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Original Study

Frequency and Predictors of Potential Drug - Drug Interactions in Hospitalized Patients With Parkinson's Diseases

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SUMMARY

Introduction: Patients with Parkinson's disease are exposed to higher number of drugs on average than other elderly persons. Levodopa, of the mainstay of Parkinson's disease therapy, is frequently interacting with numerous drugs.
Aim: The aim of this study was to identify predictors of potential drug-drug interactions (pDDIs) in hospitalized patients suffering from Parkinson's disease (PD).
Material and Methods: This was a academic retrospective cross-sectional study in PD patients hospitalized at the Clinic of Neurology, Clinical Center Kragujevac. Medical records of hospitalized patients during the period 1.1.2017 - 31.12.2019 were analysed. The pDDIs were identified by means of Micromedex andLexi-Interact online softwares, and multivariate regression methods were used to reveal potential predictors of number of pDDIs per patient.
Results: Micromedex detected 160 different pDDIs in 77.8% of 72 patients with PD. The most frequent pDDIs were those that involved aspirin (with bisoprolol, sertraline and perindopril). Predictors of pDDIs in general was total number of drugs, while use of antidepressants presented a significant risk factor for major pDDIs. Lexi-Interact revealed 310 pDDIs in 98.6% of patients. The three most common pDDIs were with levodopa (bisoprolol, clonazepam, perindopril). Total number of drugs, number of co-morbidities, hospitalization at the neurodegenerative ward, and use of antipsychotics were identified as the relevant predictors of pDDIs. Lexi-interact software detected significantly more pDDIs than Micromedex ($p<0.001$).
Conclusion: Neurologists should pay special attention when deciding whether to administer new drug to a PD patient with multiple comorbidities, hospitalized in a neurodegenerative ward and/or taking antidepressant or antipsychotic drugs.

Keywords: Parkinson's Disease, Potential Drug-Drug Interactions, Predictors, Micromedex, Lexi-Interact

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INTRODUCTION

Patients with Parkinson's disease (PD) are exposed to higher number of drugs on average than other elderly persons because apart from chronic non-communicable diseases that usually go with advanced age they need several drugs for controlling symptoms of the disease itself [1,2]. The conventional pharmacotherapy of Parkinson's disease includes a variety of drugs that act by different mechanisms with the common outcome – increase in the level and activity of dopamine in central nervous system (CNS) (levodopa combined with DOPA decarboxylase inhibitors, dopamine agonists, catechol-O-methyltransferase (COMT) inhibitors, monoamine oxidase B (MAO-B) inhibitors, etc.) [3]. Since PD is usually associated with a number of physical and mental disorders, especially in the elderly, favoring the simultaneous use of many other drugs, such as cardiovascular drugs, antidiabetic drugs, psychotropic drugs (i.e. antipsychotics, antidepressants, sedatives, anti-dementia drugs), analgesics, antibiotics, etc., drug-drug interactions are likely to occur [4].

Drug-drug interactions represent the changes in the effects of one drug which occur as a consequence of concomitant therapy with another drug. Contraindicated and major interactions to be avoided have the greatest clinical relevance, although moderate interactions also should be monitored with extreme caution [5]. Nowadays, potential drug-drug interactions (pDDIs) could be detected by online checkers such as Micromedex® [6], Lexi-Interact [7], Medscape [8], Epocrates [9], etc.
Numerous potential drug-drug interactions (pDDIs) interactions of antiparkinsonian medications are well-known. Levodopa is prone to pharmacokinetic interactions at the level of absorption (neutral amino acids, antacids, proton pump inhibitors and iron preparations), distribution (aromatic amino acid decarboxylase inhibitors) or metabolism (MAO and COMP inhibitors) [10]. Particularly serious are potential interactions of levodopa with MAO inhibitors, whose simultaneous use should be avoided due to the high risk of hypertensive crisis [11]. Due to pDDIs, concomitant use of antiparkinsonian drugs with diuretics and calcium channel blockers in patients with PD and associated hypertension is certainly not desirable [12]. Also, possible occurrence of serotonin syndrome is the reason why selegiline should not be used concomitantly with fluoxetine and tricyclic antidepressants [13,14].

Certain risk factors for occurrence of pDDIs in hospitalized patients were previously recognized, such as higher number of prescribed medications, longer duration of hospitalization and comorbidity [5,15,16]. However, to our best knowledge there are no published studies that have investigated potential drug-drug interactions in patients with PD. Therefore, this study was aimed at determining the prevalence and risk factors for each category of pDDIs in hospitalized patients with PD.

MATERIAL AND METHODS

Ethical principles

This research was approved by Ethics Committee of Clinical Center Kragujevac (CCK) (No.01/14886).

Study design and setting, patients and data collection

This study was designed as an academic retrospective cross-sectional study in PD patients admitted to the Clinic of Neurology, Clinical Center Kragujevac (CCK). We reviewed medical records of patients with PD who were hospitalized during the period 1.1.2017 - 31.12.2019.
Inclusion criteria were diagnosis of PD and patients with two or more prescribed drugs during the hospitalization. The study also included patients hospitalized for another reason unrelated to PD if they had been previously diagnosed with the disease. The only exclusion criterion was death of a patient during hospitalization.
The following data were collected from the patient medical files: demographic characteristics (gender and age in years), characteristics of hospitalization (reason for hospitalization, ward where the patient was treated (neurological intensive care unit (NICU) or department for neurodegenerative disease), length of hospitalization (in days)), clinical characteristics of PD (bradykinesia, muscular rigidity, resting tremor, postural instability, duration of disease in years), non-motor symptoms and signs of PD (cognitive impairment, pain, falls, uro-

genital dysfunction, orthostatic hypotension, sleep disorder, constipation, hallucinations), comorbidities (hypertension (HTA), other cardiovascular diseases (coronary artery disease, arrhythmia, valve disease, heart failure), diabetes mellitus 2 (DM2), drug-related allergies, thyroid disorder), laboratory parameters during the first day of hospitalization (glycaemia, creatinine, urine ketone bodies) and characteristics of prescribed drugs (number of drugs, pharmacological group of drugs such as antiplatelet drugs, antihypertensive drugs, antidepressants, antipsychotics, antacids, antiparkinsonian drugs, …).

Identificiation and classification of the potential drug-drug interactions

The potential drug-drug interactions (pDDIs) from medical files were identified by online interaction checker softwares Micromedex® [6] and Lexi-Interact [7]. Micromedex® 2.0 classifies pDDIs into 4 categories according to severity (contraindicated, major, moderate, minor) and in 3 categories according to scientific evidence (excellent, good, fair). Lexi-Interact interaction checker recognizes the following categories of pDDIs: combination of drugs to be avoided (x), major (d), pDDIs which require monitoring of therapy (c), interactions with no action needed (b) and without evidence of interaction (N/A). According to scientific documentation, thisese checker divides the pDDIs into those with excellent, good, fair and poor evidence. After the pDDIs were recorded, additional variables were determined: number of pDDIs discovered by both checkers as well as the number of pDDIs by category with respect to severity and scientific documentation. The proportion of patients who were exposed to each type of pDDIs, the frequency of each individual pDDIs and type of pDDI were the most frequent were also determined.

Statistical analysis

Descriptive data were summarized as percentages, median with interquartile rank and mean with standard deviation. A multiple linear regression, method of backward elimination was used to analyze potential risk factors for the number of pDDIs per patient. The statistical significance of the regression model was determined based on the values of F (analysis of variance) and R2 (percentage of variability of the outcome explained by the model). The extent of the impact of potential risk factors on the number of pDDIs per patient was estimated by unstandardized B coefficients and 95% confidence intervals (CI). The statistical analysis was done in the statistical program, SPSS version 18.

RESULTS

A total of 72 patients were included in this study and they were admitted to the hospital for the following reasons: (1) to clearly confirm a diagnosis of PD, (2) to treat the exacerbation of PD or (3) to treat comorbidities, such as acute ischemic stroke (AIS) (14 patients - 19.44%), cerebral small blood vessels disease (3 - 4.17%), brain tumors (1 - 1.39%) and spinal cord with peripheral nervous system disorders (8 - 11.11%). Most patients who were hospitalized in the neurological intensive care unit (NICU) were admitted for AIS while most of the other patients were treated at the department of neurodegenerative diseases. All patients with PD had bradykinesia. Non-tremor dominant type of PD was present in 60.0% of patients. At least one non-motor symptom or sign of PD was observed in 45 (62.5%) patients. Each patient from the study group received at least one antiparkinsonian drug. Other demographic, clinical, and laboratory characteristics of patients as well as the characteristics of hospitalization and prescribed drugs are shown in the Table 1.

Micromedex® identified at least one pDDIs in 77.8% of patients. Majority of patients were exposed to moderate (62.5%) and major (58.3%) pDDIs. A total of 159 different pDDIs were classified as following: contraindicated 1 (0.63%), major 67 (42.14%), moderate 84 (52.83%), and minor pDDIs 7 (4.40%). Lexi-Interact detected pDDIs in 98.6% of patients. The highest proportions of patients were exposed to major (41.7%) interactions and interactions that required therapy monitoring (93.1%). A total of 310 pDDIs were detected with this checker in the following order: those to be avoided (x) - 2 (0.64%), major interactions (d) 33 (10.64%), interactions requiring therapy monitoring –(c) 247 (79.68%), no action required (b) 27 (8.71%), and unknown interactions - a 1 (0.32%) Fair scientific evidence was shown for the majority of pDDIs (Micromedex® - 68.1%, Lexi-Interact – 93.1%) (Table 2).Lexi-interact software detected significantly

Table 1. Characteristics of the study sample of patients with Parkinson´s disease

IQR - interquartile range
NICU - neurological intensive care unit
PD - Parkinson´s disease

Demographic characteristics	
Gender	Male 38 (52.8%) Female 34 (47.2%)
Age (median(IQR)); Mean ± SD	73.0 (67.25-79.5); 72.99 ± 8.25
Characteristics of hospitalization	
Cause of hospitalization	Diagnostics of PD 15 (20.8%) Exacerbation of PD 31 (43.1%) Other causes 26 (36.1%)
Department	NICU 17 (23.6%) Others 55 (76.4%)
Length of hospitalization	13.00 (9.00-17.00); 14.29 ± 7.86
Number of diagnosis	5.00 (3.00-6.00); 5.03 ± 2.39
Clinical characteristics of patients with PD	
Muscular rigidity	59 (90.8%)
Postural instability	46 (68.7%)
Rest tremor	33 (50.8%)
Duration of PD (years)	6.5 (1.00-10.00); 6.75 ± 5.66
Tremor dominant PD	26 (40.0%)
Age (median(IQR)); Mean ± SD	73.0 (67.25-79.5); 72.99 ± 8.25
Non-motor symptoms of PD	
Cognitive impairment	23 (31.9%)
Pain	16 (22.2%)
Falls	15 (20.8%)
Urogenital dysfunction	7 (9.7%)
Orthostatic hypotension	6 (8.3%)
Sleep disorder	5 (6.9%)
Constipation	4 (5.6%)
Hallucination	3 (4.2%)
Comorbidities	
Hypertension	46 (63.9%)
Cardiovascular disease	30 (41.7%)
Diabetes mellitus 2	17 (23.6%)
Drug allergies	14 (19.4%)
Thyroid disorder	5 (6.9%)
Laboratory parameters	
Hyperglycemia	27 (38.6%)
High creatinine level	17 (24.6%)
Urine ketone bodies	12 (21.1%)
Characteristics of prescribed drugs	
Number of prescribed drugs	7.00 (5.00-9.75); 7.61 ± 3.30
Receiving antiplatelet drugs	48 (66.7%)
Receiving antidepressants	28 (38.9%)
Receiving antipsychotics	15 (20.8%)
Receiving antacids	15 (20.8%)
Number of antiparkinsonian drugs	One - 31 (43.1%) Two - 33 (45.8%) Three - 8 (11.1%)

more pDDIs than Micromedex® (χ22=54. 000, p<0.001).

The most common types of pDDIs according to severity and scientific evidence for both checkers are shown in the Table 3. The contraindicated and pDDIs to be avoided

are also shown in the Table 3. Aspirin was the most frequent drug engaged in pDDIs with an occurrence of 38 (23.90%) of all pDDIs), according to Micromedex®. According to Lexi-Interact checker, levodopa was the most frequent drug involved in pDDIs (37 (11.93%)).

The following independent and confounding variables were entered into 6 models to test their effect on the rate of pDDIs: demographic characteristics (gender, age), characteristics of hospitalization (reason, ward, length of hospitalization), non-motor symptoms of PD (cognitive impairments), comorbidities (total number of patient's diagnosis, HTA or other cardiovascular diseases), laboratory parameters (serum creatinine level), characteristics of prescribed drugs (total number of drugs used simultaneously, use of antidepressants, antipsychotics and antiplatelet drugs, number of antiparkinsonian drugs, and drug allergy. The total number of pDDIs according to Micromedex® and Lexi-interact checker respectively was used as dependent variable in a linear regression model. Significant factors identified by the regression model based on Micromedex® findings ((R2 = 0.765, F = 70.376, p < 0.001) were number of drugs, number of antiparkinsonian drugs and HTA. The same factors were included in the model for the number of major pDDIs (R2 = 0.584, F = 22.437, p < 0.001) and significance was found for number of drugs and number of patient's diagnosis. When we examined the influence of these factors on the number of moderate pDDIs (R2 = 0.696, F = 49.721, p < 0.001) number of drugs and use of antidepressants turned to have significant influence. Predictors of the total number of pDDIs according to Lexi-interact (R2 = 0.849, F = 57.974, p = 0.000) were number of drugs, a ward where the patient was treated, number of comorbidities per patient, and use of antiplatelet drugs and antipsychotics. In the linear regression model for the number of major pDDIs (R2 = 0.534, F = 18.364, p < 0.001), potential predictors were number of drugs and use of antipsychotics. For moderate pDDIs(R2 = 0.807, F = 52.535, p < 0.001), the important factors were number of drugs, hospitalization in the neurodegenerative ward, number of comorbidities and use of antiplatelet drugs. Unstandardized B coefficients, 95% CIs and p values were shown only for factors that were significant (Table 4).

DISCUSSION

The most commonly identified pDDIs with Micromedex® were those that involved aspirin (with bisoprolol, sertraline, perindopril). Only one contraindicated pDDI (pCDDI) was found, i.e. amantadine with potassium chloride. Predictor of pDDIs in general was number of drugs, while use of antidepressants was significant risk factor for major pDDIs. The

Micromedex®				Lexi-Interact			
pDDI[1]	Number and % of patients	Median (IQR[2])	Mean (±SD[3])	pDDI	Number and % of patients	Median (IQR)	Mean ±SD
Number of pDDIs	56 (77.8%)	3.00 (1.00-6.75)	4.32 (4.99)	Number of pDDIs	71 (98.6%)	8.5 (4.00-17.50)	11.64 (9.45)
pCDDIs[4]	3 (4.2%)	0.00 (0.00-0.00)	0.4 (0.20)	Avoid (x)	4 (5.6%)	0.00 (0.00-0.00)	0.6 (0.231)
Major	42 (58.3%)	1.00 (0.00-3.00)	1.76 (2.43)	Major (d)	30 (41.7%)	0.00 (0.00-1.00)	0.79 (1.21)
Moderate	45 (62.5%)	1.00 (0.00-3.00)	2.35 (3.04)	Monitor therapy (c)	67 (93.1%)	7.00 (3.25-14.00)	9.64 (8.14)
Minor	9 (12.5%)	0.00 (0.00-0.00)	0.15 (0.43)	No action (b)	50 (69.4%)	1.00 (0.00-1.00)	1.11 (1.18)
Excellent	22 (30.6%)	0.00 (0.00-1.00)	0.47 (0.87)	No known interaction (a)	3 (4.2%)	0.00 (0.00-0.00)	0.4 (0.20)
Good	41 (56.9%)	1.00 (0.00-2.75)	1.57 (2.01)	Excellent	18 (25.0%)	0.00 (0.00-0.75)	0.40 (0.80)
Fair	49 (68.1%)	1.00 (0.00-3.00)	2.29 (2.87)	Good	39 (54.2%)	0.0 (0.00-2.00)	1.14 (1.48)
				Fair	67 (93.1%)	7.0 (3.00-13.00)	9.18 (7.75)
				Poor	44 (61.1%)	1.00 (0.00-1.00)	0.85 (0.90)

Table 2. Potential drug-drug interactions detected by Micromedex® and Lexi-Interact checkers

[1] potential drug-drug interactions
[2] interquartile range
[3] standard deviation
[4] potentially contraindicated drug-drug interactions

Table 3. Examples of the most frequent potential drug-drug interactions detected by Micromedex® and Lexi-Interact

[1] potential drug-drug interactions

Micromedex			Lexi-Interact		
The most frequent pDDIs[1]			The most frequent pDDIs		
Drug 1-Drug 2	Scientific evidence	No and % of patients	Drug 1-Drug 2	Scientific evidence	No and % of patients
Aspirin-Bisoprolol	Good	20 (27.78)	Levodopa-Bisoprolol	Fair	26 (36.11)
Aspirin-Sertraline	Excellent	13 (18.05)	Levodopa-Clonazepam	Poor	20 (27.78)
Aspirin-Perindopril	Fair	12 (16.7)	Levodopa-Perindopril	Fair	15 (20.83)
Aspirin-Furosemide	Good	11 (15.28)	Levodopa-Ropinirol	Fair	13 (18.05)
Aspirin-Metformin	Fair	9 (12.5)	Aspirin-Sertraline	Fair	13 (18.05)
Bisoprolol-Metformin	Good	6 (8.33)	Levodopa-Amlodipine	Fair	13 (18.05)
Metformin-Perindopril	Fair	6 (8.33)	Levodopa-Furosemide	Fair	12 (16.7)
Aspirin-Diclofenac	Fair	6 (8.33)	Levodopa-Lorazepam	Poor	12 (16.7)
Contraindicated pDDI			Avoid (x)		
Amantadine-Potassium chloride	Fair	3 (4.17)	Potassium chloride-Clozapine	Fair	3 (4.17)
Major pDDIs			Potassium chloride-Risperidone	Fair	1 (1.39)
Aspirin-Sertraline	Excellent	13 (18.05)	Major (d)		
Aspirin-Furosemide	Good	11 (15.28)	Levodopa-Clozapine	Excellent	10 (13.89)
Aspirin-Metformin	Fair	9 (12.5)	Aspirin-Diclofenac	Good	5 (6.94)
Moderate pDDIs			Monitor therapy (c)		
Aspirin-Bisoprolol	Good	20 (27.78)	Levodopa-Bisoprolol	Fair	26 (36.11)
Aspirin-Perindopril	Fair	12 (16.7)	Levodopa-Perindopril	Fair	15 (20.83)
Bisoprolol-Metformin	Good	6 (8.33)	Levodopa-Ropinirol	Fair	13 (18.05)
Metformin-Perindopril	Fair	6 (8.33)	Aspirin-Sertraline	Fair	13 (18.05)
Minor pDDIs			Levodopa-Amlodipine	Fair	13 (18.05)
Aspirin-Ranitidine	Excellent	3 (4.17)	No action (b)		
Cyanocobalamin-Ascorbic acid	Good	2 (2.78)	Levodopa-Clonazepam	Poor	20 (27.78)
Folic-Ascorbic acid	Good	2 (2.78)	Levodopa-Lorazepam	Poor	12 (16.7)

most frequently identified pDDIs with Lexi-Interact were levodopa/ bisoprolol, levodopa/ clonazepam and levodopa/perindopril). Potassium chloride participated in 2 pCDDIs (with clozapine and risperidone). Total number of drugs, number of comorbidities, hospitalization at the neurodegenerative ward, and use of antipsychotics were identified as relevant predictors of pDDIs.

A large number of studies investigated prevalence and risk factors for the occurrence of pDDIs, but as mentioned previously, none of them was devoted to patients with PD so far. The frequency of potential interactions among neurological patients in the literature ranged from 35,5% (16) to 96% [17], which is consistent with our study. Also, predictors of number of interactions per patient in our study almost coincide with the results of the other authors. Higher number of prescribed medications and comorbidities increased the risk of pDDIs both among neurological patients [5,16,17] and patients treated for other diseases [15,18]. Certain drug groups, such as antiplatelet drugs [19] and antipsychotics [20], showed high potential for drug-drug interactions due to their specific pharmacokinetic and pharmacodynamic profile. This could explain our results where use of antipsychotics was associated with the occurrence of major pDDIs detected by Lexi-Interact tool, while the use of antiplatelet drugs contributed to the major pDDIs identified by Micromedex®.

Psychosis is one of the most common non-motor disorders in PD patients, which occurs in a small number of patients as a consequence of the adverse effects of antiparkinsonian drugs [21]. It is well-known

pDDI[1] checker used and severity of pDDIs	Predictor variable	Unstandardized coefficients	CI[2] (95%)	Sig. p
Number of Micromedex pDDIs	Number of drugs	1.389	1.190 - 1.587	0.000
	Number of antiparkinsonian drug	-0.901	−1.780 - −0.023	0.044
	HTA3	-1.351	−2.564 - −0.138	0.030
Number of Micromedex major PDDIs	Number of drugs	0.495	0.348 - 0.642	0.000
	Antidepressants	1.021	0.182 - 1.859	0.018
Number of Micromedex moderate pDDIs	Number of drugs	0.767	0.641 - 0.894	0.000
	Antidepressants	-1.114	−1.979 - −0.250	0.012
Number of Lexi-interact pDDIs	Number of drugs	2.276	1.925 - 2.627	0.000
	Department	-4.430	−6.819 - −1.988	0.001
	Number of diagnosis	0.669	0.173 - 1.165	0.009
	Antiplatelet	-2.681	−4.841 - −0.521	0.016
	Antipsychotics	3.163	0.872 - 5.455	0.008
Number of Lexi-Interact major pDDIs	Number of drugs	0.158	0.084 - 0.232	0.000
	Antipsychotics	1.742	1.221 - 2.264	0.000
Number of Lexi-Interact monitor therapy pDDIs	Number of drugs	1.801	1.466 - 2.136	0.000
	Department	-3.160	−5.259 - −1.061	0.004
	Number of diagnosis	0.520	0.055 - 0.985	0.029
	Antiplatelet	-2.074	−4.019 - −0.130	0.037

Table 4. Predictors of pDDIs discovered by multivariate linear regression

[1] potential drug-drug interactions
[2] confidence interval
[3] hypertension

that typical antipsychotics, being predominantly antagonists of the dopamine receptors are contraindicated for use in patients with PD [22]. Therefore, atypical antipsychotics with marked antagonistic effect on 5-HT2A serotonin receptors, such as clozapine and quetiapine are being used today to treat psychosis in PD patients [21]. Several studies indicate that clozapine effectively treats psychosis in patients with PD and even improves tremor without exacerbating other motor symptoms of the disease [23,24]. However, rare cases of worsening of the motor symptoms of the disease have been reported following clozapine administration [25]. This impairment is due to antagonistic effect of clozapine on dopamine receptors (although less intense than typical antipsychotics, clozapine binds to dopamine receptors), which weakens the effect of levodopa; this happened potentially in 10 patients from our study who used clozapine and levodopa simultaneously. In addition, regular blood counts are required in patients using clozapine due the neutropenia that often accompanies its use [24]. Therefore, the first step in treating psychosis in patients with PD should be to reduce the dose of existing antiparkinsonian drugs to the minimum effective, and only then to administer atypical antipsychotics [21].

By analyzing the pDDIs of our patients in Lexi-Interact tool, interactions between levodopa and antihypertensive drugs were particularly frequent. Concomitant use of levodopa with antihypertensive drugs increases the risk of orthostatic hypotension. Although interactions of levodopa with drugs from all major antihypertensive drug groups (diuretics, calcium antagonists, and angiotensin-converting-enzyme (ACE) inhibitors) are categorized as moderate, Bitner et al [12] believe that the first-line therapy of hypertension in PD should be based ACE inhibitors or beta-blockers, because of the lowest risk for hypotension.

Micromedex® and Lexi-Interact checkers are among the most sensitive and specific tools for detecting and evaluating of pDDIs [26,27]. It is known that there are important differences between various types of checkers [27,28]. We also have to emphasize significant differences between Micromedex® and Lexi-Interact online checkers in detecting potential interactions among patients with Parkinson's disease. Much higher number of potential interactions was detected by means of Lexi-Interaction checker (310 pDDIs) compared to Micromedex® (159 pDDIs). The pDDIs of levodopa with antihypertensive drugs detected by Lexi-Interact were not detected using Micromedex®. Furthermore, only 10.64% of the interactions detected by Lexi-Interact were major severity, while major interactions in Micromedex® were more prevalent (42,14%). Significant differences were also observed previously after comparing Micro-

medex® with Epocrates and Medscape interaction checkers [15]. Although each of these screening tools has satisfactory sensitivity and specificity, there is a need for the combined use of two or more checkers to avoid misdetection of pDDIs.

Our study was retrospective, so limited number of available variables, could have influenced the results. The study was single-centered and with relatively small number of patients, which limits generalizability of the results. Only hospitalized patients were included in the study, and their therapy was influenced by the availability of drugs at the hospital's pharmacy, introducing certain degree of bias.

CONCLUSION

This study revealed high frequency of pDDIs in patients with PD. Performance of the two online checkers used in the study was very different, underlying necessity to use them both, otherwise some important pDDIs could be missed. The main predictors of pDDIs were total number of drugs, number of comorbidities, hospitalization at the neurodegenerative ward and therapy with antidepressants or antipsychotics. Neurologists should pay special attention when deciding whether to administer new drug to a PD patient with multiple comorbidities, hospitalized in a neurodegenerative ward and/or taking antidepressant or antipsychotic drugs.

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CONFLICT OF INTEREST

All authors declare no conflict of interest.

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Učestalost i prediktori potencijalnih interakcija između lekova kod hospitalizovanih pacijenata sa Parkinsonovom bolešću

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KRATAK SADRŽAJ

Uvod: Bolesnici sa Parkinsonovom bolešću su u proseku izloženi većem broju lekova u odnosu na ostale starije osobe. Levodopa, koja predstavlja glavni oslonac u terapiji Parkinsonove bolesti, često stupa u interakcije sa brojnim lekovima.
Cilj: Cilj ove studije je bio da se identifikuju prediktori potencijalnih interakcija između lekova (PIL) kod hospitalizovanih pacijenata sa Parkinsonovom bolešću (PB).
Metodologija: Ovo je bila akademska retrospektivna studija preseka na pacijentima sa Parkinsonovom bolešću koji su bili hospitalizovani na Klinici za neurologiju, Kliničkog centra u Kragujevcu. Analizirani su medicinski kartoni pacijenata koji su bili hospitalizovani u periodu od 01.01.2017.- 31.12.2019. godine. PIL su identifikovane pomoću Micromedex i Lexi-Interact onlajn softvera, a metode multivarijantne regresije su korišćene za otkrivanje prediktora za pojavu PIL-ova.
Rezultati: Micromedex-om je otkriveno 160 različitih PIL-ova kod 77,8% od ukupno 72 pacijenta sa PB. Najčešće PIL su bile one koje su uključivale aspirin (sa bisoprololom, sertralinom i perindoprilom). Prediktori za pojavu svih oblika PIL-ova bili su ukupan broj lekova, dok je upotreba antidepresiva bila značajan faktor rizika za teške PIL. Primenom Lexi-Interact-a otkriveno je 310 različitih PIL-ova kod 98,6% pacijenata. Tri najčešće PIL uključivale su levodopu (sa bisoprololom, klonazepamom i perindoprilom). Ukupan broj lekova, broj komorbiditeta, hospitalizacija na odeljenju za neurogenerativne bolesti i upotreba antipsihotika identifikovani su kao relevantni prediktori za pojavu PIL-ova. Lexi-Interact softver je otkrio statistički značajno više PIL-ova od Micromedexa ($p<0,001$).
Zaključak: Neurolozi treba da obrate naročitu pažnju kada se odlučuju da li će primeniti novi lek pacijentu sa PB koji ima višestruke komorbiditete, koji je hospitalizovan na odeljenju za neurodegenerativne bolesti i/ili uzima antidepresive ili antipsihotike.

Ključne reči: Parkinsonova bolest, potencijalne interakcije između lekova, prediktori, Micormedex, Lexi-Interact

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