

## PREGLED LEK-LEK INTERAKCIJA IMUNOSUPRESIVNIH LEKOVA KOD PACIJENATA SA TRANSPLANTIRANIM BUBREGOM

**Maša Jović<sup>1\*</sup>, Katarina Danković<sup>1</sup>, Ivana Damnjanović<sup>2</sup>, Nikola Krstić<sup>1</sup>, Branka Mitić<sup>3,4</sup>, Nikola Stefanović<sup>2</sup>**

<sup>1</sup> Medicinski fakultet Niš, Univerzitet u Nišu, Srbija

<sup>2</sup> Katedra Farmacije, Medicinski fakultet, Univerzitet u Nišu, Niš, Srbija

<sup>3</sup> Katedra Interna medicina, Medicinski fakultet, Univerzitet u Nišu, Niš, Srbija

<sup>4</sup> Klinika za nefrologiju, Univerzitetski Klinički centar Niš, Niš, Srbija

\*jovic.98.masa@gmail.com

Lek-lek interakcije se često registruju kod pacijenata sa transplantiranim bubregom zbog polifarmacije i upotrebe imunosupresivnih lekova (1). Identifikovanje interakcija imunosupresiva je od velikog značaja zbog povećanog rizika za nastanak neželjenih efekata (2,3). Cilj našeg rada bio je pregled učestalosti i ozbiljnosti interakcija između imunosupresivne terapije i drugih propisanih lekova u toku prve godine nakon transplantacije bubrega. Istraživanje je obuhvatilo 99 pacijenata na trostrukoj imunosupresivnoj terapiji, koja se sastojala od takrolimusa, mikofenolat-mofetila/mikofenolne kiseline i kortikosteroida. Pregled lek-lek interakcija izvršen je na osnovu korišćenja tri različite baze podataka: British National Formulary (BNF), Lexicomp i Epocrates. Utvrđena je učestalost i ozbiljnost interakcija za svakog pacijenta pojedinačno u toku prve post-transplantacione godine. U cilju poređenja baza, izvršena je podela svih interakcija na blage, umerene i ozbiljne. Identifikovano je ukupno 130 interakcija, pri čemu je 33 utvrđeno BNF (24,24% ozbiljnih), 67 Lexicomp (ozbiljne nisu uočene) i 108 Epocrates bazom (11,11% ozbiljnih). Prosečan broj interakcija po pacijentu prema BNF-u je bio  $2,30 \pm 1,59$ , od toga blagih  $1,88 \pm 1,10$ , umerenih  $0,23 \pm 0,47$  i ozbiljnih  $0,19 \pm 0,67$ . Prema Lexicomp-u prosečan broj interakcija je bio  $7,00 \pm 2,36$ , blagih  $1,07 \pm 0,43$ , umerenih  $5,93 \pm 2,20$ . Razmatrajući Epocrates bazu, prosečan broj interakcija po pacijentu je bio  $12,72 \pm 3,82$ , blagih  $3,28 \pm 1,66$ , umerenih  $8,04 \pm 2,71$  i ozbiljnih  $1,39 \pm 0,98$ . Rezultati istraživanja su pokazali da je najveća učestalost umerenih interakcija, koje prema Lexicomp i Epocrates zahtevaju praćenje i/ili modifikaciju terapije. Pretraživanje različitih izvora informacija o interakcijama lekova doprinosi identifikaciji i proceni ozbiljnosti interakcija lekova, u cilju optimizacije imunosupresivne terapije.

### Literatura

1. Pehlivanli A, Eren-Sadioglu R, Aktar M, Eyupoglu S, Sengul S, Keven K, et al. Potential drug-drug interactions of immunosuppressants in kidney transplant recipients: comparison of drug interaction resources. Int J Clin Pharm 2022; 44(3):651-62
2. Moradi O, Karimzadeh I, Davani-Davari D, Shafiekhani M, Sagheb MM, Raees-Jalali GA. Drug-Drug Interactions among Kidney Transplant Recipients in The Outpatient Setting. Int J Organ Transplant Med 2020; 11(4):185-95.

3. Bril F, Castro V, Centurion IG, Espinosa J, Keller GA, Gonzalez CD, et al. A Systematic Approach to Assess the Burden of Drug Interactions in Adult Kidney Transplant Patients. Curr Drug Saf 2016; 11(2):156-63.

### **Zahvalnica**

Autori se zahvaljuju Ministarstvu nauke, tehnološkog razvoja i inovacija Republike Srbije (Br: 451-03-47/2023-01/200113), autori se takođe zahvaljuju Klinici za nefrologiju Univerzitetskog Kliničkog centra Niš.

## **REVIEW OF DRUG-DRUG INTERACTIONS OF IMMUNOSUPPRESSIVE DRUGS WITHIN KIDNEY TRANSPLANT RECIPIENTS**

**Maša Jović<sup>1\*</sup>, Katarina Danković<sup>1</sup>, Ivana Damnjanović<sup>2</sup>, Nikola Krstić<sup>1</sup>, Branka Mitić<sup>3,4</sup>, Nikola Stefanović<sup>2</sup>**

<sup>1</sup> Faculty of Medicine, University of Niš, Niš, Serbia

<sup>2</sup> Department of Pharmacy, Faculty of Medicine, University of Niš, Niš, Serbia

<sup>3</sup> Department of Internal Medicine, Faculty of Medicine, University of Niš, Niš, Serbia

<sup>4</sup> Clinic of Nephrology, Faculty of Medicine, University of Niš, Niš, Serbia

\*jovic.98.masa@gmail.com

Drug-drug interactions are frequently observed in kidney transplant recipients due to polypharmacy and the use of immunosuppressive drugs (1). Identifying the interaction of immunosuppressants is of great importance since they can increase the risk of adverse effects (2,3). This study aimed to review the frequency and severity of interactions between immunosuppressants and other prescribed drugs during the first year after kidney transplantation. The research included 99 patients on triple immunosuppressive protocol consisting of tacrolimus, mycophenolate mofetil/mycophenolic acid, and corticosteroid. Drug-drug interactions were identified by three different databases: British National Formulary (BNF), Lexicomp, and Epocrates. The frequency and severity of interactions were determined for each patient during the first post-transplantation year. To facilitate comparison between databases, all interactions were categorized as mild, moderate, or severe. The total number of identified interactions was 130, with 33 BNF (24.24% severe), 67 Lexicomp (without severe), and 108 Epocrates (11.11% severe). The average number of interactions per patient according to the BNF was  $2.30 \pm 1.59$ , whereas  $1.88 \pm 1.10$  were mild,  $0.23 \pm 0.47$  moderate, and  $0.19 \pm 0.67$  severe. According to the Lexicomp, the average number of interactions was  $7.00 \pm 2.36$ , of which  $1.07 \pm 0.43$  were mild, and  $5.93 \pm 2.20$  moderate. Considering Epocrates the average number of interactions was  $12.72 \pm 3.82$ , whereas  $3.28 \pm 1.66$  were mild,  $8.04 \pm 2.71$  moderate, and  $1.39 \pm 0.98$  severe. The findings showed that moderate interactions were the most frequent, which according to the Lexicomp and Epocrates require monitoring and/or modification of therapy. The exploration of various sources regarding drug interactions is necessary due to their identification assessment, but also to optimize immunosuppressive therapy.

### **References**

1. Pehlivanli A, Eren-Sadioglu R, Aktar M, Eyupoglu S, Sengul S, Keven K, et al. Potential drug-drug interactions of immunosuppressants in kidney transplant recipients: comparison of drug interaction resources. *Int J Clin Pharm* 2022; 44(3):651-62
2. Moradi O, Karimzadeh I, Davani-Davari D, Shafiekhani M, Sagheb MM, Raees-Jalali GA. Drug-Drug Interactions among Kidney Transplant Recipients in The Outpatient Setting. *Int J Organ Transplant Med* 2020; 11(4):185-95.
3. Bril F, Castro V, Centurion IG, Espinosa J, Keller GA, Gonzalez CD, et al. A Systematic Approach to Assess the Burden of Drug Interactions in Adult Kidney Transplant Patients. *Curr Drug Saf* 2016; 11(2):156-63.

### **Acknowledgements**

The authors would like to thank the Ministry of Science, Technological Development and Innovation of the Republic of Serbia (Grant No: 451-03-47/2023-01/200113), the authors would also like to thank the Clinic of Nephrology, Clinical Center Niš.