila ograničena samo na varfarin. DOAKs su ispitivani u velikim, prospektivnim randomizovanim kliničkim studijama i potvrđeno je da su ovi lekovi efikasni i bezbedni u lečenju i profilaksi EP. Primena ovih lekova u kliničkoj praksi donosi određene prednosti u terapiji antikoagulantnim lekovima. DOAKs imaju povoljan odnos efikasnosti i bezbednosti, imaju stabilan i predvidiv antikoagulantni efekat. Nadalje, DOAKs imaju direktan antikoagulantni efekat (dabigatran je inhibitor trombina; rivaroksaban i apiksaban inhibišu F Xa) i njihov antikoagulantni efekat je brz i predvidiv, imaju manje interakcija sa hranom i drugim lekovima u poređenju sa varfarinom. U bezbedonosnom profilu DOAKs je najvažnije to da ovi lekovi ređe izazivaju intrakranijumske hemoragije (za 50% manje od varfarina).
Međutin, za određenu grupu bolesnika, posebno kod kojih je visok rizik za tromboze, varfarin je i dalje lek izbora.

Characteristics of pharmacotherapy in emergency cariology

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Acute pulmonary embolism (PE) still causes significant morbidity and mortality in coronary care unit (CCU). According to the NEW GUIDELINES, fast diagnosis end prompt fibrinolytic or/and anticoagulant therapy is necessary. Low molecular weight heparin (LMWH) bridging to warfarin, has been a standard treatment for PE. Because warfarin needs almost five days or longer to achieve therapeutic effect (INR between 2 and 3), overlapping with LMWH is necessary. Regular monitoring of INR is necessary as long as warfarin is used.

Before direct oral anticoagulant drugs (DOACs) were discovered, the only option for prolonged oral anticoagulation was limited to warfarin therapy. DOACs have been tested in large randomized prospective trials and proven to be efficient and safe for pulmonary embolism treatment, as well as in prophylaxis. The addition of these new medications has advantage in anticoagulation therapy. DOACs have good efficacy/safety ratio, a stable and predictable anticoagulant effect, without the need for regular coagulation monitoring. Further, DOACs have direct anticoagulant effect (dabigatran inhibit thrombin; rivaroxaban and apixaban inhibit F Xa) and their anticoagulant effect is prompt and predictable, they have fewer food and drugs interactions compared to warfarin. The most important, safety profile of DOACs is less intracranial hemorrhages (50% less than warfarin).

However in certain groups of patients, especially if high thromboembolic risk exists, warfarin use is still indicated.

Strukturna i diskriminaciona validnost mernih skala rizika za tešku koronarnu arterijsku bolest kod žena u menopauzi

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Dobro su poznati mnogobrojni faktori rizika za koronarnu arterijsku bolest (KAD) u opštoj ljudskoj populaciji, ali je utvrđeno da postoji različit intenzitet ovih rizika kod žena u odnosu na muškarce. Faktori rizika za KAD mogu se podeliti na one koji proizilaze iz stila života, ali veoma često se govori i o aterosklerotskim faktorima rizika kao što dijabetes, gojaznost, hiperlipoproteinemija ili metabolički sindrom. Pol i starost predstavljaju važne kovarijate u istraživanjima koja imaju za zadatak proučavanje novih aterosklerotskih i/ili neaterosklerotskih faktora rizika za KAD. Međutim, problemi i bajasi koji nastupaju u interpretaciji rezultata u studijama koje se bave proučavanjem pomenutih rizika (aterosklerotskih /ili neateroskl erotskih) proizilaze iz njihove gotovo obavezne udruženosti u nastanku KAD, a sve zbog prethodnog nepoznavanja njihove latentne strukture i izostanka eventualnog pokušaja njihovog optimalnog skaliranja. Primera radi, uloga arterijskih kalcifikacija dojki (medijalne arterijske kalcifikacije) u nastanku KAD kod žena u menopauzi je kontraverzna, od izveštaja da jesu ili opet da nisu od uticaja, do izveštaja da ove promene iako nisu aterosklerotske, imaju klinički značaj samo onda kada se jave zajedno sa aterosklerozom. Otuda je neophodna konstrukcija mernih skala rizika za KAD kako bi se maksimalno zadržala informativnost iz skupa podataka, a izbegli bajasi ili neadekvatna interpretacija dobijenih rezultata.

Structural and discriminatory validity of measuring risk scales for severe coronary arterial disease in women in menopause

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Many risk factors for coronary artery disease (CAD) in the general human population are well known, but it has been found that there is a different intensity of these risks in women compared to men. Risk factors for CAD can be divided into those that come out of a life style, but very often there are discussions about atherosclerotic risk factors such as diabetes, obesity, hyperlipoproteinemia, or metabolic syndrome. Gender and age are important covariates in research whose task is to study new atherosclerotic and / or non-atherosclerotic risk factors for CAD. However, problems and bias that occur in the interpretation of the results in studies studying these risks (atherosclerotic / non-atherosclerotic) arise from their almost obligatory association in the onset of CAD, all due to the previous ignorance of their latent structure and the absence of any attempt at their optimal scaling. For example, the role of breast arterial calcification (medial arterial calcification) in the onset of CAD in women in menopause is controversial, from reports that they are or are not yet affected, to the report that these changes, although not atherosclerotic, have clinical relevance only when they occur together with atherosclerosis. Hence, the construction of measuring risk scales for CAD is necessary in order to maximize the information from the dataset, while avoiding bias or inadequate interpretation of the results obtained.

Psihofarmakoterapija poremećaja povezanih sa stresom

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Poremećaji povezani sa stresom su česti psihijatrijski poremećaji, javljaju se kao reakcija na stresogene životne događaje, sa pretežno anksioznim i depresivnim simptomima. Neurobiologija stresa je povezana sa neurotransmiterskim sistemima CNS, te medikacija menja transmisiju impulsa u serotonergičkom, noradrenergičkom i GABA sistemu. Noviji terapijski pristupi uključuju glutamatni sistem, hormone i neurotransmitere HPA osovine, voltažno senzitivne jonske kanale kao potencijalna mesta za delovanje lekova. GCP vodiči kao terapiju prvog reda označavaju lekove sa delovanjem na 5HT i NA sistem, odnosno SSRI i SNRI antidepresive, u terapiji drugog reda su antidepresivi drugačijeg mehanizma delovanja, benzodijazepini i pregabalin. Dodatna medikacija su hipnotici iz grupe “Z-drugs”, atipični antipsihotici, ß i α adrenergički blokatori. U teraporezistentnim slučajevima moguća je kombinacija antidepresiva iz različitih grupa. U tretmanu različitih vrsta ovih poremećaja postoje specifičnosti. Kod akutnih reakcija na stres se preporučuje kratkotrajna primena benzodijazepina, ß blokatori neposredno posle traume i SSRI odmah i tokom sledeća tri meseca. Tretman PTSP je složen, dugotrajan, često nedovoljno uspešan. Pored primene antidepresiva prve i druge linije, neophodna je dodatna medikacija i kombinovana medikacija. Novije kliničke studije ističu α1 adrenergički blokator Prazocin kao značajnije efikasan za tretman flesh- back-ova nego dosadašnja medikacija. Medikamentozni tretman se najčešće dopunjava psihoterapijskim intervencijama- CBT i EMDR.

Psychopharmacotherapy in stress induced dissorders

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Stress-related disorders are frequent psychiatric disorders, which occur as a reaction to stressed life events, with predominantly anxiety and depressive symptoms. Neurobiology of stress is associated with numerous neurotransmitter systems in the CNS, and the medication of these disorders is associated with the modulation of impulse transmission at the serotonergic, noradrenergic and GABA systems. Recent therapeutic approaches include the glutamate system, hormones and neurotransmitters of the HPA axes, ion sensitive channels as potential sites for the drugs action. Good clinical practice guidelines as first-line therapy mean drugs with action on the 5HT and NA system, that is, SSRI and SNRI antidepressants, while in the second-line therapy, antidepressants of a different mechanism of action, benzodiazepines and pregabalin. Augmented medication are hypnotic from the group “Z-drugs”, atypical antipsychotics, ß and α adrenergic blockers. In theraporezistent cases, a combination of antidepressants from different groups is possible. There are specificities in the treatment of various types of stress-related disorders. In acute stress reactions, short-term administration of benzodiazepines is common, ß-blockers immediately after trauma and SSRI is recommended immediately and over the next three months. PTSD treatment is complex and long-lasting, often not sufficiently successful. In addition to the use of first and second line antidepressants, augmented medication or combined medication are often necessary. Recent clinical studies suggest α1-adrenergic blocking agent Prazocin as significantly effective for the treatment of flesh-back in relation to current medication. Medical treatment usually needs to be supplemented by psychotherapy interventions such as CBT and EMDR.

Supstituciona terapija opijatskih zavisnika - indikacije i dileme

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Opijatska zavisnost je hronični recidivantni psihijatrijski poremećaj sa epidemijskim razmerama. Potrebe za lečenjem su uslovile razvoj različitih metoda tretmana a njihova uspešnost je ograničena karakteristikama poremećaja. Vodiči dobre kliničke prakse su definisali visoko i nisko zahtevne programe gde terapija supstitucije opijatskim agonistima zauzima značajno mesto. Njeni ciljevi su smanjenje upotrebe ilegalnih droga i mortaliteta, prevencija transmisionih bolesti i kriminogenosti. Indikacije za uključivanje u program supstitucije su: starost 18 godina, zavisnički staž najmanje 5 godina, ispunjeni dijagnostički kriterijumi MKB 10, više bezuspešnih lečenja, psihijatrijski i telesni /HIV, HCV/ komorbiditet, udruženost sa kriminogenim ponašanjem, motivacija za program. Pored jasnih smernica i dobiti postoje i ograničenja i problemi. Uspešnost je i dalje kompromitovana visokom stopom recidivizma, sa svojim brojnim uzrocima i faktorima rizika. Zadržavanje u programu je ugroženo nedovoljnom saradnjom pacijenata sa čestim zahtevima za povećanje doza i sledstveno pojavom ilegalne prodaje opijatskih supstituta. Pojavljuje se demotivacija pacijenata i terapeuta za primenu psihosocijalnih intervencija sa nedovoljnom promenom zavisničkih obrazaca. Neophodna je revizija odluka u vezi različitih terapijskih modaliteta za svakog pacijenta ponaosob i da se u okviru supstitucionih programa pacijenti prevode u druge oblike terapije /detoksikacija i održavanje antagonistima opijatskih receptora/. Insistira se na primeni sveobuhvatnog modela lečenja /ostala psihofatrmakoterapija uz supstitucionu, psihosocijalne intervencije, porodična terapija, KBT/.

Supstitution in opiate addicts- indications and dilemas

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Opioid dependence is a chronic recurrent psychiatric disorder with epidemic proportions. The need for treatment has led to the development of different treatment methods and their performance is limited by the characteristics of the disorder. Good clinical practice guides have defined high and low-demanding programs where substitution therapy for opiate agonists takes a significant place. Its goals are to reduce the use of illegal drugs and mortality, the prevention of transmission diseases and criminality. Indications for the treatment in substitution program are: 18 years of age, opiate dependency for at least 5 years, complete ICD 10 diagnostic criteria, more unsuccessful treatments, psychiatric and physical / HIV, HCV / co-morbidity, association with criminal behavior, motivation for the program. In addition to guidelines and benefits, there are limitations and problems. Performance is still compromised by a high rate of recidivism, with its numerous causes and risk factors. Retention in the program is compromised by inadequate collaboration with patients and higher dosing requirements and the consequent occurrence of illegal sales of opiate substitutes. Demotivation of patients and therapists for the application of psychosocial interventions with insufficient change of addictive patterns appears. It is necessary to revise the decisions regarding different therapeutic modalities for each patient individually and in the substitution programs patients are translated into other forms of therapy / detoxification and maintenance of opiate receptor antagonists/. Comprehensive model of treatment / other psychopharmacotherapy with substitution, psychosocial interventions, family therapy, CVT / is needed and an imperative.

Pružanje kliničko farmakoloških informacija u KC Vojvodine

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Pružanje informacija o lekovima predstavlja jednu od osnovnih delatnosti iz oblasti kliničke farmakologije koja se sprovodi na Zavodu za farmakologiju, toksikologiju i kliničku farmakologiju Medicinskog fakulteta u Novom Sadu. Pored lekara i farmaceuta, informacije se pružaju i opštoj populaciji na teritoriji Vojvodine.

Udeo opšte populacije u zahtevima za informacijoma o lekovima je ispod 3% u odnosu na ukupan broj, a najčešća pitanja su se odnosila na interakcije, neželjena delovanja, doziranje i način primene lekova.

Od strane profesionalaca iz oblasti medicine ili farmacije, najveći broj zahteva (oko 30%) se odnosio na klinički značaj interakcija lekova. Informacije o neželjenim dejstvima lekova bile su predmet oko 12% zahteva. Bezbednost upotrebe lekova u trudnoći i dojenju razmatrana u oko 15% zahteva. Maksimalno dozvoljene doze i način/režim doziranja bili su predmet 11% upućenih zahteva. Preostali zahtevi su bili u vezi sa farmakokinetikom leka, terapijom prvog izbora za određene bolesti, kao i sa doziranjem u posebnim populacionim grupama (najčešće u dečijem uzrastu).

Pružanje kliničko farmakoloških informacija je prepoznato od strane zdravstvenih profesionalaca kao neophodnost u rešavanju pitanja efikasnosti i bezbednosti farmakoterapije i predstavlja potrvdu značaja kliničkog farmakologa u sistemu zdravstvene zaštite u našoj sredini.

Providing of clinical pharmacology information in Clinical Center of Vojvodina

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Providing information of drugs is one of the main activities in the field of clinical pharmacology conducted at the Department of Pharmacology, Toxicology and ClinicalPharmacology, Faculty of Medicine, University of Novi Sad.
The share of general population in drug information requests is below 3% in relation tothe total number, and the most frequent questions were related to drug interactions, adverse effects, dosing and method of administration.
From doctors and pharmacists, the highest number of requests (around 30%) were related to the clinical significance of drug interactions. Information related to adverse drug reactions were subject to around 12% of the requirements. The safety of the use of drugs in pregnancy and breastfeeding was considered in about 15% of the requirements. Maximal doses and dosage regimens were subject to 11% of requests. The remaining requirements were related to the pharmacokinetics of the drug, recommended therapy for certain diseases, and dosing in special population groups (usually in children). Providing of clinical pharmacology information has been recognized by health professionals as a necessity in addressing the issue of efficacy and safety ofpharmacotherapy and is a confirmation of the importance of the clinical pharmacologist in the health care system in our community.

Korelacija između rezistencije i potrošnje antibiotika u Srbiji i pojedinim zemljama Evropske unije

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Nedavni dokazi o razlozima sve veće rezistencije dolaze od meta-analiza koje ukazuju na udruženost između potrošnje antibiotika i rezistencije mikroorganizama na njih.
Cilj ove studije je bio da se odredi potrošnja antibiotika u Grčkoj, Srbiji i Švedskoj od 2012. do 2015. godine i da se utvrdi udruženost između potrošnje i rezistencije određenih sojeva bakterija u istim zemljama.
Ovo je retrospektivna, opservaciona, studija preseka sa rutinski prikupljenim podacima o potrošnji antibiotika (od 2012. do 2015.) i stopama rezistencije u Grčkoj, Srbiji i Švedskoj (2014.).
Rezultati za 2015. su pokazali da je Švedska zemlja sa najmanjom potrošnjom antibiotika, a zatim Srbija, pa Grčka. Dodatno, Grčka i Srbija imaju trend porasta potrošnje antibiotika u ispitivanim godinama, dok Švedska nasuprot njima ima trend smanjenja. U sve tri zemlje beta laktami/penicilini su grupa antibiotika sa najvećom potrošnjom. Takođe, rezultati iz ove studije su potvrdili udruženost između potrošnje i rezistencije na antibiotike. Ova studija je istakla jačinu korelacije između stopa potrošnje antibiotika i stopa rezistencije na sojeve E. coli, Acinetobacter spp. i MRSA.

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The correlation between resistance and antimicrobial consumption in Serbia and certain countries of the European Union

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Recent evidence comes from meta-analyses that report positive associations between antimicrobial consumption and the development of resistance at both population and individual levels.
The aim of this study was to measure the consumption of antimicrobial drugs in Greece, Serbia and Sweden from 2012 to 2015 and to evaluate relationship between that consumption and resistance of selected bacterial strains in same countries.
This was a retrospective, observational, cross-sectional, population-based study of routinely collected data for consumption of antimicrobial drugs (from 2012 to 2015) and national antimicrobial resistance rates in Greece, Serbia and Sweden (2014).
The results for year 2015 have shown that Sweden is the country with the lowest consumption of antimicrobial drugs, followed by Serbia and finally Greece. Results for trends in antibiotics use it can be noticed that both Greece and Serbia have increasing rates of consumption in the years 2012-2015, whereas Sweden has a decreasing tendency. From the analysis of antibacterials subgroups it can be seen that beta lactam/penicillins are the drugs of choice in all three countries. Furthermore, results from this study confirmed the relationship between community antimicrobial consumption and serious resistant infections in patients. This study has emphasized the strength of correlation between community consumption rates and antimicrobial resistance rates in E. coli, Acinetobacter spp. and MRSA.

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Finansijski menadžment u anesteziologiji i reanimatologiji u Kliničkom centru Srbije

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Здравље је значајно за сваког појединца и друштво. Систем здравствене заштите претставља један од стубова друштвеног система, мерило квалитета, нивоа и укупне друштвене перспективе. Анализа трошкова има важну улогу у изградњи ефикасног финансирања здравства. Методологија обрачуна трошкова није стандардизована у клиничким центрима.
Упоредили смо директне трошкове (плате,лекове,медицински и немедицински материјала, неопходне анализе и медицинске опреме) Центра за анестезиологију и реаниматологију у Клиничком центру Србији, установи терцијалног нивоа здравствене заштите, у 2006 и 2015 години.
Резултати су показали десетоструко смањење персоналних трошкова, уз пораст трошкова лекова и анализа. Видљива је несагласност у методологији израчунавања анестезиолошких услуга али и константног, хроничног и прогресивног обезбређивања струковног рада у директним трошковима. Услуге анестезиолога видљиве су само током рада у операционој сали. Нису приказане остале анестезиолошке услуге током: преоперативне процене и припреме, непосредном постоперативном и одложеном, хроничном лечењу критично оболелих болесника.
Квалитет статистичких података који су презентовани указује на незаинтересованост болничке администрације за анализу презентованих података у циљу смањења и рационализације трошкова здравствене заштите.

Financial Management in Anesthesiology and Reanimatology at the Clinical Center of Serbia

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Health is important for every individual and society. The health care system is one of the pillars of the social system, a measure of quality, level and overall social perspectives. Analysis of the expenses has an important role in building effective health financing. Costing methodology is not standardized in clinical centers.

We compared direct costs (salaries, drugs, medical and non-medical materials, necessary analyzes and medical equipment) of the Center for Anesthesiology and Reanimatology at the Clinical Center of Serbia, establishment of tertiary level of health care in 2006 and 2015.

The results showed a ten-fold decrease in personnel costs, with a rise in drug costs and analysis. Disagreement is apparent in the methodology of calculating anesthetic services, but also by constant, chronic and progressive securing of professional work in direct costs. Anesthetist services are only visible during operation in the operating room. No other anesthetic services were provided during: preoperative assessment and preparation, immediate postoperative and delayed, chronic treatment of critically ill patients.

The quality of the statistical data presented is indicative of the lack of interest of the hospital administration in analyzing the presented data in order to reduce and rationalize health care costs.

Primena RIA i IRMA tehnika u medicini

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Radioimunološke (RIA) i imunoradioimetrijske (IRMA) tehnike omogućavaju određivanje supstancija kliničkog i biološkog značaja. Ove tehnike imaju značajan uticaj na medicinsku dijagnostiku zbog lakoće kojom se mogu izvoditi, istovremeno obezbeđujući preciznost, specifičnost i osetljivost. Osetljivost se postiže primenom radionuklida a specifičnost je u vezi sa imunohemijskim reakcijama. Ove tehnike se uglavnom koriste za merenje biološki aktivnih jedinjenja prisutnih u niskim koncentracijama, kao što su hormoni, proteini, lekovi, mikroorganizmi itd.
Radioimunološka (RIA) tehnika se koristi za određivanje velikog broja hormona, enzima, antigena i lekova koji se nalaze u minimalnim količinama (10-9-10-12M) u ljudskoj plazmi, likvoru... Ova metoda ima visoku specifičnost jer je imunološka reakcija između antigena i antitela je visoko specifična. Tačnost metode zavisi od različitih eksperimentalnih faktora, kao i specifičnosti reakcije antigen-antitelo. Na preciznost RIA tehnika utiču greške u pipetiranju reagenasa, hemijskom razdvajanju kompleksa i merenju radioaktivnosti.
IRMA u odnosu na RIA ima mnogo veću osetljivost, tj, mogućnost tačnog određivanja veoma niskih koncentracija hormona, što je u nekim slučajevima (npr. u TSH) veoma značajno. Zbog upotrebe monoklonskih antitela i u prvoj fazi reakcije (inkubacije) ovaj sistem ima znatno bolju specifičnost, čime se znatno smanjuju greške zbog ukrštenih reakcija sa drugim hormonima.
Osnovni nedostatak ovih tehnika je upotreba radionuklida jer predstavljaju opasnost po zdravlje, zahtevaju posebnu pažnju tokom rukovanja, dobro obučeni kadar i dobro definisano skladištenje otpada. Zbog toga što primenjeni radionuklidi imaju kratko vreme poluraspada, kompleti imaju kratak rok trajanja. Merenje radioaktivnosti zahteva posebnu instrumentaciju i može trajati dugo vremena.

Application of RIA and IRMA techniques in medicine

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A radioimmunoassay (RIA) and an immunoradiometric assay (IRMA) are the most commonly used techniques which allow the measurement of a wide range of materials of clinical and biological importance. These techniques have a significant impact on medical diagnosis due to the ease with which the tests can be carried out, while assuring precision, specificity and sensitivity. These techniques achieve sensitivity through the use of radionuclides and specificity that is uniquely associated with immunochemical reactions. They are largely used for measuring biologically active compounds present in low concentrations, such as hormones, proteins, drugs, microorganisms, etc.
The radioimmunoassay (RIA) method is employed to determine numerous hormones, enzymes, antigens, and drugs in minute quantities (10-12–10-9 M) in human plasma in order to assess various disease conditions. In RIA, the immunologic reaction between the antigen and the antibody is highly specific, and hence the method has high specificity. The accuracy of the method depends on various experimental factors and the specificity of the antigen–antibody reaction. The precision of RIA is affected by experimental errors in pipetting of reagents, chemical separation of the complex, and counting.
IRMA is much more sensitive to RIA, which in some cases (e.g. in TSH) is very significant. Because of the use of monoclonal antibodies in the first phase of the reaction, this system has a much better specificity, which significantly reduces errors due to cross-reactions with other hormones.
Although they are highly sensitive and precise, they are also associated with several disadvantages. Among the drawbacks, the use of radioactive tracers is of most concern because they present a health hazard, require special attention for handling, well-trained staff and well-defined waste storage. Moreover, because radioisotopes have a limited half-life, the kits have limited shelf lives, and radioactive counting can be time-consuming and requires special instrumentation.

Specifičnosti transfuzije kod trudnica sa autoimunim bolestima

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Autoimune bolesti su 2 puta češće zastupljenije kod žena. Najćešće se javljaju u reproduktivnom period žene. Mogu biti izazvane infekcijom, štetnim uticajima sredine a pogoduje im ishrana bogata mastima i šećerima takozvana zapadnoevropska ishrana. Autoimune hronične inflamatorne bolesti su factor rizika za aloimunizaciju na eritrocitne antigene.
Istraživanja su pokazala da oko 16% pacijenata muškog pola sa autoimunim bolestima nakon transfuzije razvija antieritrocitna antitela. Transfundovani pacijenti muškog pola sa autoimunim bolestima 2 puta češće formiraju antieritrocitna antitela u odnosu na pacijente bez autoimmune bolesti. Kod žena je rizik dvostruko veći a kod trudnica je rizik za aloimunizaciju dodatno povećan zbog prisustva fetalnih antigena. Najčešća antitela koja se razvijaju kod transfundovanih pacijentat su na sledeće eritrocitne antigeme: D, K, E, C, Fya, Jka, M.
Poseban entitet predstavljaju trudnice sa hematološkim oboljenjima kao što su imunska trombocitopenijska purpura (ITP) i autoimuna hemolizna anemija (AIHA). Transfuzija koncentratima trombocita se, kod ITP zbog opasnosti od formiranja dodatnih HLA antitela, primenjuje samo u vitalnim indikacijama, dok je u AIHA transfuzija koncentratima eritrocita terapija izbora.
Autoimune bolesti kod trudnica mogu dovesti s jedne strane do krvarenja a s druge do tromboembolijskih komplikacija Tako da pacijenti sa trombocitopenijom i lupus antikoagulansom (LA) nakon transfuzije trombocitnim koncentratom razvijaju tromboembolijske komplikacije. Iz tog razloga pre primene transfuzije koncentrovanim trombocitima treba odrediti LA kako bi se prevenirala tromboembolijska komplikacija. S druge strane u nekim slučajevima je opisan antifosfolipini sindrom sa trombocitopenijom koji je doveo do krvarenja.
Za prevenciju krvarenja ili tromboembolijskih koplikacija kod trudnica koje zahtevaju transfuziju trombocita bitno je odrediti testove hemostaze i LA, a u cilju smanjenja rizika od aloimunizacije na najmanju moguću meru od neophodne važnosti je kod trudnica sa autoimunim oboljenjima uraditi proširenu fenotipizaciju eritrocita na antigene Rh sistema (C,c, E, e) i Kell (K,k) sistema i primenjivati deleukocitovane komponente krvi.

Specific features of transfusion in pregnant women with autoimmune diseases

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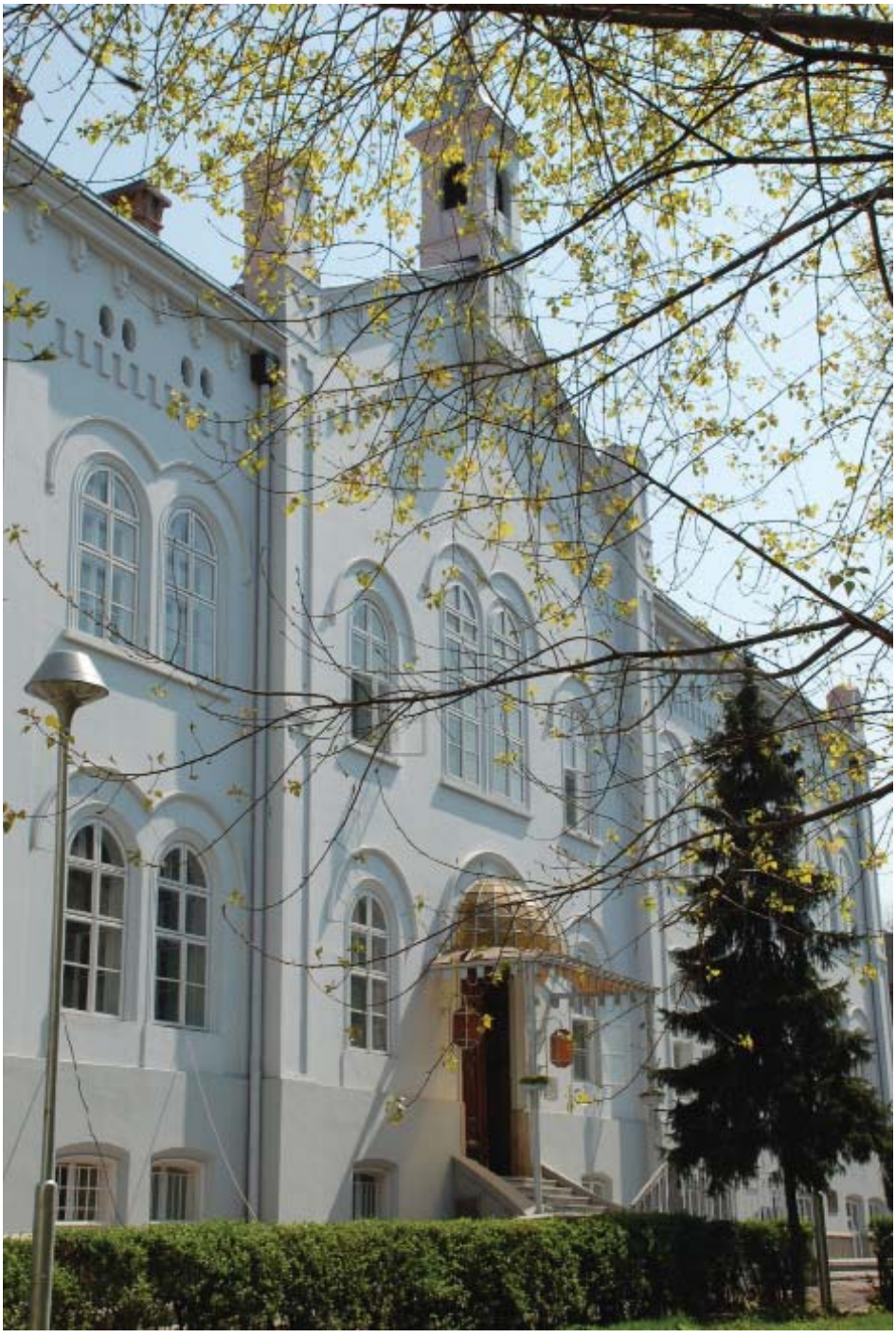

Neadherencija kod vanbolničkih pacijenata sa dijabetes melitusom tip 2

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Cilj ove studije bio je da se proceni neadherencija pacijenta prema antidijabetičnoj terapiji na nivou primarne zdravstvene zaštite u istočnom delu Bosne i Hercegovine (BiH).
Metode: Ispitivanje je obuhvatilo retrospektivni pregled zdravstvenih kartona 323 pacijenata sa dijabetes melitusom tipa 2 (T2DM) u primarnom zdravstvenom centru opštine Foča u istočnom delu BiH i praćena je adherencija prema antidijabetičnoj terapiji metodom brojanja tableta.
Rezultati: Većina pacijenata je lečeno oralnim antidijabeticima (84,21%). Polovina pacijenata (48%) nisu bili adherentni prema svojoj antidijabetičnoj terapiji, a pacijenti lečeni kombinacijom oralnim antidijabeticima i insulinom pokazali su bolju adherenciju od pacijenata na samo oralnoj terapiji antidijabeticima. Starost (B = -0,749; p = 0,004), doplata cene leka (B = 0.549; p = 0.028) i oralna terapija (B = 0.827; p = 0.045) bili su značajni prediktori neadherencije.
Zaključak: Oko polovine bolesnika nije bilo adheretno prema svojoj antidijabetičnoj terapiji. Intervencije koje su orijentisane na promene zdravtsvene politike u pogledu dostupnosti antidijabetičkih lekova putem smanjenja doplate na cenu leka i obezbeđivanja edukativnih intervencija mlađim pacijentima kao i onima na oralnoj terapiji antidijabeticima može doprineti do bolje adherencije pacijenata sa T2DM-a prema njihovoj antidijabetičnoj terapiji u istočnom delu BiH.

Ovaj rad je podržan od strane Ministarstva prosvete i nauke Republike Srbije, projekat broj 42012.

Non-adherence among type 2 diabetic patients in primary care setting in eastern Bosnia and Herzegovina

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The aims of this study were to assess patients' non-adherence and associated factors to antidiabetic medication in the primary care setting in the eastern part of Bosnia and Herzegovina (BiH).
Methods: We conducted a retrospective chart review of 323 patients with type 2 diabetesmellitus (T2DM) attending the primary health care center of the Foča municipality in eastern part of BiH and measured adherence to antidiabetic medication. Adherence was measured using a pill count method.
Results: The majority of patients were treated with oral therapy (84.21%). Half of the patients (48%) treated pharmacologically were non-adherent and patients on oral and insulin combination therapy showed better adherence than those on oral therapy. Age (B = −0.749;p = 0.004), copayment (B = 0.549; p = 0.028) and oral therapy (B = 0.827; p = 0.045) were the strongest predictors of poor adherence.
Conclusion: About half of the patients were non-adherent to antidiabetic medication. Interventions oriented towards policy changes regarding availability of antidiabetic medication through copayment reductions, and providing healt education to younger population and patients on oral therapy could lead to better adherence among T2DM patients in eastern part of BiH.

This work was supported by the Ministry of Science and Technological Development, Serbia (project No. 41012).

Analiza upotrebe lekova u terapiji respiratornih oboljenja u republici Srbiji u periodu 2011-2016.

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Uvod: Hronične nezarazne bolesti postale su jedan od najvažnijih uzroka umiranja širom sveta,a nastaju kao rezultat interakcije između pojedinca i njegove okoline. U ovu grupu spada i hronična opstruktivna bolest pluća. Stoga je razumljivo da lekovi u terapiji ove bolesti zauzimaju značajan udeo potrošnje.
Cilj rada: Cilj rada je bio da se analiziraju podaci o potrošnji lekova u terapiji opstruktivne bolesti pluća u Srbiji u periodu od 2011 do 2016. godine kao i da se potrošnja ovih lekova uporedi sa Norveškom i Finskom zemljama koja ima razvijenu farmakoterapijsku praksu.
Materijal i metode: Podaci o potrošnji lekova u Srbiji za period od 2011. do 2016. godine preuzeti su od Agencije za lekove i medicinska sredstva Srbije. Podaci o potrošnji lekova u Norveškoj preuzeti su sa zvanične internet stranice Norveškog instituta za javno zdravlje i podaci o potrošnji lekova u Finskoj preuzeti su sa zvanične internet stranice Finske agencije za lekove – Fimea.
Rezultati: Ukupna potrošnja lekova u Srbiji u terapiji respiratornih oboljenja za period od 2011. do 2016. godine bila je manja nego potrošnja iste grupe lekova u Norveškoj i Finskoj u istom periodu. U sve tri zemlje, potrošnja lekova R grupe beleži rast. U odnosu na podgrupe, na prvom mestu se nalaze lekovi u terapiji hronične opstruktivne bolesti pluća (R03).
Zaključak: Ukupna potrošnja lekova u periodu od 2011. do 2016. godine bila je veća u Norveškoj i Finskoj nego u Srbiji. Na osnovu dobijenih podataka može se zaključiti da u Srbiji ne postoji adekvatna upotreba lekova i da ona nije u skladu sa farmakoterapijskom praksom koja postoji u zemljama sa dobro razvijenom farmakoterapijskom praksom.

Ključne reči: farmakoepidemiologija, hronična opstruktivna bolest pluća, respiratorni sistem

Zahvalnica: Ovaj rad je podržan od strane projekata Pokrajinskog sekretarijata za visokoobrazovanje i naučno-istraživačku delatnost AP Vojvodina br. 142-451-3630/2017-01 i 142-451-2459/2018-03.

Analysis of the use of drugs in therapy of respiratory diseases in the republic of serbia in the period 2011-2016

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Introduction: Non infectious chronic diseases become one of the most frequent cause of morbidity all around the world and they are results of interactions between man and his environment. This group of diseases includes also chronic obstructive pulmonary disease, which explains why medications for the treatment of this disease take a large part in the consumption.
Objective: The aim of this study was to analyze the consumption of medications in chronic obstructive pulmonary disease in Serbia in period from 2011 to 2016, as well as comparing the consumption in our country with the consumption in Norway and Finland that has developed farmacoterapeutic practice.
Material and methods: The data about the use of medications in Serbia from 2011 to 2016 were taken from the Agency for Drugs and Medical Devices of the Republic of Serbia. The data about the use of medications in Norway were taken from official website of the Norwegian healthcare system and the data about the use of medications in Finland were taken from official website Finnish Medicines Agency - Fimea.
Results: Total consumption of medications for the treatment of respiratory diseases in Serbia from 2011 to 2016 was lower than the comnsumption of the same medications in Norway and Finland in the same period. In all three countries, the consumption of drugs in the R group is growing. In relation to subgroups, in the first place are drugs in the treatment of chronic obstructive pulmonary disease (R03).
Conclusion: Total drug consumption in the period from 2011 to 2016 was higher in Norway and Finland than in Serbia. Based on the obtained data, it can be concluded that there is no adequate use of medicines in Serbia and that it is not in line with the pharmacotherapeutic practice that exists in countries with well-developed pharmacotherapeutic practices.

Keywords: pharmacoepidemiology, chronic obstructive pulmonary disease, the respiratory system

Acknowledgements: This research was supported by projects for Scientific and Technological Development of Vojvodina No. 142-451-3630/2017-01 and 142-451- 2459/2018-03.

Znanje, stavovi i odnos pacijenata prema analgeticima u Srbiji

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Pacijenti širom sveta sve češće koriste lekove za smanjenje bolova, bez prethodne konsultacije lekara. Stoga cilj ove studije je da se utvrdi znanje, stavovi i ponašanje pacijenata u vezi sa upotrebom analgetika u Srbiji.
Materijal i metode: Anketa je sprovedena na slučajnom uzorku od 160 odraslih ispitanika koji su posetili lekare opšte prakse u domovima zdravlja opštine Bačka Topola. Upitnik je obuhvatao pitanja o demografskim karakteristikama, znanju, stavovima i ponašanju prema upotrebi analgeticima. Ispitivanje je odobreno od Etičkog komiteta Medicinskog fakulteta u Novom Sadu kao i Doma zdravlja Bačka Topola.
Rezultati: Prosečna starost ispitanika je bila 50,06 godina, a 65% ispitanika bile su žene. Čak 75% ispitanika je koristilo analgetike tokom prethodne godine, a 34% njih jednom mesečno. Najčešće indikacije bile su: glavobolja 52%, bolovi u zglobovima 33% i bolovi u krstima 41%. Najčešće su koristili ibuprofen 47%, diklofen 28% i acetilsalicilnu kiselinu 21%. 48% ispitanika je izjavilo da su koristile analgetike bez prethodne konsultacije lekara (samomedikacija), jer bol nije bio dovoljno jak, a 32% ispitanika je koristilo analgetike na osnovu prethodnog iskustva. 77% ispitanika je tvrdilo da su upoznati sa nuspojavama analgetika, ali samo 40% ispitanika je nabrojalo neželjena dejstva.
Zaključak: U daljoj racionalizaciji upotrebe analgetika, neophodna je efikasna edukacija opšte populacije u cilju menjanja njihovih stavova i ponašanja prema analgeticima.

Ovaj rad je podržan od strane Ministarstva prosvete i nauke Republike Srbije, projekat broj 42012.

Public knowledge, beliefs and behavior regarding the use of antibiotics in Serbia

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Introduction: Using painkillers without previous consultation with family physician has been ever more common among patients in many countries. The objective of this study was to investigate the patients' knowledge about painkillers, their attitude and behaviour regarding the use of painkillers in Serbia.
Material and methods: The survey was conducted on a random sample of 160 adult subjects who consulted general practitioners (GP) at health centers. A self-administered questionnaire included questions on demographic characteristics, knowledge about painkillers, beliefs and behaviours toward painkillers use. The study was approved by the Ethical Committees of the Medical Faculty in Novi Sad and the Health Center Bačka Topola.
Results: The mean age of patients was 50.06 years, of which 65% were women. 75% of the study subjects used painkillers last year, 34% used painkillers once a month. Most common indications were headache 52%, joint pain 33% and back pain 41%. The most commonly used pain reliever is ibuprofen 47% followed by diclofen 28% and aspirin 21%. While 65% subjects of study have asked to seek advice from a family physician, 48% of our subjects do not seek advice from their family physician (self-medication) because the pain is not too strong, 32% of the subjects referred to earlier experience. 77% of subjects said they know side effects of analgesics, but only 40% of them wroted it.
Conclusion: The educational campaigns about the behaviour of patients towards painkillers are the key elements to ensure judicious, quality and knowledge based use of drugs.

This work was supported by the Ministry of Science and Technological Development, Serbia (project No. 41012).

Stavovi i ponašanja studenata medicine i farmacije o samomedikaciji

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Uvod: Samomedikacija je uobičajena pojava među budućim zdravstvenim radnicima, a njihovi stavovi prema konvencionalnoj i komplementarnoj medicini mogu bi uticati na njihovu buduću farmakoterapijsku praksu. Cilj ovog istraživanja bio je da se istraže stavovi i učestalost samomedikacije među populacijom studenata prvih i završnih godina studija medicine i farmacije.
Materijal i metode: Ova studija preseka sprovedena je na Medicinskom fakultetu Univerziteta u Novom Sadu i obuhvatila je uzorak od 192 studenta medicine i farmacije prve i završne godine studija. Studenti su popunili upitnik o demografskim podacima i samomedikaciji koji je razvijen u svrhu ovog istraživanja.
Rezultati: Samomedikacija je zabeležena kod 81.3% studenata. Lekovi koji su se najčešće uzimali samoinicijativno bili su konvencionalni lekovi. Faktori rizika za samomedikaciju identifikovani u logističkoj regresionoj analizi su szavršna godina studija (OR 7.29, CI 95% 2.282-22.899), samostalno stanovanje (OR3.463, CI 95% 1.437-8.343) i konzumiranje cigareta (OR 8.55, CI 95% 1.053-69.384). Studenti završne godine imali su više poverenja u konvencionalnu medicinu u poređenju sa biljnim lekovima i bolje znanje o sigurnosti i riziku zajedničke primene biljnih i konvencionalnih lekova.
Zaključak: Samomedikacija je veoma zastupljena među studenatima medicine i farmacije, naročito među studentima završne godine. Nije utvrđena razlika u stavovima i ponašanju u odnosu na studijski program.

Ovaj rad je podržan od strane Pokrajinskog sekretarijata za visokoobrazovanje i naučno-istraživačku delatnost Autonomne pokrajine Vojvodine projekat broj 114-451-2178/2016-03.

Self-medication attitudes and behaviour among medicine and pharmacy students

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Introduction: Self-medication was reported to be common among future health care professionals and attitudes towards conventional and complementary medicine could have effect on their future pharmacotherapy practice. The aim of this research was to determine attitudes and prevalence of self-medication among population of first and finishing year medicine and pharmacy students.
Material and Methods: Research was performed as a cross-sectional study at the faculty of Medicine, University of Novi Sad and it included 192 first and last year students of medicine and pharmacy. Students filled out a demographic and self-medication questionnaire created for the purpose of this research.
Results: Self-medication was reported by 81.3% students. The most frequently self-prescribed medications were conventional drugs. Independent risk factors for self-medication identified in the logistic regression analysis were last year of studies (OR 7.29, CI 95% 2.282-22.899), living alone (OR3.463, CI 95% 1.437–8.343) and consumption of cigarettes (OR 8.55, CI 95% 1.053-69.384). Last year students had more confidence in conventional medicine compared to herbal drugs, and had better knowledge about safety and risks of co-administration of herbal and conventional drugs.
Conclusions: Self-medication is an important issue among population of medical students, especially among final year students. No difference in attitudes and behavior was found in relation to study program.

This work was supported by the Provincial Secretariat for Higher Education and Scientific Research, Autonomous Province of Vojvodina project No. 114-451-2178/2016-03

Timski rad - osnova uspeha bolničke farmakologije

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Klinička farmakologija je medicinka disciplina nastala sredinom XX veka, podrazumeva najefikasniju primenu leka, te bi se slobodno moglo reći da predstavlja završnicu svih terapijskih pristupa u medicini. Reč je o oblasti koja se spontano pojavila na medicinskom terenu i od prvog momenta ima jedinu perspektivu u jedinstvu prakse i nauke. Specijalisti i subspecijalisti klinicke farmakologije rade se lekarima specijalistima svih oblasti, farmaceutima, farmaceutskim magnatima, ljudima iz regulative, proizvodnje.
U multidisciplinarnim timovima postižu rezultate u oblasti drug discovery, pretkliničkim, kliničkim ispitivanjia, kliničkoj farmakoterapiji, farmakoekonomiji, razvoju medicinskih sredstava. Spontano, poslednju deceniju razvija se multidisciplinarna bolnička farmakologija.
Sabrani rezultati i iskustva nakon decenija primene leka su veliki doprinos znanju koje pomaže da se zdravije i kvalitetnije živi.

Team work - the base of the success of Hospital Pharmacology

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Clinical pharmacology is a medical discipline that arrised in the mid-20th century, it means the most effective use of the drugs, and it could be freely said to represent the completion of all therapeutic approaches in medicine. It is a matter that spontaneously emerged on the medical field and from the first moment has the only perspective in the unity of practice and science. Specialists and subspecialists of clinical pharmacology work with doctors specialized in all areas, pharmaceuticals, pharmaceutical magnates, people from regulation, production.
In multidisciplinary teams, results are achieved in the field of drug discovery, preclinical, clinical trials, clinical pharmacotherapy, pharmacoeconomics, development of medical devices. Spontaneously, the last decade has developed a multidisciplinary hospital pharmacology.
Collecting results and experiences after decades of drug application are a great contribution to knowledge that helps to live healthier and better lives.

Bezbedna primena metamizola: aktuelno stanje

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Metamizol je neopioidni analgetik koji ima analgetsko, antipiretsko, spazmolitičko i antiinflamatorno dejstvo, pa je mesto primene našao u terapiji postoperativnog i kancerskog bola, lečenju kolika i kod migrene. Smatra se da je za analgetski efekat odgovorna inhibicija enzima ciklooksigenaze (COX) i stimulacija kanabinoidnih receptora. Ima sličnu analgetsku efikasnost kao i ostali analgetici koji se najčešće koriste za lečenje umerenog i jakog postoperativnog bola.
Njegova primena je kontroverzna zbog rizika od nastanka agranulocitoze. U nekim zemljama je strogo zabranjen njegov promet (SAD, Velika Britanija, Švedska, Japan). Internacionalna epidemiološka studija o agranulocitozi i aplastičnoj anemiji je pokazala da je ukupna godišnja incidenca agranulocitoze procenjena na 4,4 slučaja na million korisnika, sa prosečnim mortalitetom od 0,4 na million korisnika. Na osnovu podataka SZO, najčešće prijavljivani neželjeni efekti na metamizol su oni vezani za kožu i potkožno tkivo (raš, urtikarija, pemfigus vulgaris, toksična epidermalna nekroliza). Na osnovu podataka ALIMS-a koji se odnose na prethodni petogodišnji period, od 50 prijavljenih neželjenih reakcija na metamizol 30% su bile one koje su se odnosile na kožu i potkožno tkivo. Analiza potrošnje metamizola u periodu od 2010 - 2015. godine, izražena kao broj definisanih dnevnih doza na 1000 stanovnika na dan (DDD/1000 stanovnika na dan), ukazuje na postepen, ali konstantan pad u posmatranom periodu u našoj zemlji.

Safety of metamizole utilization: current views

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Metamizole is a nonsteroidal anti-inflammatory drug, with analgesic, antipyretic, spasmolytic, and weak anti-inflammatory properties and it can be used to treat postoperative pain, cancer and colic pain, and migraine. The analgesic effect of metamizole seems to be based on the inhibition of cyclooxygenase (COX) enzyme activity and stimulation of cannabinoid receptors. Metamizole appears to be of similar efficacy to analgesics which are frequently used in the treatment of moderate to severe postoperative pain.
The use of metamizole is controversial, mainly due to the appearance of metamizole-induced agranulocytosis. Metamizole is withdrawn from the market in some countries (United States of America, United Kingdom, Sweden, Japan). The international epidemiological study of agranulocytosis and aplastic anemia showed that the overall annual incidence of agranulocytosis was 4.4 cases per million users, with an annual mortality rate of 0.4 per million users. The most common adverse events of metamizole, reported by the WHO, were the skin and subcutaneous tissue disorders (rash, urticaria, pemphigus vulgaris, toxic epidermal necrolysis). Based on the data obtained from ALIMS in the last five years, 30% of 50 cases of metamizole adverse reactions was reported as skin and subcutaneous tissue disorders. Analysis of total consumption of metamizole in Serbia in the period from 2010 – 2015, expressed as the number of defined daily doses per 1000 inhabitants per day (DDD / 1000 inhabitants per day), indicated a gradual, but constant decline in metamizole consumption in the observed period in our country.

Faktori koji doprinose pojavi i održanju narkomanije

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Definicija ilegalnih droga u ovom radu podrazumeva: marihuanu (kanabis), hašiš, amfetamine, LSD ili druga halucinogena sredstva, krek, kokain, ekstazi, heroin, magične pečurke, trodon i ostale analgetike, GHB, inhalanse, alkohol u kombinaciji sa lekovima i sedative.
Čak 15,1% učenika prvih razreda srednjih škola navodi da su tokom života bar jednom upotrebljavali neku od prethodno navedenih ilegalnih droga. Učenici iz Beograda u najvećem procentu navode da su upotrebljavali bilo koju ilegalnu drogu tokom života (17,1%). Takođe, upotreba ilegalnih droga tokom života je češća među mladima iz velikih i malih gradova (15,9% i 14,2%, redom), u odnosu na omladinu iz ruralnih naselja (13,3%). Ne uočavaju se značajne razlike u upotrebi ilegalnih droga među mladićima i devojkama, s tim što nešto veći procenat devojaka (15,3%), nego mladića (14,8%) prijavljuje upotrebu neke ilegalne droge tokom života.
Koliko će mladi eksperimentisati sa drogama zavisi između ostalog od dostupnosti droga, zakonske regulative, roditelja, školskih vlasti, mogućnosti koje pruža lokalna zajednica za kreativno provođenje slobodnog vremena, veština kojima raspolažu mladi za izlaženje na kraj sa stresom, sposobnost rešavanja problema, informisanost mladih o posledicama upotrebe droga, i sl. Ovo su ujedno zaštitni faktori od posrtanja mladih ljudi. Zbog nespremnosti roditelja i socijalne sredine da pravilno reaguju, vaspitavaju i učestvuju u životu mladih jesu i faktori održavanja droge.
Prevencija: promocija zdravih stilova života, kvalitetan odnos u porodici i rešavanje konfliktnih situacija unutar porodice, edukacija o efektima droge dece i roditelja. U prevenciji treba da učestvuju ministarstava zdravlja, unutrašnjih poslova, prosvete, i škole. Potrebno je pojačati bolnička odeljenja za bolesti zavisnosti i učiniti ih dostupnijim mladim ljudima.

Contributing factors of substance abuse

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The definition of illegal drugs in this paper includes: marihuana (cannabis), hashish, amphetamine, LSD or other hallucinogenic agents, crack, cocaine, ecstasy, heroin, magic mushrooms, trodone and other analgetics, GHB, inhalants, alcohol in combination with medications and sedatives.
Even 15.1% of primary school pupils say that at least once they used one of the previously mentioned illegal drugs. The pupils in Belgrade say that they used no matter what illegal drugs during their lifetime (17.1%). Also, the use of illegal drugs throughout life is more common among young people from large and small towns (15.9% and 14.2%, respectively), compared to youth from rural settlements (13.3%). There are no significant differences in the use of illegal drugs among boys and girls, with a slightly higher percentage of girls (15.3%) than boys (14.8%) reporting the use of an illegal drug during their lifetime
How young people will experiment with illegal drugs depends on the availability of drugs, legislation, parents, school authorities, opportunities provided by the local community for the creative spending free time, the skills that young people have in dealing with stress, ability to solve problems, informing young people about the consequences of illegal drug use, ect. At the same time these are protective factors of the demolition of young people. Due to the unwillingness of the parents and the social environment to properly react, educate and participate in the lives of young people these are also the factors of illegal drugs abuse.
Prevention: promotion of healthy lifestyles, quality family relationships and the resolution of conflict situations within the family, education about effects of drugs for children and parents. The ministries of health, police, education, and schools should also take part in prevention. It is necessary to strengthen hospital departments for addictions and make them more accessible to young people.

Antimikrobna svojstva industrijske konoplje: pretkliničkа ispitivanja

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Konoplja je jedna od prvih biljaka koje su korišćene kao lekovi, prve primene se spominju u izvorima starim preko 5000 godina. Veliki broj potencijalnih proizvoda može se izolovati iz ovog višenamenskog useva, povećavajući mu konkurentnost u odnosu na pamuk i sintetička vlakna. Ovaj pregledni rad će se fokusirati na pretkliničke studije koje su istraživale antimikrobna svojstva industrijske konoplje kako bi se postavile osnove za buduća istraživanja i ponudili dokaze koji podržavaju razvoj antibakterijskih proizvoda zasnovanih na industrijskoj konoplji.
Pretraga je uključivala pregled baza Medline i Google scholar sa ključnim rečima: konoplja; *Cannabis sativa*; antimikrobno; antibiotik; bakterija. Dokazi pokazuju da je pre-kanabidol moćan fitoantibiotik, kao i da drugi nepsihotropni kanabinoidi kanabikromen, kanabirol i kanabidiol, kao i psihotropni agens D9-tetrahidrokanabinol u različitim stepenima, pokazuju antibakterijsku aktivnost (MIC vrednosti u 0,5-2 mg / mL). Antibakterijska aktivnost je posebno izražena prema MDR sojevima, uključujući MRSA. Rezultati ukazuju da kanabinoidi verovatno nisu supstrati za najčešće mehanizme rezistencije na trenutno dostupne antibiotike. Ispitivanja 5 različitih eteričnih ulja konpolje pokazala su skromnu antimikrobnu aktivnost. Nasuprot tome, ekstrakt cele biljke Cannabis sativa, inhibirao je rast i Gram pozitivnih i Gram negativnih mikroroganizama. Pojedini autori su ipak pronašli samo efekte na *S. Aureus*. Može se zaključiti da različiti preparati konolje ispoljavaju animikrobno dejstvo, a kanabinoidi i njihovi prekursori su najverovatnije najpotentniji antibakterijski agensi prisutni u industrijskoj konoplji.

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Antimicrobial properties of industrial hemp: preclinical evidence

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Cannabis is one of the first plants to have been used as a medicine, with the first reported use dating back 5000 years. A large number of potential complementary products can be derived from this multi-use crop which can significantly enhance its competitiveness to cotton and synthetic fibers. This review will focus on preclinical studies investigating antimicrobial properties of industrial hemp in order to lay ground for future research and offer up to date evidence to support the development of antibacterial products based on industrial hemp. Search was performed in the Medline and Google scholar bases using keywords: hemp; Cannabis sativa; antimicrobial; antibiotic; bacteria. Evidence shows that pre-cannabidiol is a powerful plant antibiotic and that other nonpsychotropic cannabinoids cannabichromene, cannabigerol and cannabidiol, as well as the psychotropic agent Δ9-tetrahydrocannabinol to various degrees, exhibit antibacterial activity (MIC values in the 0.5-2 μg/mL range). Antibacterial activity was especially pronounced in MDR strains, including MRSA. Cannabinoids are probably not substrates for the most common resistance mechanisms to current antibacterial agent. Experiments with 5 different essential oils showed modest antimicrobial activity. The extract of the whole plant of Cannabis sativa inhibited growth of both Gram negative and positive organisms, in contrast some authors who found only effects on S. Aureus. To conclude, different preparations of Cannabis sativa exhibit antimicrobial properties, and cannabinoids and their precursors are the most likely antibacterial agents present in hemp.

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12-MKH: novi pristup u terapiji metaboličkog sindroma

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Studije su pokazale da žučne kiseline nisu samo modifikatori apsorpcije nutritivnih lipida već i važni signalni molekuli koji ispoljavaju brojne fiziološke funkcije. 12 - monoketoholat (12-MKH) je stabilna polusintetska so žučne kiseline niske toksičnosti. Pokazala je značajan hipoglikemijski efekat i potencijal da pospeši apsorpciju različitih agenasa koji se koriste u tretmanu metaboličkih poremećaja. Ovaj rad daje pregled aktuelnih istraživanja o 12-MKH i potencijalnoj primeni u metaboličkom sindromu (MS).
Pretraga je uključivala pregled baza Medline i Google scholar sa ključnim rečima: žučne kiseline, 12-MKH, dijabetes, gojaznost, metabolizam. Na modelu dijabetesa tipa 1 (T1DM) kod pacova, pokazano je da primena samog 12-MKH dovodi do značajnog hipoglikemijskog efekta. Pregledom brojnih studija o 12-MKH kao potencijalnom adjuvansu primećeno je da nakon oralne primene kod T1DM pacova 12-MKH potencira efekat steviozida, u kombinaciji sa gliklazidom ispoljava jači efekat od samog 12-MKH i da pojačava nazalnu permeaciju insulina. Skorašnja studija je pokazala da kombinacija 12-MKH i gliklazida obezbeđuje čak i bolju kontrolu glikemije kod pacova prethodno tretiranih probioticima nego kod onih koji nisu bili podvrgnuti pretretmanu. Uprkos nerazjašnjenom mehanizmu interakcije, očigledan je značajan sinergistički efekat između 12-MKH, gliklazida i probiotika. 12-MKH može da ponudi novi terapijski pristup u lečenju dijabetesa, gojaznosti i drugih komponenata MS.

Ovaj rad je podržan od strane Ministarstva prosvete, nauke i tehnološkog razvoja Republike Srbije, projekat broj III 41012.

12-MKC: a novel approach for metabolic syndrome treatment

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Recent studies have revealed that bile acids are not only modificators of dietary lipid absorption but also important signaling molecules exerting multiple physiological functions. 12-monoketocholate (12-MKC) is a stable semisynthetic bile acid salt with low toxicity. It has shown significant hypoglycemic activity and the potential to enhance absorption of various agents using in treatment of metabolic disorders. This review summarizes recent analyses of 12-MKC and its potential therapeutic application in metabolic syndrome (MS).
The research was performed in the Medline and Google scholar bases using the following key words: bile acids, 12-MKC, diabetes, obesity, metabolism. It has been demonstrated that administration of 12-MKC alone to a rat model of type 1 diabetes (T1DM) resulted in a significant hypoglycemic effect. Overviewing numerous studies about 12-MKC as a potential adjuvant it has been derived that after oral administration in T1DM rats, 12-MKC has a promotory effect on the action of stevioside, in combination with gliclizide exerts a better effect than 12-MKC alone and that it enhances nasal permeation of insulin. A recent study has shown that the combination of 12-MKC and gliclazide exhibits even a better glycemic control in probiotic pretreated T1DM rats compared to those without pretreatment. Despite the unclear mechanism of interaction, a meaningful synergistic effect between 12-MKC, gliclazide and probiotics in T1DM is obvious. 12-MKC may serve as a potent therapeutic approach for the treatment of diabetes, obesity, and other MS components.

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Interakcije između gliklazida i probiotskih bakterija u *in vitro* uslovima

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Uvod: Veliki broj dokaza ukazuje na ulogu crevne mikroflore u interindividualnim razlikama u metabolizmu lekova. Gliklazid pripada derivatima sulfoniluree i karakterišu ga velike interindividualne razlike u terapijskom odgovoru. Stoga, cilj rada je da se postave preliminarne pretpostavke o uticaju mikroflore na terapijski odgovor gliklazida na osnovu *in vitro* procene transporta i biotransformacije gliklazida u probiotskim bakterijama.
Metode: Uzorci gliklazida sa probiotskim bakterijama inkubirani su 24h na 37°C. Nakon odgovarajuće pripreme uzorka, određen je HPLC metodom intracelularni i ekstracelularni sadržaj gliklazida u sedam vremenskih tačaka. Biotrasnformacija i potencijalni produkti gliklazida ispitani su odgovarajućim softverskim paketima.
Rezultati: Tokom 24h-inkubacije sa probiotskim bakterijama, u svim vremenskim tačkama primećena je statistički značajno niža koncentracija gliklazida u ekstracelularnom sadržaju u poređenju sa kontrolnom grupom. U skladu sa tim, koncentracija gliklazida u ćelijama se povećavala tokom vremena. Nakon 24h, ukupna koncentracija gliklazida dostigla je 70% vrednosti početne koncentracije. Reakcije hidrolize i hidroksilacije su predloženi putevi biotransformacije gliklazida u probiotskim bakterijama
Zaključak: Može se zaključiti da postoje interakcije između gliklazida i probiotskih bakterija, kako na nivou aktivnog i pasivnog transporta, tako i na nivou biotransformacije enzimskom aktivnošću probiotskih bakterija. Efekat ovih interakcija na konačan terapijski odgovor gliklazida trebalo bi dalje ispitati i potvrditi u *in vivo* uslovima

Zahvalnica: Ovaj rad je podržan od strane HORIZON 2020 MEDLEM projekta br.690876 i od strane Pokrajinskog sekretarijata za visokoobrazovanje i naučno-istraživačku delatnost APV-a br. 114-451-2072-/2016-02.

In vitro study of gliclazide-probiotic bacteria interactions

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Background: The growing body of evidence pointed to the role of gut microflora in interindividual differences in drug metabolism. Gliclazide belongs to sulfonylurea family and is characterized by large interindividual differences in therapeutic response. Therefore, the aim of this study was to make assumptions of gut microflora influence on interindividual differences in gliclazide response based on *in vitro* assessment of gliclazide transport and biotransformation in probiotic bacteria.
Methods: Samples of gliclazide with probiotic bacteria were incubated for 24 hours at 37°C. After adequate sample preparation, intracellular and extracellular concentrations of gliclazide were determined in seven time points by HPLC. Gliclazide biotransformation and potential metabolic products were examined by appropriate software packages.
Results: During the twenty-four-hour incubation with probiotic bacteria, in all time points, statistically significantly lower concentrations of gliclazide in extracellular content were observed compared to controls. Accordingly, concentration of gliclazide increased in probiotic cells over time. After 24 hours, total concentration of gliclazide, as a sum of intracellular and extracellular content, reached about 70% of concentration from the beginning of the experiment. Potential metabolic pathways of gliclazide biotransformation by enzymatic activity of probiotic bacteria involve reactions of hydrolysis and hydroxylations.
Conclusion: It can be concluded that there are important interactions between gliclazide-probiotic bacteria, both at the level of active and passive transport into the cells, and at the level of drug biotransformation by enzymatic activity of probiotic bacteria. The effect of these interactions on the final therapeutic response of gliclazide should be further studied and confirmed in *in vivo* conditions.

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Znanje studenata medicine o upotrebi kanabisa u terapijske svrhe

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Uvod: Legalizacija upotrebe kanabisa u terapijske svrhe je sve aktuelnija kako širom sveta, tako i u Srbiji.
Cilj: Steći uvid u znanje i stavove studenata medicine o upotrebi kanabisa u terapijske svrhe.
Metode: Anketa je sprovedena na uzorku od 316 studenata treće, pete i šeste godine medicine Medicinskog fakulteta, Univerziteta u Novom Sadu.
Rezultati: Kanabis su znatno više koristile osobe muškog pola (p=0,007), dok razlika u upotrebi nije postojala između studenata različitih godina studija (p=0,830). Studenti koji su nekada koristili kanabis su upoznatiji sa terapijskim i neželjenim delovanjima (p=<0,001). Studenti koji nikada nisu koristili koristili smatraju da upotreba kanabisa u terapijske svrhe može izazvati zavisnost (p=<0,001), da može otvoriti prostor zloupotrebi (0,031) kao i da može biti put ka upotrebi težih droga (p=0,001). Studenti koji su koristili kanabis su upoznatiji sa aktuelnošću legalizacije kanabisa u Srbiji (p=0,006) i značajno veći broj njih u odnosu na one koji nikad nisu koristili kanabis smatra da upotrebu kanabisa u terapijske svrhe treba legalizovati u Srbiji (p=0,006). Najčešće terapijske indikacije koje su navodili su: hronična bol (194, 75,2%) i karcinom (190, 73,6%), a najčešća neželjena dejstva: slabljenje memorije (117, 57,1%), tahikardija (109, 53,2%) i mučnina (102, 49,8%). 302 studenta, odnosno 96% smatra da ukoliko bi se legalizovala upotreba u terapijske svrhe, izdavanje bi trebalo da bude samo na recept.
Zaključak: Znanje studenata je bilo u korelaciji sa prethodnom konzumacijom kanabisa, dok godina studija nije imala nikakav značaj. Studenti koji su probali kanabis su imali znatno veće znanje o terapijskim i neželjenim efektima, kao i o legalizaciji kanabisa u terapijske svrhe. Studenti koji nisu probali kanabis su bili više upoznati sa mogućim zloupotrebama..

Ovaj rad je podržan od strane Pokrajinskog sekretarijata za visokoobrazovanje i naučno-istraživačku delatnost Autonomne pokrajine Vojvodine projekat broj 114-451-2178/2016-03.

Medical school students' knowledge about the use of cannabis in medical purposes

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Introduction: The legalization of cannabis for medical use is gaining momentum all around the globe and such is the case for Serbia.
Aim: To determine the knowledge and attitudes of medical students' regarding medical cannabis.
Methods: An anonymous questionnaire was conducted among a sample of 316 students of the third, fifth and sixth year at the Faculty of Medicine, University of Novi Sad.
Results: Cannabis was significantly more used by the male students (p=0.007), whereas no apparent difference was found based on which year of studies they were enrolled into (p=0.830). The students who had used cannabis before were more familiar with the medical and adverse effects (p=<0.001). The students who had never used cannabis thought that the medical use of cannabis can cause addiction (p=<0.001); that it may lead to substance misuse (0.031) and to the use of hard drugs (p=0.001). The students who had used cannabis before were more informed about the process of legalization of cannabis in Serbia (p=0.006), and a significantly higher number of students who had used cannabis before consider that the medical use of cannabis should be legalized in Serbia (p=0.006). The most frequent medical indications stated were: chronic pain (194, 75.2%), and cancer (190, 53.2%); the most frequent adverse effects were: memory loss (117, 57.1%), tachycardia (109, 53.2%), and nausea (102, 49.8%). 302 students, i.e. 96% of them think that if the medical use of cannabis was legalized, a medical prescription should be dispensed.
Conclusion: There was significant correlation between the students' knowledge and their previous use of cannabis, whereas the year of study had no significant effect. The students who had tried cannabis before were more informed about the medical and adverse effects, as well as the legalization of cannabis for medical use. The students who had not tried cannabis before were more familiar with potential misuse.

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Povećanje potrošnje biljnih lekova u Srbiju u periodu od 2006. do 2016.

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Uvod: Postoje istraživanja koja pokazuju da biljni lekovi mogu biti dobar izbor za lečenje nekih bolesti. U svetu postoji trend rasta potrošnje ove grupe lekova, a cilj ove studije bio je da se pronađe trend potrošnje u Srbiji.
Metoda: Podaci o potrošnji biljnih lekova tokom posmatranog perioda u Srbiji, uzeti su sa zvanične internet stranice Agencije za lekove i medicinska sredstva Srbije.
Rezultati: Apsolutna potrošnja biljnih lekova (izražena u evrima) u 2016. godini u odnosu na 2006. godinu povećana je za 1466,63%, dok je relativna potrošnja (u odnosu na ukupnu potrošnju svih lekova) u istom periodu povećana za 811,11%. Istovremeno, povećanje potrošnje biljnih lekova, nije praćeno i povećanjem prisustva savremenih farmaceutskih formulacija i prisustvom savremenih nosača lekova koji doprinose povećanju efikasnosti ovih lekova.
Zaključak: Na osnovu dobijenih podataka uočava se visok procenat povećanja potrošnje biljnih lekova u Srbiji. Takođe, iz navedenog se može očekivati povećanje trenda upotrebe biljnih lekova i u budnućnosti. Dobijeni rezulatati upućuju na zaključak da Srbija prati svetski trend u povećanju upotrebe biljnih lekova.

Ključne reči: fitoterapija, fitopreparati, promet biljnih lekova

Zahvalnica: Pisanje ovog rada je podržalo Ministarstvo prosvete, nauke i tehnološkog razvoja Republike Srbije (projekati broj OI 172058 i OI 41012)

The growth rate of consumption of herbal medicines in Serbia in the period from 2006 to 2016

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Introduction: There are studies showing that herbal remedies can be a good choice for the treatment of some diseases. There is a growing trend in the consumption of this group of drugs in the world, and the aim of this study was to find a trend of consumption in Serbia.
Method: Data on the consumption of herbal remedies during the observed period in Serbia were taken from the official website of the Agency for Medicines and Medical Devices of Serbia.
Results: Absolute consumption of herbal medicines (expressed in euros) in 2016 compared to 2006 increased by 1466.63%, while relative consumption (in relation to total consumption of all drugs) increased by 811.11% in the same period. At the same time, the increase in herbal drugs consumption is not accompanied by an increase in the presence of modern pharmaceutical formulations and the presence of modern drug carriers that contribute to the increase in the efficacy of these drugs.
Conclusion: Based on the obtained data, a high percentage of increase in consumption of herbal medicines in Serbia is observed. Also, the above can be expected to increase the trend of the use of herbal remedies and in the future. The obtained results point to the conclusion that Serbia is following the world trend in increasing the use of herbal medicines.

Keywords: phytotherapy, phytopraparations, consumption of herbal medicines

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Ispitivanje profila brzine rastvaranja paracetamola iz različito formulisanih tableta sa trenutnim oslobađanjem

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Uvod: Poznavanje uticaja pomoćnih supstanci na profil brzine oslobađanja aktivnog sastojka iz farmaceutske formulacije, važno je sa aspekta obezbeđivanja najvišeg stepena efikasnosti same formulacije. Cilj ovog rada bio je da se ispita uticaj ekscipijenasa na kinetiku osobađanja aktivne supstance iz četiri formulacije paracetamola prisutne na tržštu.
Materijal i metoda: Disolucioni profili su određeni uz pomoć Disolucionog testera, metodom sa lopaticama, i korišćenjem fosfatnog pufera (pH=6,8) kao medijuma za rastvaranje. Oslobađanje paracetamola je praćeno u šest vremenskih tačaka, u toku 60 minuta. Sadržaj je određen merenjem na UV/VIS spektrofotometru na 243 nm. Poređenje dobijenih profila rađeno je na tri načina: model nezavisnom metodom, statističkom obradom (ANOVA, t-test parova), i model zavism metodama.
Rezultati: Sve formulacije su u prvih 45 minuta oslobodile više od 85% sadržaja. Formulacija D, koja je sadržl superdezintegrator, oslobodila čak 90% sadržaja u prvih 5 minuta. Iako vrednosti faktora razlike i sličnosti (f1 i f2) upućuju da su disolucioni profili isti, ANOVA testom pokazano je da se formulacije A i B, B i C, kao i B i D razlikuju u svih 6 ispitanih što znači da imaju paralelne profile. Dalje model zavisni metod je pokazao da oslobađanje paracetamola iz formulacije A i D najbolje opisuje model kinetike prvog reda, dok oslobađanje paracetamola iz formulacije B i C logistički model.
Zaključak: Prema ovom istraživanju, sredstva za dopunjavanje i sredstva za raspadanje imaju najveći uticaj na disolucioni profil paracetamola. Takođe, može se uočiti da i ostali ekscipijensi poput sredstava za kliženje imaju uticaj na kinetiku osobađanja aktivnog sastojka iz tableta sa trenutnim oslobađanjem.

Ključne reči: ekscipijensi, kinetika osobađanja aktivnog sastojka, acetaminofen

Zahvalnica: Pisanje ovog rada je podržalo Ministarstvo prosvete, nauke i tehnološkog razvoja Republike Srbije (projekat broj OI 41012)

Investigation of dissolution profiles of paracetamol from various immediate release tablet formulations

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Introduction: Knowing the influence of excipients on the dissolution profile of the active pharmaceutical ingredient from the pharmaceutical formulation is important from the aspect of ensuring the highest degree of efficiency of that formulation. The aim of this study was to investigate the effect of excipients on the kinetics of active substance individuals from the four formulations of paracetamol present on the market.
Material and Method: Dissolution profiles were determined using a Dissolution tester,method with paddles, and phosphate buffer (pH = 6.8) as a solvent medium. The release of paracetamol was monitored at six time points within 60 minutes. The content was determined by measuring by the UV / VIS spectrophotometer at 243 nm. A comparison of the obtained profiles was done in three ways: by the model independent method, statistical processing (ANOVA, t-test pairs), and the model dependent methods.
Results: All formulations are in the first 45 minutes liberated more than 85 % of the label content. Formulation D, which contained superdesintegrator, released 90% of content in first 5 minutes. Though based on values of difference and similarity factors formulations are, not significantly different, ANOVA-based method showed that formulation A and B, B and C, as well as formulation B and D do statistically differ in all 6 time points, meaning they have parallel profiles. The release of paracetamol from formulations A and D is best described by the first order kinetic model, while the release of formulations B and C logistic model.
Conclusion: According to this study, diluents and desintegrants have the greatest effect on the paracetamol dissolution profile. Also, it can be noticed that other excipients, as glidants, have an effect on the kinetics of active pharmaceutical ingredients from the immediate release tablets.

Keywords: excipients, release kinetics of active pharmaceutical ingredient, acetaminophen

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Antioksidativna aktivnost rtanjskog čaja (*Satureja montana, L.*)

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Uvod: Zahvaljujući prisustvu sekundarnih metabolita kao što su flavonoidi, steroli, etarska ulja i tanini, pripadnici roda Satureja poseduju lekovita svojstva i svrstavaju se u grupu tradicionalnih preparata za ublažavanje poremećaja mnogih organskih sistema. Novija istraživanja ukazuju na potencijalno korisna farmakodinamska delovanja jednog od pripadnika roda Satureja, rtanjskog čaja, kao što su antigljivično i antibakterijsko delovanje, sposobnost neutralisanja reaktivnih kiseoničnih vrsta, antidijabetesno, antihiperlipidemijsko kao i ekspektorantno i vazodilatatorno dejstvo.
Cilj: Ispitati uticaj ekstrakta rtanjskog čaja na biohemijske parametre, pokazatelje funkcije jetre i bubrega u serumu i antioksidativni potencijal na modelu belih, laboratorijskih pacova, izloženih oksidativnom stresu primenom toksičnih doza paracetamola.
Materijal i metode: Ispitivanje je sprovedeno na polno zrelim, belim laboratorijskim pacovima soja Wistar, podeljenih u četiri grupe od po 6 jedinki. Životinje su pretretirane per os tokom 7 dana, ekstraktom rtanjskog čaja i fiziološkim rastvorom nakon čega su dobili toksičnu dozu paracetamola. Pacovi su žrtvovani nakon čega je urađena kompletna obdukcija, dobijena krv je korišćena za određivanje biohemijskih parametara, a homogenat jetre za određivanje enzima oksidativnog stresa.
Rezultati: Primena toksične doze paracetamola je statistički značajno povećala aktivnost jetrenih transaminaza u serumu u odnosu na kontrolu, $p<0,05$. Aktivnost enzima oksidativnog stresa bila je značajno veća kod životinja koje su pre toksične doze paracetamola bile tretirane fiziološkim rastvorom u odnosu na kontrolu, $p<0,05$. Pokazatelji jetrenih i bubrežnih funkcija kao i koncentracija enzima oksidativnog stresa bili su značajno niži kod životinja koje su pre toksične doze paracetamola tretirane rtanjskim čaja u odnosu na grupu koja je dobila samo paracetamol.
Zaključak: Toksična doza paracetamola dovodi do značajnog poremećaja biohemijskih parametara, pokazatelja funkcije jetre i bubrega i pokazatelja oksidativnog stresa, u serumu laboratorijskih pacova. Pretretman ekstraktom rtanjskog čaja pre primene toksične doze paracetamola doveo je do nižih vrednosti biohemojskih i parametara oksidativnog stresa.

Ključne reči: rtanjski čaj, pacovi, paracetamol, antioksidativno dejstvo

Ovaj rad je podržan od strane Ministarstva prosvete, nauke i tehnološkog razvoja Republike Srbije, projekat broj III 41012.

Antioxidant activity of Winter savory extract (*Satureja montana, L.*)

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Introduction: Because of the presence of secondary metabolites such as flavonoids, sterols, essential oils and tannins, the Satureja family has medicinal properties and is classified as a group of traditional preparations for alleviating the disorders of many organic systems. Recent studies indicate potentially useful pharmacodynamic effects of one of the members of the genus Satureja, Satureja montana, L., such as antifungal and antibacterial activity, the ability to neutralize reactive oxygen species, antidiabetic, antihyperlipidemic as well as the expectorant and vasodilatory effect.
Aim: Enquier into the influence of winter savory extract on biochemical parameters, liver function and kidney function in the serum, and antioxidant potential on white, laboratory rats exposed to oxidative stress using toxic doses of paracetamol.
Materials and Methods: The research was conducted on the half-mature white Wistar laboratory rats, divided into four groups of 6. The animals were orally pretreated for 7 days, with winter savory extract and saline followed by a toxic dose of paracetamol. Rats were sacrificed, after which complete autopsy was performed, the blood obtained was used to determine biochemical parameters, and liver homogenate to determine oxidative stress enzymes.
Results: The application of the toxic dose of paracetamol statistically significantly increased the activity of liver transaminases in the serum relative to control, $p < 0.05$. The activity of oxidative stress enzyme was significantly higher in animals that were treated with physiological saline compared with control, $p < 0.05$, before the toxic doses of paracetamol. Indicators of hepatic and kidney functions, as well as the concentration of oxidative stress enzymes, were significantly lower in animals that were treated with rats compared with the paracetamol group alone prior to the toxic dose of paracetamol.
Conclusion: The toxic dose of paracetamol leads to a significant disorder of biochemical parameters, liver and kidney function indicators and oxidative stress indicators in the serum of laboratory rats. Pre-treatment with winter savory extract prior to the administration of the toxic dose of paracetamol led to lower biochemical and oxidative stress parameters.

Key Words: Winter savory extract, rats, paracetamol, antioxidant effect

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Isplativost primene preparata gvožđe (II)-glukonat, mangan--glukonat, bakar-glukonata u odnosu na preparat gvožđe (III) hidroksid polimaltozni kompleks u uslovima u Srbiji

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Uvod: Anemija uzrokovana nedostatkom gvožđa leči se preparatima gvožđa u trajanju od 3 do 6 meseci. Od preparata gvožđa za peroralnu primenu u Republici Srbiji na doplatnoj Listi lekova RFZO nalaze se gvožđe (II) fumarat i gvožđe (III) hidroksid polimaltozni kompleks.
Cilj: Cilj studije je da se utvrdi isplativost stavljanja na pozitivnu listu preparata gvožđe (II)-glukonat, mangan-glukonat, bakar-glukonata u odnosu na preparat gvožđe (III) hidroksid polimaltozni kompleks.
Materijal i metode: U analizi isplativosti korišćen je matematički model stabla odluke napravljen pomoću TreeAge Pro® softvera. Za komparator sa A1 liste, uzet je preparat gvožđe (III) hidroksid polimaltozni kompleks. Rezultat farmakoekonomske analize je predstavljen kao inkrementalni odnos troškovne isplativosti (ICER) po uspešno lečenom pacijentu (dostignute ciljne vrednosti hemoglobina > 110g/L). U analizu su uključeni troškovi lekova, pregledi lekara opšte prakse (prvi i kontrolni), specijalistički pregledi (prvi i kontroni), troškovi laboratorijskih nalaza (KKS, Gvožde, Feritin, Transferin i TIBC/UIBC) i pripadajućih procedura prema dostupnom cenovniku RFZO. Budući da se analiza radi iz perspektive RFZO, uzeti su u obzir samo direktni troškovi.
Rezultati: Uzimajući napred navedene faktore u obzir, kao i podatak da je prosečna cena terapijskog ciklusa preparatom gvožđe (II)-glukonat, mangan-glukonat, bakar-glukonata 5.778,05 RSD, dobijamo da je ukupni trošak terapije ovim preparatom 21.505,95 RSD. Takođe nalazimo da u identičnim uslovima i sa cenom prosečnog terapijskog ciklusa u iznosu od 3.798,48 RSD ukupni trošak preparatom gvožđe (III) hidroksid polimaltozni kompleks iznosi 24.662,31 RSD.U slučaju korišćenja preparata gvožđe (II)-glukonat, mangan-glukonat, bakar-glukonata došlo bi do ušteda u iznosu od 3.156,36 RSD u odnosu na preparat gvožđe (III) hidroksid polimaltozni kompleks po jednom uspešno lečenom pacijentu.
Zaključci: Terapija preparata gvožđe (II)-glukonat, mangan-glukonat, bakar-glukonata predstavlja isplativu strategiju u odnosu na terapiju preparatom gvožđe (III) hidroksid polimaltozni kompleks u Srbiji.

The cost-effectiveness of the iron (II)-gluconate, manganese--gluconate, copper-based preparations for iron (III) hydroxide polymaltose complex in Serbia

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Introduction: Anemia caused by iron deficiency is treated with iron preparations for 3 to 6 months. On positive list of Republic health fund of Serbia (RHFS), there are two iron preparations for oral use: iron (II) fumarate and iron (III) hydroxide polymaltose complex.
Objective: The aim of the study was to determine the cost-effectiveness of iron preparations for oral use: iron (II) -gluconate, manganese-gluconate, copper-gluconate compared to the iron (III) hydroxide polymaltose complex.
Material and Methods: In the cost-effectiveness analysis, a mathematical model of a decision tree using the TreeAge Pro® software was used. The result of the pharmacoeconomic analysis is presented as an incremental cost-effectiveness ratio (ICER) per successful treated patient (hemoglobin target value> 110g / L). The analysis includes the cost of medicines, general medical examinations (first and control), specialist examinations (first and controles), costs of laboratory findings (KKS, iron, feritine, transferin and TIBC / UIBC) and associated procedures according to the available RHFS pricelist. Since the analysis is based on the RHFS perspective, only direct costs were taken into account.
Results: Taking the aforementioned factors into consideration, as well as the fact that the average price of was5,778.05 RSD for the therapeutic cycle with iron (II) -glutonate, manganese-gluconate, copper-gluconate, the total cost of therapy with this preparation is 21.505.95 RSD . Under the same conditions and with the price of the average therapeutic cycle of 3,798.48 RSD, the total cost of treatment with iron (III) hydroxide polymalose complex is 24,662.31 RSD. In the case of the use of iron (II) -glutonate, manganese gluconate, copper gluconate instead of iron (III) hydroxide polymaltose complex, the posible savings are 3,156.36 RSD per one successfuly treated patient.
Conclusions: The treatment with iron (II)-gluconate, manganese-gluconate, copper-gluconate preparations is a cost-effective strategy in relation to the treatment of the iron (III) hydroxide polymaltose complex in Serbia.