

Drug interactions – a cross-section of the situation at the primary level of health care in Montenegro

Ninoslava Lalatovic^{1*}, Snezana Pantovic¹, Masa Marojevic²

¹ University of Montenegro, Faculty of Medicine, Krusevac bb 81000 Podgorica, Montenegro

² Special Hospital for Orthopedics, Neurosurgery and Neurology "Vaso Čuković", Risan, Montenegro

Introduction

Polypharmacy, the simultaneous use of several drugs by one person, is becoming more common among the elderly. That is due to the presence of multiple comorbidities in such patients, which requires a more complex treatment regimen (Wastesson et al., 2018). As much as polypharmacy is justified in some situations, it in itself carries a risk. The frequency of side effects and drug interactions is higher, and the compliance is worse. When you use more than five drugs together, in theory, there is a 50% probability that an interaction will occur and when using more than seven drugs, the odds increase to 100%. 20% of these interactions consider having clinical significance (Nobili et al., 2009; Rollason and Vogt, 2003). A clinically significant interaction is the one where a particular therapeutic combination leads to an unexpected change or condition in the patient. They most often occur at the level of metabolism (pharmacokinetic interaction) or at the level of the target site of action (pharmacodynamic interaction), which can increase or decrease the activity of the drug, which can result in either side effects or lack of therapeutic effect. Given that these are interactions that can seriously endanger the patient's condition, it is necessary to take adequate measures to prevent them, in which pharmacists can play an important role (Seymour and Routledge, 1998). Due to the growing popularization of "nutrients, dietary supplements" in the media, patients often take additional preparations in addition to prescribed medications. That is why it is crucial to know what the patient uses from over-the-counter (OTC) medications since these medications can also have a high potential for interacting with prescribed medications (Delafuente, 2003). Considering the above, we wanted to examine the frequency of drug interactions in patients in Podgorica. The research was

conducted in 2018 and 2021 on patients in the primary level of health care (PHC) in Podgorica to correlate the frequency of interactions.

Materials and methods

Materials

The prospective study was conducted on patients in primary health care institutions in Podgorica in the period November 2018 - February 2019 and May 2021 - April 2022. The inclusion criteria for the study were that respondents voluntarily agreed to participate and that they were confident in the type of drug they used on the day of the survey. After that, they started filling out a questionnaire in which they had to state: their gender, age in years, medicines, supplements, and herbal medicines they use.

Method

After obtaining the data, we split the respondents into two groups those who were older and those who were younger than 65 years old. Then we enter the data from the questionnaire into an excel spreadsheet. After that, for each respondent individually at the website www.drugs.com, Interaction checker section, we enter the complete therapy that the respondent was using. Only the so-called major interactions, clinically significant interactions (CSI) that could be even life-threatening, were taken into account. After that, we processed the data in Microsoft Excel.

Results and discussion

In the 2018 survey, 106 respondents participated, 39 men (36.8%) and 67 women (63.2%). Out of the total

*nina.lalatovic32@gmail.com

number, 62.3% were ≥ 65 years old, of which 34.9% of the respondents were male. The mean age of participants < 65 years was 55 ± 8 years, while the average age of participants ≥ 65 years was 75 ± 6 years. The average number of drugs used by subjects ≥ 65 years is 7 ± 2 , compared to subjects < 65 years where 5 ± 1 (Lalatovic and Duborija Kovacevic, 2019).

In the 2021 survey, 110 respondents met the conditions for participation, namely 68 men (61.82%) and 42 women (38.18%). Out of the total number, 48.18% were ≥ 65 years old, of which 60.38% of the respondents were male. The mean age of subjects < 65 years was 55 ± 6 , while the mean age of participants ≥ 65 years was 69 ± 3 years. The average number of drugs used by subjects ≥ 65 years is 7 ± 2 , compared to subjects < 65 years, where it was 5 ± 2 .

When we compare these data, we conclude that 22.67% fewer respondents older than 65 years old participated in the 2021 survey, that they were younger on average, and that the participation of male respondents was more dominant compared to 2018. On the other hand, the average number of used drugs was almost the same in both studies.

In the 2018 study, we observed at least one CSI in 15% of respondents < 65 and in 34.8% of respondents ≥ 65 years of age. The average number of interactions in younger participants was two interactions per patient and 1.7 interactions per patient in older group. The minimum number of registered interactions was 1, while the maximum number of observed interactions was 5 in subjects < 65 and 4 in subjects ≥ 65 years. Most interactions were of the pharmacodynamic type (spironolactone and ramipril) or pharmacokinetic at the metabolic level (amiodarone and simvastatin) (Lalatovic and Duborija Kovacevic, 2019).

One CSI was observed in 8.77% of subjects < 65 years, while in subjects ≥ 65 , 18.87% was observed, with an average number of 1.3 interactions per patient in older subjects, showing data from 2021. The minimum number of registered interactions was 1, while the maximum number of observed interactions in the participants ≥ 65 years was 3. All interactions were pharmacodynamic, usually between spironolactone and angiotensin-converting enzyme inhibitors or angiotensin receptor antagonists, antiplatelet drugs and anticoagulants, or amiodarone and diuretics.

When we compare these data, we can see that the frequency of CSI in both studies was higher in respondents older than 65 years, by 56.9% and 53.53%, respectively, which is the consequence of using more drugs in this population. We also observed 45.78% fewer interactions in patients ≥ 65 years and 41.53% fewer in subjects < 65 years of age in 2021 compared to 2018 data. However, it should be taken into account that in the

research from 2018, there were more patients older than 65, so this percentage reduction in the number of interactions is realistically less but certainly less than the one from 2018. What could be noticed is that the use of supplements (vitamins and minerals) is much higher in 2021 compared to 2018, which is probably due to the COVID 19 pandemic.

Conclusion

The results of this research indicate that the frequency of CSI in PHC is still higher among respondents ≥ 65 years, with the fact that compared to the results from 2018, this percentage is significantly lower. The reason may be a higher degree of adherence to EU therapeutic guidelines when prescribing therapy, better cooperation and communication between doctors and also, doctors and pharmacists. The results of our research indicate the need to create a database that would include reference institutions such as the Institute of Medicines and Medical Devices of Montenegro, the Institute of Public Health, and primary health care institutions for further monitoring and reducing the incidence of CSI to a minimum, and thus savings in health care.

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