UVODNIK

Na letošnjem 5. simpoziju Sekcije kliničnih farmacevtov SFD že drugo leto zapored predstavljamo povzetke raziskav s področja klinične farmacije. Letos je, v skladu s pričakovanji, teh prispevkov manj kot lansko leto. Razveseljiva je kakovost prispevkov ter dejstvo, da prispevki prihajajo ne samo iz Slovenije, ampak tudi iz sosednje Hrvaške. Sodelovanje s tujino predstavlja priložnost za izmenjavo znanj in dobrih praks ter seveda možnost za sodelovanje tudi na raziskovalnem področju. Večina povzetkov je iz bolnišničnega okolja, kar pa seveda ne pomeni, da so raziskave s področja klinične farmacije omejene samo na bolnišnično okolje. Prav nasprotno, tako kot se mora klinična farmacija izvajati na vseh ravneh zdravstvenega sistema, se morajo tudi raziskave. Izvajanje raziskav s področja klinične farmacije moramo v čim večji meri umestiti v okvir našega rednega dela. Tako bomo spodbudili raziskovanje, ki je temelj razvoja. Farmacevti moramo dobro premisliti, katere naše, tudi tradicionalne naloge, lahko predamo drugim profilom oziroma centrom ali pa jih celo prenehamo izvajati, pridobljen čas pa namenimo kliniki in seveda raziskovanju. Seveda pa potem izsledki našega raziskovalnega dela ne smejo ostati pozabljeni na računalniku, ampak predstavljeni širši strokovni javnosti!

Verjamem, da je dobrih raziskav, ki bi si zaslužile predstavitev v našem Farmacevtskem vestniku in bi jih kolegi z veseljem prebrali, še veliko. Že sedaj vas lepo vabim, da se v prihodnjem letu odzovete na vabilo k objavi vaše raziskave v našem Farmacevtskem vestniku. Pri načrtovanju in izvedbi raziskav pa ne pozabite na našo matično Fakulteto za farmacijo, ki nam tudi po zaključku študija nudi podporo.

Sedaj pa vam v upanju, da se med branjem prispevkov utrne ideja za sodelovanje, nadgraditev vašega dela ali izvedbo raziskave, želim prijetno branje!

Član gostujočega uredniškega odbora: Janez Toni, mag. farm.

1 **Marijana Fortuna Lužar, Marjana Bernot, Simona Borštnar, Simona Hotujec, Petra Tavčar, Igor Virant, Monika Sonc, Andreja Eberl, Mina Kovačevič, Samo Rožman**
Smernice zdravljenja ekstravazacije s protirakavimi zdravili na oil in pregled vseh dokumentiranih primerov ekstravazacije v obdobju 2010 - 2013 108

2 **Ivana Marinović, Vesna Bačić Vrca, Srećko Marušić, Iva Mucalo, Mateja Klarić, Jadranka Morović-Vergles**
The analysis of pharmacotherapy at hospital admission and discharge 109

3 **Tanja Tomšič**
Zdravljenje zunajbolnišnične pljučnice na infekcijskem in pljučnem oddelku Splošne bolnišnice Novo mesto 109

4 **Sanja Smontara, Slaven Falamić, Ivana Samardžić, Vesna Bačić-Vrca**
Do patients seek proffesional help in treating headache with medications? 111

5 **Erika Stariha**
Poročanje neželenih dogodkov pri zdravljenju z zdravili v Kliniki Golnik 111

6 **Maja Jošt, Mihaela Zidarn, Mitja Košnik**
Hereditary angioedema- how can medicines reach the patient? 112

7 **Matej Dobravc Verbič, Kristina Homec, Aleš Mrhar**
Ocena pojavnosti in ukrepov ob pojavu hematoloških neželenih učinkov pri bolnikih zdravljenih v gastro-onkološki ambulanti UKC Ljubljana 113

8 **Ivona Capjak, Ana Kučak, Ivanka Gujić**
Stablity of dextran diluted in water for injection at two temperatures 114

9 **Lea Knez, Aleksander Sadikov, Andraž Jakelj, Katja Mohorčič, Nina Turnšek Hitij, Tanja Cufer**
Overall survival in advanced lung cancer patients proposed to receive initial chemotherapy according to actual chemotherapy delivery 115

10 **Lea Knez, Mojca Kerec Kos, Tanja Cufer**
Drug interactions in cancer treatment: measures for their identification and prevention in routine clincal practice 115

11 **Lea Knez**
Good clinical pharmacy practice in oncology: the experience from University Clinic Golnik, Slovenia. 116

12 **Ana Šarčević, Erika Stariha, Viktorija Tomič, Stanislav Šuškovič, Aleš Mrhar**
Antimicrobial therapy of community-acquired pneumonia at the University Clinic Golnik 117

13 **Tomaž Vovk, Boštjan Guštin, Daniela Milosheska, Bogdan Lorber, Jurij Trontelj, Iztok Grabnar**
Terapevtsko spremljanje koncentracij lamotrigina in njegovega presnovka 2-N glukuronida s pomočjo posušenih krvnih madežev 118

POVZETKI RAZISKAV s področja klinične farmacije

SMERNICE ZDRAVLJENJA EKSTRAVAZACIJE S PROTIRAKAVIMI ZDRAVILI NA OIL IN PREGLED VSEH DOKUMENTIRANIH PRIMEROV EKSTRAVAZACIJE V OBDOBJU 2010-2013

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UVOD

Na Onkološkem inštitutu v Ljubljani (OIL) je bila ustanovljena delovna skupina za pripravo standardov za ravnanje v primeru ekstravazacijie s protirakavimi zdravili. Standard omogoča strokovno, pravilno in hitro ukrepanje v primeru ekstravazacije s protirakavim zdravilom, poleg tega pa je standard nujno potreben za enotno zdravljenje bolnikov, ki prejemajo protirakava zdravila v ostalih bolnišnicah v Sloveniji. Ekstravazacija je zaplet zdravljenja s protirakavimi zdravili. Protirakavo zdravilo, ki ga bolnik prejme v obliki infuzije v veno, nenamerno uhaja iz vene v okolno tkivo in na njem povzroči poškodbo. Klinična slika je različna, od neznatnih simptomov do hudih tkivnih poškodb.

NAMEN

Na podlagi napisanega standarda smo izdelali algoritme zdravljenja ekstravazacije in obrazec za dokumentiranje ekstravazacije s protirakavimi zdravili. Statistično smo obdelali vse dokumentirane ekstravazacije s protirakavimi zdravili od januarja 2010 do septembra 2013.

MATERIALI IN METODE

Na OIL smo v izbranem obdobju bolnike zdravili s 47 protirakavimi zdravili. Pri nastanku standardov smo pregledali že obstoječe tuje smernice, članke ter posamezne študije in Smpc za posamezno zdravilo kot npr. ESMO-EONS Clinical Practice Guidelines,PubMed, UpToDate 2012, COG (Children´s Oncology Group) Pharmacy Committee, Extravasation of Cytotoxic Agents Compendium for Prevention and Management.

REZULTATI IN RAZPRAVA

Protirakava zdravila smo razdelili v tabelo glede na možnost povzročitve tkivne poškodbe ob ekstravazaciji med nevezikante, iritante in vezikante in določili ukrepe zdravljenja. Za posamezno protirakavo zdravilo so določeni ukrepi ob ekstravazaciji, povezani z njegovo razvrstitvijo in poznavanjem delovanja zdravila kot antidota. Protirakava zdravila iz iste skupine imajo podobne stranske učinke. Na podlagi pregledane literature smo v naš standard vključili tri antidote dimetilsulfoksid (DMSO), hialuronidaza (Hylase) in deksrazoksan (Savene). Poleg ukrepov z antidoti je smiselno simptomatsko zdraviti rdečino s kortikosteroidno kremo in bolečino s sistemskimi in lokalnimi analgetiki. V našem standardu je o 47 protirakavih zdravil: 16 nevezikantov, 10 iritantov in 10 vezikantov , 8 zdravil je vezikant/iritant in 3 iritant/nevezikant. Hladne obkladke uporabimo pri 20 zdravilih, pri 4 zdravilih uporabimo tople obkladke, pri 18 zdravilih obkladki niso potrebni, pri 5 zdravilih so obkaldki lahko hladni ali topli glede na delovanje protirakavega zdravila. Najpogosteje prijavljena ekstravazirana protirakava zdravila so: doksorubicin (antraciklini) 28 %, fluorouracil (antimetabolit) 17 % in paklitaksel (taksani) 14%. Od tega je bilo 59 % vezikantov , 17 % iritantov ter 24 % nevezikantov. Pri 60 primerih je bila potrebna aplikacija antidota, pri 77 aplikacija obkladkov in v 32 primerih so bili potrebni dodatni ukrepi. V 48 % smo kot antidot uporabili dimetilsulfoksid, v 41 % hialuronidazo in v 11 % deksrazoksan.

ZAKLJUČKI

Smernice zdravljenja so nujno potrebne za enotno zdravljenje bolnikov, ki prejemajo protirakava zdravila tako na

OIL kot tudi v ostalih bolnišnicah po Sloveniji. Algoritem zdravljenja omogoča strokovno in učinkovito ukrepanje v najhitrejšem možnem času. Poleg tega je vsak dogodek ekstravazacije dokumentiran po enotnem vprašalniku.

OBJAVLJENO V:
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THE ANALYSIS OF PHARMACOTHERAPY AT HOSPITAL ADMISSION AND DISCHARGE

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INTRODUCTION
In order to develop a program that includes medication reconciliation at the Clinic of Internal Medicine, research on the analysis of pharmacotherapy at the hospital admission and discharge has been started and will be conducted for 6 months.

METHODS
Patients being admitted to the Clinic of Internal Medicine are interviewed and the Best Possible Medication History (BPMH) is created. BPMH is compared to the prescribed therapy at the time of hospital admission and discharge. In communication with physicians we identified all unintentional discrepancies. We also evaluated the potential seriousness of these discrepancies[1]. In order to optimize pharmacotherapy residents of clinical pharmacy are doing interventions during hospital admission.

RESULTS
During the 2-month period, 70 patients were enrolled in research. 37 unintended discrepancies were identified and classified according to type of discrepancy. The most common type of discrepancy was omission of drug (59,5%). Most discrepancies (48,7%) had the potential to result in severe discomfort or clinical deterioration (class 3). On 405 prescribed medications, residents of clinical pharmacy made 33 interventions. Intervention acceptance rate by physicians was 48,7%.

CONCLUSION
Our analysis has shown high incidence of unintentional discrepancies with the potential to result in severe discomfort or clinical deterioration (class 3). Residents of clinical pharmacy made a large number of interventions in order to optimize the therapy.

We evaluated patients' knowledge and understanding of medications in use and the rate of patients' adherence to medication which indicate the need for introducing counselling at discharge from hospital.

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ZDRAVLJENJE ZUNAJBOLNIŠNIČNE PLJUČNICE NA INFEKCIJSKEM IN PLJUČNEM ODDELKU SPLOŠNE BOLNIŠNICE NOVO MESTO

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UVOD
Letno slovenske bolnišnice zaradi zunajbolnišnične pljučnice sprejmejo okoli 6000 bolnikov, med temi največji delež predstavljajo bolniki starejši od 65 let. Smrtnost bolnikov z zunajbolnišnično pljučnico zdravljenih v bolnišnici znaša okrog 10%, ta številka pa je znatno večja pri starostnikih in bolnikih s kroničnimi boleznimi. Za obravnavo zu-

najbolnišnične pljučnice smo v letu 2010 v Sloveniji dobili prenovljena in dopolnjena priporočila, ki naj bi bila osnova za pripravo kliničnih poti v posameznih ustanovah in glavno vodilo pri zdravljenju zunajbolnišnične pljučnice.

NAMEN

Namen te naloge je bil pregledati zdravljenje zunajbolnišnične pljučnice v Splošni bolnišnici Novo mesto, poiskati pomanjkljivosti v zdravljenju in omogočiti pripravo načrta za izboljšave.

MATERIALI IN METODE

V raziskavo smo vključili vse bolnike, ki so se zdravili na Infekcijskem in Pljučnem oddelku Splošne bolnišnice Novo mesto v obdobju januar – junij 2012 zaradi zunajbolnišnične pljučnice. Podatki so bili pridobljeni iz popisov bolnikov, programa za analizo podatkov v zdravstveni organizaciji – K22 in programa Birpis. Glede na pridobljene podatke je bila narejena ocena resnosti pljučnice po sistemu PSI, opredeljen klinični izid, ocenjena skladnost izbire protimikrobnega zdravljenja s smernicami in čas protimikrobnega zdravljenja. Na podlagi veljavnih smernic je bila v sodelovanju s specialisti infektologije/pulmologije pripravljena klinična pot.

REZULTATI IN RAZPRAVA

V raziskavo smo vključili 74 bolnikov, pri tem so starejši od 65 let predstavljali 78,4% vključenih bolnikov. Največ zajetih bolnikov je bilo po sistemu PSI uvrščenih v razred IV (42%), sledi razred V (27%), potem razreda II (12%) in III (12%) ter z najmanj bolniki razred I (7%). Delež bolj ogroženih bolnikov (PSI IV in V) je bil v primerjavi z literaturo visok in vsi bolniki, ki so med zdravljenjem umrli, so sodili med bolj ogrožene bolnike. Zdravljenje v bolnišnici je bilo uspešno za 89% bolnikov, vendar le za 62% s prvotno predpisanim antibiotikom. Skladnost s smernicami glede na izbiro protimikrobnega zdravila je znašala 49%, pri tem so bili klinični izidi primerljivi z literaturo. Čas protimikrobnega zdravljenja v bolnišnici je v povprečju znašal 9,4 dni, kar je znotraj smernic, vendar je bil razpon velik (od 2 do 34 dni). Pomanjkljivo so bili zabeleženi podatki o kajenju in ob odpustu iz bolnišnice je bilo samo sedmim bolnikom svetovano cepljenje, priporočilo pa bi bilo smotrno še za vsaj 54 bolnikov.

ZAKLJUČKI

Izidi zdravljenja zunajbolnišničnih pljučnic v Splošni bolnišnici Novo mesto so primerljivi z literaturo, vendar pa je naloga vseeno opozorila na nekatere pomanjkljivosti pri obravnavi bolnikov. Za izboljšanje kakovosti zdravljenja je bila pripravljena klinična pot, ki opozarja na vse korake obravnave zunajbolnišničnih pljučnic in olajša sledenje smernicami. Uporaba klinične poti lahko prispeva k skrajšanju časa hospitalizacije, časa protimikrobnega zdravljenja in k zmanjšanju stroškov, tudi če ne vpliva na izboljšanje kliničnih izidov.

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DO PATIENTS SEEK PROFFESIONAL HELP IN TREATING HEADACHE WITH MEDICATIONS?

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INTRODUCTION

Headaches are among the most prevalent neurological disorders (1). According to International Headache Society (IHS) headaches are classified into three main groups (primary, secondary and cranial neuralgias, facial pain and other headaches). It is a very common symptom of varius diseases and conditions and one of the main reasons for analgetics use. Appropriate treatment of headache disorders requires professional training of health professionals, accurate diagnosis and recognition of the condition, appropriate treatment with cost-effective medications, lifestyle modifications and patient education (2). In the headache treatment pharmacists should play an important role (3).

PURPOSE OF THE STUDY

The aim of this observational community pharmacy-based study was to analyze pharmacotherapy given to treat headache and the type of recommendation for its use.

METHODS

The study was conducted in public pharmacies during the period of one month. Consecutive patients dispensed with drugs to treat headache were included in the analysis and interviewed at site.

RESULTS

The study enrolled 163 patients (62% women). The average age of patients was 53.3 (range 19-86). The most commonly used analgesic was ibuprofen (35%), followed by a combination of propyphenazone, paracetamol, codein and caffeine (19.6%). Ketoprofen and paracetamol in monotherapy were used by 13.5% and 12.3% of patients, respectively. 104 patients agreed to fill out a questionnaire (63.8%) which showed that 49% of patients treated headache once a month, 32.7% once a week, 12.5% more than once a week and 5.8% less than once a month. Patients reicived recommendation for headache therapy mostly from their doctors (55.8%). Recommendations received from pharmacists (22.1%) and other sources (22.1%) were equally represented.

CONCLUSION

Even though majority of patients in our study used medications which do not require prescription, most of patients consulted health proffesionals for treating headache.

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POROČANJE NEŽELENIH DOGODKOV PRI ZDRAVLJENJU Z ZDRAVILI V KLINIKI GOLNIK

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UVOD

Neželeni dogodki pri zdravljenju z zdravili so nenamerne napake pri predpisovanju, izdaji, pripravi, dajanju ali spremljanju učinka zdravil, ki povzročijo nek neželen dogodek pri zdravljenju bolnika. Te dogodke pa se da preprečiti (1,2,). V Kliniki Golnik neželene dogodke pri dajanju zdravil medicinske sestre poročajo že od leta 2005, v letu 2014 pa so s poročanjem neželenih in t.i. skorajšnjih dogodkov pri pripravi in izdaji zdravil pričeli tudi farmacevti. Skorajšnji dogodki (ang. near misses) so napake, ki so se zgodile v procesu zdravljenja z zdravili, vendar niso dosegle bolnika

(3). Namen naše analize je kategorizacija napak iz zbranih poročil ter predlagati izboljšave sistema poročanja in sistemskega ukrepanja.

METODE

Pregledali smo zbrana poročila od leta 2005 do konca leta 2014. Bolj podrobno smo pregledali poročila za leto 2014, kjer smo napake razvrstili v kategorije in pregledali tudi evidentirane razloge, ki so privedli do napake. Preverili smo tudi popolnost izpolnjenih obrazcev s strani zdravnika. Rezultate smo predstavili na komisiji za kakovost (KZK), medicinskih sestram ter zdravnikom.

REZULTATI

Skupno je bilo v 10 letih zbranih 183 poročil. V letu 2005 je bilo izpolnjenih 5 poročil pri 5436 hospitalizacijah, v letu 2014 pa 52 poročil pri 6843 hospitalnih obravnavah. Od 52ih poročil je bilo 15 poročil o skorajšnjih dogodkih pri pripravi ali izdaji zdravil iz lekarne, ki niso podrobneje predstavljeni v tem prispevku. Vrste napak pri ostalih neželenih dogodkih so bile: zamenjava odmerka ali poti aplikacije (15/37), zamenjava bolnika (7/37), zamenjava zdravila (7/37), zdravilo ni bilo dano pravočasno (4/37), zdravilo dano kljub ukinitvi na terapevtskem listu (4/37). Pri trinajstih neželenih dogodkih je bilo možno iz poročila ugotoviti razlog za napako, in sicer: nečitljiva pisava (4/13) , moteče okolje (3/13), slaba predaja službe (3/13), stiska s časom (2/13) in izolacija bolnika (1/13). Klinična pomembnost napake je bila s strani zdravnika ocenjena pri 30ih poročilih, od tega samo enkrat kot velika klinična pomembnost. Ugotovili smo velik razpon pomembnosti napak znotraj ocene »majhna klinična pomembnost« ter, da so se podobne napake pojavljale na različnih oddelkih, vendar sistemske rešitve niso bile razvidne iz poročil.

DISKUSIJA

Na podlagi ugotovitev analize smo v letu 2014 pripravili prenovljen obrazec, ki zajema vse procese pri zdravljenju z zdravili, razširja možnost poročanja vseh zdravstvenih delavcev, ki so vključeni v proces zdravljenja z zdravili, omogoča in spodbuja poročanje skorajšnjih dogodkov ter kot skrbnika poročanja napak in sistemskega reševanja le-teh postavlja farmacevta. Skorajšnje dogodke se lahko poroča tudi anonimno saj želimo zmanjšati morebitne zadržke posameznikov (občutek krivde, strah pred posledicami). Na prenovljenem obrazcu je tudi razširjena rubrika o oceni klinične pomembnosti, s kratkim opisom, da zdravniku olajša odločitev in hkrati poenoti kriterije. Obrazec je v mesecu decembru potrdil strokovni svet klinike in se ga od tedaj uporablja. Nekaj sistemskih ukrepov za preprečitev najpogostejših napak zamenjave odmerka in zamenjave bolnika je bilo na podlagi rezultatov že izpeljanih, in sicer rizična zdravila smo pričeli opremljati z nalepkami: »preveri odmerek-nevarnost zamenjave« ter pripravili plakate, ki bolnike v bolnišnici seznanijo o pomembnosti pravilne identifikacije. Nenazadnje je porast števila poročil odraz skupnega dela na prepoznavanju napak pri zdravljenju z zdravili in zavedanja, da lahko s poročanjem neželenih dogodkov in skorajšnjih dogodkov bistveno prispevamo k sistemskim rešitvam, ki preprečijo neželene dogodke pri zdravljenju z zdravili v prihodnosti in s tem k večji varnosti in kakovosti zdravljena bolnikov z zdravili v Kliniki Golnik.

VIRI:

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HEREDITARY ANGIOEDEMA- HOW CAN MEDICINES REACH THE PATIENT?

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BACKGROUND

Hereditary angioedema (HAE) is a rare hereditary disease, which can be fatal without appropriate treatment of acute episodes. Accessibility of new medicines (conestat alpha and icatibant in Slovenia for the treatment of acute episodes of HAE (AE HAE) has some advantages compared to plasma-derived C1 inhibitor but also huge impact on direct costs. Our main goal was establishment of comprehensive care for HAE patients in order to enhance the quality and unified of care with control of the costs.

METHODS

The centralized care model for HAE patients was developed based on data from national lists and recommendations from literature. The data on HAE patients (20) in Slovenia were retrieved regarding supply with rescue med-

icines for AE, frequency of annual AE and consumption of medicines per patient for each AE for the last two years.

RESULTS

A **national widespread network of non-stop access points** for supply of conestat alpha in 7 ED in Slovenian hospitals was set up. **Patients were gradually switched to icatibant for AE HAE as rescue medicine.** A **logistic plan to assure sufficient stocks of AE HAE medicines with expired data minimization policy** was made. **A system for recording treatment outcomes and consumption of medicines on each patient** was developed. The safety, quality and unified of care for HAE patients was improved by preparing the **documentation**: Patient Identification Card, Recommendation for treatment the AE HAE in ED, etc.

CONCLUSION

Our model was designed in accordance to recommendations for centralized care of patients with rare diseases. It was adjusted to requirements of national health insurance and regional distribution of HAE patients in Slovenia. The comprehensive care model includes non-stop access points for HAE medicines as well as treatment outcomes recording according to medicines consumption. It represents good and necessary base for better management of HAE patients where data from large clinical trials are scarce.

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PREDSTAVLJENO NA:

8th C1- Inhibitor Deficiency Workshop, Budapest 2013, Hungary

OCENA POJAVNOSTI IN UKREPOV OB POJAVU HEMATOLOŠKIH NEŽELENIH UČINKOV PRI BOLNIKIH ZDRAVLJENIH V GASTRO-ONKOLOŠKI AMBULANTI UKC LJUBLJANA

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UVOD

Hematološki neželeni učinki (hemNU) so pogosti in resni neželeni učinki bolnikov, zdravljenih s kemoterapijo. So tudi med najpogostejšimi vzroki prilagajanj odmerkov in zamikov kemoterapije. Pravilno ukrepanje ob pojavu hemNU ima velik pomen pri doseganju optimalnih izidov zdravljenja.

NAMEN

Namen raziskave je pridobiti oceno pojavnosti hemNU in pregled ukrepov pri bolnikih, zdravljenih z intravensko kemoterapijo v gastro-onkološki ambulanti (GOA) UKC Ljubljana. Rezultati raziskave bodo služili kot osnova za pripravo priporočil za ravnanje v primeru pojava hemNU, s katerimi želimo zagotoviti ustrezno obravnavo bolnikov v teh primerih.

MATERIALI IN METODE

V raziskavo smo vključili 121 bolnikov, ki so v letu 2012 prejeli vsaj eno aplikacijo intravenske kemoterapije. Zbirali smo vrednosti hematoloških parametrov pred predvidenimi aplikacijami kemoterapij. Pri bolnikih s pojavom hemNU, ki smo jih definirali kot pojav levkopenije (število levkocitov ≤ $4{,}0 \times 10^9$/L), anemije (koncentracija hemoglobina ≤ 11,0 g/dL), trombocitopenije (število trombocitov ≤ 100×10^9/L) ali nevtropenije (število nevtrofilcev ≤ $2{,}0 \times 10^9$/L), smo spremljali prilagajanje odmerkov in zamik terapij in jih primerjali s tujimi priporočili za ravnanje ob pojavu hemNU (1, 2, 3).

REZULTATI IN RAZPRAVA

HemNU so se pojavili pri 73 bolnikih (60,3 %). Najpogosteje je prišlo do pojava anemije, in sicer pri 42,9 % bolnikov. Anemiji sta po pogostosti sledili levkopenija (33,9 % bolnikov) in nevtropenija (27,3 % bolnikov). Najredkeje se je pojavila trombocitopenija, ki je nastopila pri 20,6 % bolnikov. Glede na tuja priporočila je bila prilagoditev terapije (nižanje odmerka in/ali zamik terapije) potrebna pri 24 bolnikih (19,8 %) za skupno 64/623 (10,3 %) aplikacij kemoterapij. Nižanje odmerka je bilo predvideno za 18/64 (28,1 %), zamik terapije pa za 58/64 (90,6 %) aplikacij kemoterapij. Premajhno znižanje odmerka smo zabeležili pri 7/18 (38,9 %) aplikacijah kemoterapij. Pri 21/58 (36,2 %) aplikacijah pa ni bilo predvidenega zamika kemoterapije. Skupno smo pri 9/24 (37,5 %) bolnikih zaznali neustrezno ukrepanje ob pojavu hemNU. Večjih prilagoditev odmerkov ter daljših zamikov terapij, kot jih navajajo priporočila, nismo smatrali kot neskladnih – navedeni ukrepi so bili namreč lahko uvedeni zaradi drugih vzrokov, ki jih v raziskavi nismo obravnavali.

ZAKLJUČKI

Pojavnost anemije in trombocitopenije med bolniki zdravljenimi v GOA so bili primerljivi z rezultati podobnih raziskav, pojavnost nevtropenije pa je bila v tej raziskavi nekoliko nižja. (4) Visoko število odstopanj od priporočil pri prilagajanju terapije ob pojavu hemNU nakazuje potrebo po postavitvi internih priporočil ter po vključitvi kliničnega farmacevta v pregled predpisane kemoterapije glede na vrednosti hematoloških parametrov pred aplikacijo kemoterapije.

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STABLITY OF DEXTRAN DILUTED IN WATER FOR INJECTION AT TWO TEMPERATURES

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INTRODUCTION

Dextran solutions are commonly used as blood plasma volume expanders and blood flow improvers. In neurology dextran solutions are used after stroke, in condition of disturbances in arterial and venous blood flow.

PURPOSE OF THE STUDY

The behaviour of dextrans low molar mass (40,000) at different temperatures in aqueous solutions was investigated.

One of the major problems is that the solution properties change with time. At the same temperature, the hydrodynamic radius and the intrinsic viscosity are higher for different molecular weights, while these properties decrease with an increase of temperature at the same molecular weight (1).

Namely, if solutions of clinical-type dextrans are stored for prolonged periods of time, partial precipitation takes place (2). The aim of this research is to study stability of water solutions of dextrans under different conditions in order to enhance our understanding of behaviour of dextrans in water. The degree of branching increases with increasing molar mass (2).

Viscosity of in water solution polysaccharides depends on intrinsic characteristics of the biopolymer (such as molecular weight, volume, size, shape, surface charge, deformation facility, esterification degree, and galacturonic content) and on ambient factors (such as pH, temperature, ionic strength, solvent, etc.).

METHODS

Solution of dextran 40.000 was stored at 25°C ± 2°C/60 % RH ± 5 % (long term stability conditions) and 40°C ± 2°C/75 % RH ± 5 % RH (accelerated stability conditions). Samples were collected at 0, 3, and 6 months after storage at each temperature. Dextran content was measured in triplicate from each of sample at each temperature by

stability-indicating parameters, were intrinsic viscosity is the most important parameter.

RESULTS AND DISCUSSION

After 3 month storage at 25°C, the dextran content in was 100.7 g/L (99,80 % of the original concentration at 25°C) C. After 3 month storage at 40°C the dextran content was the same; 100.7 g/L. The intrinsic viscosity after three months shows decline of 5.56 % but no difference at two storage temperature. Dextrans are polysaccharides consisting essentially of α-l.6-1inked D-glucose units. They show a varying degree of branching at the 2-, 3- and/or 4-positions in the glucose residues.

CONCLUSIONS

The results indicate that the solution of dextran in water for injection is stabile with no limts of storage temperature.

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OVERALL SURVIVAL IN ADVANCED LUNG CANCER PATIENTS PROPOSED TO RECEIVE INITIAL CHEMOTHERAPY ACCORDING TO ACTUAL CHEMOTHERAPY DELIVERY

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BACKGROUND

The benefits of chemotherapy in advanced lung cancer patients are well known. However, after evaluating patient eligibility, not all patients proposed for chemotherapy by multidisciplinary tumour board (MTB) actually receive it. In routine clinical practice, it is important to review the impact of this decision on patient survival and hospital cancer registry serve this function perfectly. Thus, the aim of the study was to evaluate the overall survival (OS) of advanced lung cancer patients according to delivery of initial chemotherapy between January 2010 and December 2013 at a single institution.

METHODS AND MATERIALS

The study included advanced lung cancer patients (adenocarcinoma, squamous cell lung cancer, small-cell lung cancer; SCLC) that were proposed for initial chemotherapy by a MTB (n=483). Patients that refused chemotherapy (n=11) or failed to come to the first appointment (n=27) were excluded, resulting in a final 445 patients included. All data were retrieved from our hospital lung cancer registry.

RESULTS AND DISCUSSION

As expected, patients receiving chemotherapy (361/445; 81%) had a significantly longer mOS (9.6 vs 1.7 mo; log-rank, $p<0.001$). This effect sustained across all tumour histologies (11.0 vs 1.8 mo for adenocarcinoma; 8.8 vs 2.3 mo for squamous; 8.9 vs 0.9 mo for SCLC; all log-rank, $p<0.001$). Also in multivariate analysis chemotherapy proved to be a strong independent factor (Cox-regression, $p<0.001$) alongside with tumour histology and performance status (PS) but not Charleson comorbidity index (CCI). Of note, this slightly differed from the factors revealed by logistic regression to be independently associated with chemotherapy delivery: patients with squamous histology ($p<0.001$), a poorer PS, as judged by the treating oncologist at the time of evaluation ($p<0.001$), and higher CCI ($p=0.014$) less often received chemotherapy.

CONCLUSION

The observed benefit of chemotherapy treatment in OS is not surprising and just proves the known. The value of patient and tumour features (CCI, histology), that impact the decision on chemotherapy treatment but not OS should be reconsidered and carefully interpreted in light of the extremely poor prognosis of advanced lung cancer patients not receiving chemotherapy.

Prispevek je bil predstavljen decembra 2014 na 14th Central European Lung Cancer Congress na Dunaju.

DRUG INTERACTIONS IN CANCER TREATMENT: MEASURES FOR THEIR IDENTIFICATION AND PREVENTION IN ROUTINE CLINCAL PRACTICE

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BACKGROUND

Cancer patients are prescribed numerous medications, including anticancer drugs, drugs for supportive care and comorbidities. Anticancer drugs are considered high risk drugs and drug interactions may have important implications for patient safety.

AIM

The presented study evaluates the management of drug interactions with anticancer drug therapy in routine clinical practice.

MATERIALS AND METHODS

The study was designed as a retrospective study and reviewed drug interactions in patients, where anticancer drug therapy was initiated in the year 2012 at the University Clinic Golnik. As part of routine clinical practice, in all patients, drug interactions were reviewed by a pharmacist, who discussed those judged to be clinically important with the patient's oncologist. As part of the study, drug interactions were reassessed using three different drug interaction databases (Lexi-comp, Stockley's Drug Interaction, Drugs.com) to record all possible interventions. Only drug interactions between drugs in systemic cancer therapy (including anticancer drugs and support care drugs) and prescription drugs for comorbidities were evaluated.

RESULTS AND DISCUSSION

Overall, the study included 223 lung cancer patients. Most patients were older (median 63 years), were taking a median of 4 drugs for treatment of comorbidities, and were prescribed a median of 6 drugs for cancer treatment. Review of drug interaction databases revealed 1416 drug interactions between drugs in systemic cancer therapy and other drugs, only 18 % of detected interventions involved anticancer drugs and only 19 % would affect the outcomes of anticancer treatment: the overwhelming number of possible drug interactions emphasise the importance of identifying clinically relevant drug interactions. The need for the critical appraisal of possible drug interactions is further evidenced by the low number of interactions (52/1416; 4 %), judged by the pharmacist as clinical important. Pharmacists more often identified as important interactions involving anticancer drugs (85 %; Chi^2, $p<0.01$) and those affecting the outcomes of anticancer therapy (79 %; Chi^2, $p<0.01$). To prevent the manifestation of drug interactions, pharmacists most often suggested a change in the treatment of comorbid conditions.

CONCLUSIONS

In the treatment with high risk drugs, all efforts should be invested to prevent adverse drug events and avoiding drug interactions falls within this aim. Review of drug interactions at initiation of anticancer drug treatment was successfully implemented into routine clinical practice. The study revealed a large number of possible drug interactions, showing the need for their critical appraisal in order to identify and prevent clinically relevant drug interactions.

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GOOD CLINICAL PHARMACY PRACTICE IN ONCOLOGY: THE EXPERIENCE FROM UNIVERSITY CLINIC GOLNIK, SLOVENIA

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INTRODUCTION

Anticancer drugs are high risk drugs that may adversely affect patient health, also when used as indicated. Moreover, cancer treatment is complex and, thus, prone to errors. To safeguard patient safety, it is of paramount importance to implement systems to reduce such errors. This may only be achieved through a multiprofessional approach with the participation of pharmacists. Herein, the role of clinical pharmacists in the treatment of oncology pa-

tients at the University Clinic Golnik and their contribution to patient safety is presented.

MATERIALS AND METHODS

Pharmacists were proactive in looking for possibilities to participate in the treatment of cancer patients. Their role is expanding: pharmacists have to obtain a drug history; pharmacists have to check for drug interactions; pharmacists have to double check every chemotherapy prescription; pharmacists consult patients prescribed with oral anticancer drugs. To argument the need for pharmacists involvement, pharmacists interventions made during chemotherapy prescription screening and interactions for which a pharmacist's advice was offered, were retrospectively reviewed during a 5-month and a 1-year period.

RESULTS AND DISCUSSION

Over the past years pharmacists' role in the treatment of oncology patients was developed from scratch to become an important member of the oncology team. The successful implementation of clinical pharmacy services into routine clinical practice is the most important result. The contribution of these services to patient care was quantified. During the screening of 506 chemotherapy prescriptions, pharmacists made 211 interventions: 31% were related to anticancer drugs, and 76% were implemented. The findings of this study served to improve clinical practice, e.g. by implementing chemotherapy order templates to reduce the number of errors in prescribing support care drugs. Cancer patients were found to be at risk of drug interactions: in 223 patients, 1416 interactions were identified and 52 were judged as clinically important, most of which (41/52) would affect anticancer therapy. Possible drug interactions have to be interpreted correctly to focus all efforts into preventing those clinically relevant.

CONCLUSION

Pharmacists have an important role in the treatment of oncology patients. The integration of clinical pharmacy services as chemotherapy prescription screening and drug interactions checking were shown to contribute to patient safety.

Prispevek je povzetek specialistične naloge Vloga kliničnega farmacevta pri obravnavi onkoloških bolnikov v Univerzitetni kliniki Golnik. Ljubljana 2014.

ANTIMICROBIAL THERAPY OF PNEUMOCOCCAL PNEUMONIA - SHORT PRESENTATION OF OUR STUDY RESULTS

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1 INTRODUCTION

Community-acquired pneumonia (CAP) is a form of an acute respiratory infection that affects the lungs of the adults either outside the hospital or up to 48 hours after hospitalization and has a high risk of fatal outcome (1, 2). We aimed to evaluate the appropriateness of treatment of CAP, caused by *S.pneumonia,* at the University Clinic Golnik in 2011 according to the Slovenian guidelines for treating CAP by analysing quality indicators (2).

2 METHODS

We conducted a retrospective cohort study by reviewing medical records of patients, who have been hospitalized at the University Clinic Golnik from 01.01.2011 until 31.12.2011. We searched patients with discharge diagnose of pneumonia caused by *S. pneumoniae* and patients with the laboratory data of isolated *S. pneumoniae* from patients' blood, sputum, tracheal aspirates or other samples in 2011. Only patients that had clinical manifestation of CAP were included.

3 RESULTS

The final study sample included 58 patients. The median age was 73 (Q1=63, Q3=80), 46,6 % of patients were smokers. Analysis of quality indicators listed in Slovenian guidelines for treating CAP showed: no patient had the pneumonia severity index (PSI/PORT) evidently determined, all patients had oxygen saturation determined on admission and for 75,9 % of patients blood cultures were collected. The choice of empiric antibiotic treatment was adequate in 89,5 %. Antibiotics were administered within 4 hours after the diagnose of CAP to 86,2 % of patients. Patients were treated empirically with amoxicillin/clavulanate (AMC) in 53,4 %, moxifloxacin was used in 22,7 % of patients and

in 8,6 % patients AMC was used in combination with azithromycin. Median duration of empiric treatment was 3,5 days. Antibiogram was done in 94,8 % of cases. Surprisingly, just 15,5 % of antibiotic therapies were changed based on the antibiogram results and only 8,4 % represented a step down to the antibiotic with a narrower spectrum of activity (e.g.penicillin V or G). Median total time of antibiotic treatment was 12 days and median length of hospital stay was 10,5 days which was in correlation with age of patients (0,561; p<0,001). Overall, 8,6 % of patients died.

4 DISCUSSION

Measured quality indicators showed fairly good compliance (above 75 %) with the guidelines. The study sample was small (58) due to inclusion criteria – patients with the discharge diagnose of pneumonia (the cause was not specified) and with no isolate of *S.pneumoniae,* were not evaluated. The most important finding of this study is that clinicians rarely (8,4 %) changed the empiric treatment of CAP to a narrower spectrum of activity. Nevertheless, a prospective study would be beneficial to explore the reason for such low rate of changing the empiric treatment to pathogen specific one.

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Prispevek je bil objavljen v zborniku Golniškega simpozija, Antimicrobial therapy of pneumococcal pneumonia – short presentation of our study results. 5th Slovenian Pnumology and Allergology Congress, October 2012: 55-58. Poster predstavljen na 36. EPSA kongresu 2013.

TERAPEVTSKO SPREMLJANJE KONCENTRACIJ LAMOTRIGINA IN NJEGOVEGA PRESNOVKA 2-N GLUKURONIDA S POMOČJO POSUŠENIH KRVNIH MADEŽEV

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UVOD

Pri terapevtskem spremljanju koncentracij (TDM) učinkovin ali aktivnih presnovkov se navadno uporabljajo vzorci krvne plazme ali seruma. Z razvojem zelo občutljivih analiznih metod, se je količina vzorca za analizo bistveno zmanjšala, kar omogoča uporabo alternativnih vzorcev. V to skupino sodijo tudi posušeni krvni madeži oz. angleško »dried blood spots« (DBS). V zadnjih nekaj letih se je vzorčenje s pomočjo DBS razširilo tudi na TDM različnih učinkovin in njihovih presnovkov npr. učinkovin za zdravljenje raka in epilepsije. Pri pripravi vzorca DBS se bolnik sam ali s pomočjo zdravstvenega osebja zbode z lanceto v prstno blazinico, kapljico krvi prenese na poseben papirček, kjer se kapljica posuši in nato papirček shrani v vrečko z nizko prepustnostjo za pline skupaj s sušilnim sredstvom. Tako pripravljen vzorec se transportira v analizni laboratorij, kjer se analizira. Glavne prednosti vzorcev DBS so enostaven in manj invaziven odvzem krvi, možnost samo-jemanja vzorcev, majhen volumen vzorca, zmanjšana možnost okužb ter zmanjšani stroški transporta in shranjevanja vzorcev.

NAMEN

Razvoj in validacija analizne metode za določanje protiepileptične učinkovine lamotrigina in njegovega glavnega presnovka 2-N-glukuronida v DBS, primerjava koncentracij vzorcev DBS s plazemskimi ter merjenje koncentracij analitov v bolnikih na terapiji z lamotriginom.

MATERIALI IN METODE

Vzorce DBS smo pripravljali iz 10 µL z analiti obogatene venske krvi zdravih prostovoljcev oz. venske krvi bolnikov,

ki se zdravijo z lamotriginom. Za ekstrakcijo analitov smo uporabili trdne nosilce, medtem ko smo koncentracijo analitov določali s pomočjo kromatografije ultra visoke ločljivosti s tandemskim masnim spektrometrom vrste trojni kvadrupol.

REZULTATI IN RAZPRAVA

Območje metode je bilo za oba analita od 0,1 do 20 µg/mL, z ustrezno linearnostjo (r^2> 0,985), točnostjo (94,0–110,6 %) in ponovljivostjo (dnevna 4,39–5,86 %; meddnevna 0,23–6,83 %). Za lamotrigin so bile plazemske koncentracije za približno 20 odstotkov nižje od koncentracij v vzorcih DBS, medtem ko so bile plazemske koncentracije lamotrigin 2-N-glukuronida približno dvakrat višje od koncentracij določenih v vzorcih DBS. Razlike v koncentracijah analitov v plazmi in polni krvi so posledica različnega porazdeljevanja analitov med plazmo in krvnimi celicami, kar je potrebno upoštevati pri klinični interpretaciji koncentracij vzorcev DBS. Bolniki, ki so prejemali od 100 do 400 mg lamotrigina na dan, so imeli v stacionarnem stanju minimalne koncentracije DBS za lamotrigin 2-N-glukuronid od 0,31 do 3,22 µg/mL in za lamotrigin od 1,83 do 9,39 µg/mL. Izmerjene koncentracije lamotrigina v vzorcih DBS so tudi ob upoštevanju 20 odstotne razlike med koncentracijo v plazmi in vzorcih DBS, v večjem delu znotraj referenčnega intervala lamotrigina, ki velja za plazmo in znaša od 2,5 do 15 µg/mL.

ZAKLJUČEK

Razvita analizna metoda se je izkazala kot enako primerna za merjenje analitov, kot metoda, ki uporablja večje volumne krvi oz. plazme, le da moramo upoštevati ugotovljeno razliko koncentracij, ki nastanejo kot posledica delne porazdelitve analitov v krvne celice. Metoda je uporabna pri individualizaciji odmerjanja lamotrigina v specifični populaciji kot so nosečnice.

VIR:

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