https://doi.org/10.31925/farmacia.2026.2.21 **ORIGINAL ARTICLE**

POTENTIALLY CLINICALLY RELEVANT DRUG INTERACTIONS IN POST-STROKE REHABILITATION PATIENTS: A PROSPECTIVE STUDY

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Manuscript received: November 2025

Abstract

Post-stroke rehabilitation patients require complex pharmacotherapy, increasing their risk of potential drug-drug interactions (pDDIs). The study aimed to assess the prevalence, types, and predictors of clinically relevant pDDIs in post-stroke patients during rehabilitation. This prospective observational study was conducted at the Institute for Physical Medicine, Rehabilitation, and Orthopaedic Surgery. Clinically relevant pDDIs were identified using Lexi-Drugs. The study included 217 post-stroke rehabilitation patients (86.2% ischaemic stroke). At least one clinically relevant pDDI was present in 96.3% of ischaemic and 76.7% of haemorrhagic stroke patients ($p < 0.001$). Ischaemic stroke history was an independent predictor for higher pDDI risk (OR 5.3; $p < 0.05$). The study revealed a high prevalence of potentially clinically relevant pDDIs in post-stroke rehabilitation patients, particularly among those with ischaemic stroke. Additionally, comorbidities such as pneumonia or constipation increased the risk of pDDIs occurrence. Given the complexity of post-stroke pharmacotherapy, systematic screening and management strategies are crucial to minimise the risk of preventable adverse drug interactions and improve rehabilitation outcomes.

Rezumat

Pacienții aflați în recuperare după accidentul vascular cerebral (AVC) necesită regimuri farmacoterapeutice complexe, ceea ce crește riscul apariției interacțiunilor medicamentoase potențiale (pDDIs). Acest studiu a avut ca obiectiv evaluarea prevalenței, tipurilor și factorilor predictivi ai pDDI la pacienții post-AVC. Acest studiu observațional prospectiv a fost realizat în cadrul Institutului de Medicină Fizică, Reabilitare și Chirurgie Ortopedică. Interacțiunile medicamentoase potențial relevante clinic au fost identificate utilizând baza de date Lexi-Drugs. În studiu au fost incluși 217 pacienți aflați în recuperare post-AVC, dintre care 86,2% au prezentat accident vascular cerebral ischemic. Cel puțin o interacțiune medicamentoasă potențial relevantă clinic a fost identificată la 96,3% dintre pacienții cu AVC ischemic și la 76,7% dintre pacienții cu AVC hemoragic ($p < 0,001$). Antecedentul de AVC ischemic a reprezentat un factor predictiv independent pentru un risc mai crescut de apariție a pDDIs (OR 5,3; $p < 0,05$). Rezultatele studiului evidențiază o prevalență ridicată a interacțiunilor medicamentoase potențial relevante clinic la pacienții aflați în recuperare după AVC, în special în rândul celor cu AVC ischemic. De asemenea, anumite comorbidități, precum pneumonia sau constipația, au fost asociate cu un risc crescut de apariție a pDDIs.

Keywords: drug-related problems, drug interactions, ischaemic stroke, haemorrhagic stroke

Introduction

Stroke rates have risen in recent decades due to poor control of known risk factors such as diabetes, smoking, ageing populations, and unequal access to health services (1, 2). Current forecasts predict that the number of stroke survivors will double by 2035. However, the highest increase is predicted for the cost of social care, namely, up to 2.5 times (3). The expenditure is due to patients' inability to work, the cost of rehabilitation, and the cost of treating the stroke or comorbidities (2-5). Post-stroke patients require complex therapy that is often associated with adverse events. Studies have reported that patients with unfavourable post-stroke functional outcomes were prescribed more medications and had more potentially inappropriate medications and more

potential drug-drug interactions (pDDIs) (6, 7). A pDDI is defined as the co-prescription of two drugs known to interact, and a manifestation could occur in the exposed patient. pDDIs have been studied in various clinical settings to determine the extent of drug-related harm and to identify factors that increase the risk of pDDIs. pDDIs are referred to as preventable drug-related complications; when manifested, they are associated with hospital admissions, increased length of hospital stays, and higher overall costs for hospitalised patients (8-10). However, drug-related problems and pDDIs have mostly been studied in patients with acute stroke in neurological intensive care units or surgical wards, compromising patient safety (11-13). Nevertheless, the studies confirmed a high prevalence of pDDIs on admission due to acute stroke, during hospitalisation, and at discharge, with rates of 61-90% (11, 14-16). In contrast, pDDIs have been less studied in the rehabilitation phase, where new rehabilitative pharmacotherapy is also introduced (17). Post-stroke patients in particular are at increased risk of pDDIs as they have multiple co-morbid conditions and take a variety of medications, as polypharmacy (concomitant use of 5 or more drugs) has been identified as a major risk factor for pDDIs. They are often exposed to drug classes with a particularly high risk of pDDIs, such as anticoagulants, antimicrobials, antiepileptics, antihypertensives, sedatives, and antidepressants (13, 17).

To our knowledge, there are no studies investigating exposure to pDDIs in neurorehabilitation, including both ischaemic and haemorrhagic stroke patients. The aim of our study was therefore to investigate the prevalence, types, and risk factors for the occurrence of clinically relevant pDDIs in post-stroke patients during the rehabilitation phase. Recognizing and treating pDDIs has become an important task for healthcare professionals in order to achieve the best possible care for this vulnerable patient group. Timely recognition and treatment of pDDIs could reduce medication errors, which are common in stroke patients due to the complexity of the medical condition and therapy, but also due to impaired patient communication (18, 19).

Materials and Methods

Study design

A prospective observational study was conducted in a 40-bed Neurorehabilitation department at the Institute for Physical Medicine, Rehabilitation and Orthopaedic Surgery "Dr Miroslav Zotović", Banja Luka, Republic of Srpska, Bosnia and Herzegovina. The study was approved by the Ethics Committee of the Institute for Physical Medicine, Rehabilitation and Orthopaedic Surgery "Dr Miroslav Zotović" (Decision number: 116-16-10645/17, 12 Dec 2017).

Subjects

Consecutively admitted patients with a history of ischaemic or haemorrhagic stroke were included in the prospective study. Patient data were collected from medical documentation for a total of 217 patients hospitalised for the first time for physical rehabilitation after a stroke, during the period from January 2018 to October 2018. The inclusion criteria were a diagnosis of stroke, first-time in-hospital post-stroke rehabilitation, the use of more than one medication, and the patient's age of over 18 years. Multiple post-stroke rehabilitations or admissions were excluded.

Procedure

Identification of pDDIs was performed using the UpToDate® Lexidrug™ electronic database, default settings (UpToDate Inc., 2025). According to the Lexidrug database, potential pDDIs of classes A (no interaction) and B (no action needed) are of academic, but not a relevant clinical concern. pDDIs of classes X (avoid combination), D (consider therapy modification), and C (monitor therapy) are considered clinically relevant, as they require healthcare professionals' attention and assessment of the benefit/risk ratio for an individual patient.

Screening for pDDIs included all medications administered during the entire rehabilitation stay. The 24-hour interval between administering two drugs was used for assessing pDDI prevalence. Medication list included regularly or as-needed administered drugs during the rehabilitation stay, including enteral and parenteral routes of administration (inhalation, topical, intravenous, intramuscular, subcutaneous, sublingual, or transdermal), as well as vitamins, herbal, and other dietary supplements. Enteral formulas were not assessed for potential drug-food interactions. Medications prescribed at discharge were not included in pDDIs screening. Medications involved in pDDIs were presented according to the Anatomical Therapeutic Chemical (ATC) classification system (chemical, pharmacological, or therapeutic subgroup).

Statistical Analysis

Continuous variables are presented as mean and standard deviation, while ordinal variables are presented as median and interquartile range (IQR), and with an overall range (minimum-maximum value). Qualitative, nominal variables are presented as the number of patients (percentage). The exposure and the number of pDDI classes were calculated per patient. The proportion of drug classes involved in pDDIs was calculated per number of pDDIs. The difference in continuous variables between ischaemic and haemorrhagic stroke patients was tested using a Mann-Whitney U-test, due to unbalanced group sizes. The difference in proportions between the two observed groups was assessed using the Chi-square test of independence (Fisher's test). The changes in the Barthel Index before and after the rehabilitation

stay were tested using the Wilcoxon Signed Rank test. Age, gender, number of drugs, number of comorbidities, presence of comorbidities, and stroke type were tested in separate univariate binary logistic regression analyses for the outcome: occurrence of X pDDI, occurrence of D pDDI, occurrence of C pDDI, or occurrence of any clinically relevant pDDI. Multivariate logistic regression was used to identify risk factors for the occurrence of clinically relevant pDDIs. Variables identified as statistically significant predictors of pDDI occurrence in univariate analysis were further entered into multivariate analyses (method: enter, to adjust for confounding). The results are presented as crude or adjusted odds ratios with 95% confidence intervals (CIs). A p-value of < 0.05 was considered statistically significant. Statistical Package for Social Sciences (SPSS, IBM Corp. Released 2013. IBM SPSS Statistics for Windows, Version 22.0. Armonk, NY: IBM Corp.) software was used for statistical analysis.

Results and Discussion

The study included 217 post-stroke rehabilitation patients, the majority of whom had a history of ischaemic stroke (187, 86.2%). The majority of patients lived at home prior to admission to rehabilitation (178, 82%), while 52 patients (24%) were transferred from other facilities – general hospitals, clinical centres, residential or nursing homes. The average age of patients was 72 years, and the average duration of rehabilitation was 26 days. The Barthel Index showed that ischaemic stroke patients had lower scores for activities of daily living at the beginning of the study, and rehabilitation led to an improvement in scores in both groups ($p < 0.001$). Alcohol consumption and smoking were statistically more common in the ischaemic group. Patients received complex therapy during the post-stroke rehabilitation phase. The median number of drugs in patients with ischaemic stroke was 11, whereas patients with haemorrhagic stroke received significantly lower numbers of medications, 6, during the rehabilitation phase. In contrast, the median number of comorbidities did not differ between the observed groups. The most common comorbidities were cardiovascular and endocrine diseases (hypertension, cardiomyopathy, diabetes mellitus, and arrhythmias). Complications such as urinary tract infections, mental disorders, constipation, and chronic pain were also highly prevalent. Although the risk factors differed between ischaemic and haemorrhagic stroke, we did not find any statistically significant differences in the presence of the recorded complications in this sample size. The detailed demographic and clinical characteristics are presented comparatively in Table I.

The exposure of patients to clinically relevant pDDIs was higher in ischaemic compared to haemorrhagic stroke patients (as shown in Table II). Interestingly, the occurrence of X pDDIs, denoting the highest risk class, was more frequent in haemorrhagic patients. In contrast, the prevalence of other types of clinically relevant pDDIs was statistically higher in ischaemic stroke patients during rehabilitation. Subsequent detailed analysis of the 2,590 clinically relevant pDDIs revealed the involvement of 33 different drug classes in pharmacotherapy, including herbal drugs and vitamins. The most common drug classes were: antihypertensives, diuretics, antidepressants, antiplatelet agents, antidiabetics, anti-infectives for systemic use, nonsteroidal anti-inflammatory drugs (NSAIDs), antiarrhythmics, and sedatives. The frequency of the drug classes involved in pDDIs is shown in Table III. Logistic regression was used to identify risk factors for the occurrence of X, D, C, or total pDDI. Age and gender were not statistically significant predictors in the univariate analysis. As summarised in Table IV, stroke type remained a significant predictor for clinically relevant pDDIs after adjusting for the number of drugs as a potential confounder. The history of ischaemic stroke increased the likelihood of any type of clinically relevant pDDI by 5.3-fold. Pneumonia (aOR 13.7) and constipation (aOR 2.5) increased the odds of D pDDIs, findings confirmed in multivariate analysis.

Table I

Demographic and clinical characteristics

	Median [IQR] (total range) Number of patients (%)			
Characteristics	**All patients (N = 217)**	**Ischaemic stroke (N = 187)**	**Haemorrhagic stroke (N = 30)**	**p-value**
Age, years	72 [66-79] (41-90)	72 [66-80.5] (43-90)	70.5 [63.5-77.5] (41-87)	0.059
≥ 65	172 (79.3%)	152 (81.3%)	20 (66.7%)	0.067
Gender, female	116 (53.5%)	103 (55.1%)	13 (43.3%)	0.231
Length of rehabilitation, days	26 [18.5-31] (1-387)	27 [21-38.5] (1-387)	13.5 [7.5-27.5] (3-53)	0.248
Barthel Index on admission	37 [13-69] (1-97)	37 [12-69] (1-91)	48.5 [21.5-79.5] (18-97)	0.259
Barthel Index at discharge	62 [22.5-83.5] (1-100)	62 [22-83.5] (1-98)	52 [25-88.5] (20-100)	0.818

	Median [IQR] (total range) Number of patients (%)			
Characteristics	**All patients (N = 217)**	**Ischaemic stroke (N = 187)**	**Haemorrhagic stroke (N = 30)**	**p-value**
Problem with speech	98 (45.2%)	80 (42.8%)	18 (60%)	0.079
Problem with swallowing	34 (15.7%)	28 (15%)	6 (20%)	0.482
Alcohol consumption	24 (11.1%)	22 (11.8%)	2 (6.7%)	0.049
Smoking	33 (15.2%)	32 (17.1%)	1 (3.3%)	0.031
Drug allergies	17 (7.8%)	15 (8.1%)	2 (6.7%)	0.570
Number of drugs	10 [7-14] (2-27)	11 [8-14] (3-27)	6 [3.5-9] (2-19)	0.039
≥ 5	204 (94%)	180 (96.3%)	24 (80%)	< 0.001
≥ 10	119 (54.8%)	106 (56.7%)	13 (43.3%)	0.173
Number of comorbidities	3 [2-5] (0-9)	4 [3-5] (0-9)	3.5 [3-4.5] (1-6)	0.282
Comorbidities				
Hypertension	182 (83.9%)	154 (82.4%)	28 (93.3%)	0.129
Cardiomiopathy	71 (32.7%)	63 (33.7%)	8 (26.7%)	0.447
Diabetes mellitus	64 (29.5%)	57 (30.5%)	7 (23.3%)	0.425
Arrhythmia	62 (28.6%)	51 (27.3%)	11 (36.7%)	0.290
Urinary tract infections	59 (27.2%)	55 (29.4%)	4 (13.3%)	0.078
Mental disorders	43 (19.8%)	38 (20.3%)	5 (16.7%)	0.641
Constipation	35 (16.1%)	33 (17.6%)	2 (6.7%)	0.181
Chronic pain	23 (10.6%)	21 (11.2%)	2 (6.7%)	0.749

IQR – interquartile range

Table II

The prevalence of clinically relevant potential drug-drug interactions

	All patients (N = 217)	**Ischaemic stroke (N = 187)**	**Haemorrhagic stroke (N = 30)**	**p-value**
Number of patients (%)				
X	33 (15.2%)	28 (15%)	5 (16.7%)	0.811
D	87 (40.1%)	80 (42.8%)	7 (23.3%)	0.044
C	202 (93.1%)	179 (95.7%)	23 (76.7%)	< 0.001
X+D+C	203 (93.5%)	180 (96.3%)	23 (76.7%)	< 0.001

Legend: C - monitor therapy; D - modify regimen; IQR – interquartile range; S.D. – standard deviation; X - avoid combination

Table III

Drug classes involved in clinically relevant potential drug-drug interactions

ATC drug class (chemical, pharmacological, or therapeutic subgroup)	**Frequency**	**Percentage**
The alimentary tract and metabolism		
Drugs for acid-related disorders	47	1.8
Drugs for functional gastrointestinal disorders (antispasmodics)	13	0.5
Drugs for functional gastrointestinal disorders (propulsives)	16	0.6
Antidiarrheals	6	0.2
Antidiarrheals (electrolytes)	16	0.6
Drugs used in diabetes	249	9.6
Vitamins	21	0.8
Mineral supplements (iron)	2	0.1
Blood and blood-forming organs		
Antithrombotic agents (platelet aggregation inhibitors excl. heparin)	262	10.1
Antithrombotic agents (vitamin K antagonists)	11	0.4
Antithrombotic agents (heparin group)	7	0.3
Antithrombotic agents (direct factor Xa inhibitors)	30	1.2
Cardiovascular system		
Cardiac therapy (antiarrhythmics)	150	5.8
Antihypertensives	430	16.6
Diuretics	298	11.5
Lipid-modifying agents (HMG CoA reductase inhibitors)	44	1.7

ATC drug class (chemical, pharmacological, or therapeutic subgroup)	**Frequency**	**Percentage**
Genito-urinary system and sex hormones		
Urologicals (drugs used in benign prostatic hypertrophy)	8	0.3
Systemic hormonal preparations, excl. sex hormones and insulins		
Corticosteroids for systemic use	12	0.5
Thyroid therapy (levothyroxine)	11	0.4
Antiinfectives for systemic use		
Antibacterials for systemic use	186	7.2
Musculoskeletal system		
Anti-inflammatory and antirheumatic products, non-steroids	154	5.9
Nervous system		
Analgesics (opioids)	14	0.5
Analgesics (other analgesics and antipyretics)	10	0.4
Antiepileptics	12	0.5
Anti-parkinson drugs	1	0.0
Psycholeptics (antipsychotics)	99	3.8
Psycholeptics (anxiolytics)	6	0.2
Psycholeptics (hypnotics and sedatives)	104	4
Psychoanaleptics (antidepressants)	269	10.4
Psychoanaleptics (anti-dementia drugs)	33	1.3
Psychoanaleptics (other anti-dementia drugs, *Ginkgo biloba*)	6	0.2
Respiratory system		
Respiratory system drugs	62	2.4
Sensory organs		
Ophthalmologicals (antiglaucoma preparations)	3	0.1

ATC - Anatomical Therapeutic Chemical classification system

Table IV

The predictors of clinically relevant potential drug-drug interactions

Variables	**X (avoid combination)**	**D (modify regimen)**	**C (monitor therapy)**	**X+D+C**
Univariate analysis, crude OR [95% CI], p-value				
Number of drugs	1.178 [1.085 -1.280] p < 0.001	1.102 [1.038 -1.172] p = 0.002	1.564 [1.245 - 1.965] p < 0.001	1.402 [1.151 - 1.708] p < 0.001
Stroke type: ischaemic	0.881 [0.311 -2.493] p = 0.811	2.457 [1.005 -6.008] p = 0.049	6.810 [2.259 - 20.527] p < 0.001	7.826 [2.518 - 24.324] p < 0.001
Comorbidities	Insomnia 14.166 [1.727 - 116.189] p = 0.014	Pneumonia 12.282 [1.326 - 113.776] p = 0.027 Constipation 2.367 [1.097 -5.108] p = 0.028	-	-
Multivariate analysis, adjusted OR [95% CI], p-value				
Number of drugs	1.177 [1.082 -1.279] p < 0.001	1.108 [1.038 -1.182] p = 0.002	1.473 [1.178 - 1.841] p < 0.001	1.320 [1.093 - 1.595] p = 0.004
Stroke type: ischaemic	-	2.322 [0.870 - 6.203] p = 0.093	4.051 [1.163 - 14.113] p = 0.028	5.280 [1.546 - 18.036] p = 0.008
Comorbidities	Insomnia 2.262 [0.473 -10.816] p = 0.307	Pneumonia 13.677 [1.474 - 126.952] p = 0.021 Constipation 2.505 [1.157 - 5.426] p = 0.020		

CI – confidence interval

Our study revealed a high prevalence of clinically relevant pDDIs in post-stroke patients during medical rehabilitation treatment. In the overall sample, the prevalence of the highest risk pDDIs was estimated at 15.2%, while the exposure was slightly but not significantly higher in the haemorrhagic stroke

group. The prevalence of class D pDDIs requiring a change in therapy was 40.1%, and the exposure was up to 20% higher in the ischaemic group than in the haemorrhagic group, which is a statistically significant difference. Finally, the prevalence of class C pDDIs requiring therapy and patient monitoring was 93.1% in the entire sample. Again, ischaemic stroke patients were 20% more likely to have D, C, or any type of clinically relevant pDDI compared to haemorrhagic stroke patients.

This was the first study to examine pDDIs during physical rehabilitation treatment and compare treatment patterns and potential drug-related harms in ischaemic and haemorrhagic stroke patients. Previous studies mostly focused on acute stroke patients and showed high rates of pDDIs on admission, during hospitalisation, or at discharge (11-16). However, pDDIs in the rehabilitation phase after stroke have not been extensively studied (20). Studies have tended to report drug-specific outcomes, such as the prevalence of pDDIs resulting from the use of antiepileptic drugs (7, 13, 19, 21, 22).

In our study, the characteristics of therapies that lead to clinically relevant pDDIs were described in more detail. Stroke patients have an increased risk of medication errors, drug-related problems, and pDDIs. Reasons for this include advanced age, high prevalence of comorbidities, polypharmacy, use of intravenous routes of administration, administration of drugs with a narrow therapeutic index, prolonged hospitalisation, and impaired communication due to aphasia (18, 23). Stroke patients receive antiplatelet agents, anticoagulants, antihypertensives, statins, hypoglycaemic agents, and anti-infectives to treat post-stroke infections (13). The therapies listed are in line with stroke treatment guidelines, but also reflect treatment options for comorbidities such as hypertension, diabetes, hyperlipidemia, arrhythmias, heart failure, and epilepsy, which are the most common (11, 23). However, our results showed that many other classes of drugs were involved in clinically relevant pDDIs in pharmacotherapy. Indeed, a variety of drugs used to treat different organ systems contributed significantly to the pDDI-related burden. As described in the literature, antiepileptic drugs should be initiated in the post-stroke phase to control seizures, and systemic anti-infectives should be used to treat post-stroke infections such as urinary tract infections or pneumonia (13, 24). Central nervous system drugs included antidepressants, antiepileptics, sedatives, antipsychotics, antidementia drugs, opioid analgesics, and antiparkinsonian drugs. In addition, delayed-onset or less severe disorders than those reported or potentially neglected in the acute phase were identified in our study as contributing to medication complexity and the occurrence of pDDIs (25). For example, post-seizure gastrointestinal disturbances included hyperacidity, cramps, dysmotility, nausea, constipation, or diarrhoea. When new drugs are added to therapy, they should be screened for clinically relevant pDDIs. Medications for the respiratory system, glaucoma, benign prostatic hyperplasia, iron deficiency, and hypothyroidism could be matched to other medications administered to achieve better disease outcomes and improve functionality in daily activities. Last but not least, herbal drugs, electrolytes, and vitamins contributed to the development of clinically relevant pDDIs and should be included in the comprehensive therapeutic evaluation of patients. A 2022 study reported that up to one-third of stroke patients take fixed-dose multivitamin supplements (23).

In addition to the variety of drug classes used in pDDIs, the complexity of the medication is described by the number of drugs per patient. As shown in Table 1, patients had a median of 10 drugs in their therapy, with patients with ischaemic stroke having almost 11 drugs and those with haemorrhagic stroke having 6 drugs in their therapy. The pharmacodynamic and pharmacokinetic properties of the drugs, together with the high total number of drugs in therapy, resulted in a high prevalence of pDDIs. We identified predictors of clinically relevant pDDIs in four separate analyses, with the dependent variables: X pDDIs, D pDDIs, C pDDIs, and total clinically relevant pDDIs. In all analyses, the number of medications remained a statistically significant predictor of pDDI occurrence, even after adjustment for other patient characteristics, as confirmed in other studies (11, 12, 26).

When controlling for the number of medications, history of ischaemic stroke remained a statistically significant predictor of the occurrence of clinically relevant pDDI by 5.3-fold. These results confirmed the susceptibility of these patients to pDDIs due to pharmacokinetic or pharmacodynamic properties (26). This association may be driven by differences in pharmacotherapy patterns, especially antithrombotic therapy. Moreover, our findings indicate that patients with pneumonia or constipation had higher odds for the occurrence of D-type pDDIs. Literature reports urinary tract infections or pneumonia as common post-stroke infections, resulting in high consumption of antibiotics, up to 80-90% in acute care (11-13). Consequently, antibiotics are reported as a frequent drug class implicated in pDDIs. Post-stroke constipation is frequently driven by drug-drug interactions involving anticholinergics, opioid analgesics, antihypertensives (calcium channel blockers), and certain antidepressants, which increase risk when combined with reduced mobility (27-31). Given the high incidence of constipation in post-stroke patients of nearly 50% (27), therapy assessment and possible therapy modifications should be addressed for each individual patient.

Although the appropriateness of medication or adherence to treatment guidelines was not the subject of the current study, we can conclude that the complexity of medication during rehabilitation treatment is very high and requires mandatory pDDI screening to plan proactive measures or modify therapy. This study is the first to investigate pDDIs in post-stroke rehabilitation, filling a gap in the literature that has so far mainly focused on stroke patients in the acute phase. The results of our study highlight the need for greater awareness and individualised treatment plans to manage complex pharmacotherapy during post-stroke rehabilitation and to improve patient safety and clinical outcomes.

Limitations

The study was conducted at a single rehabilitation institute, limiting the generalisability of the findings to other healthcare settings and populations. A multicenter approach would strengthen external validity. The clinical consequences of pDDIs were not recorded in this study. The sample sizes of ischaemic and haemorrhagic stroke patients were not balanced; therefore, we used the Mann-Whitney test for between-group comparison.

Conclusions

Our study emphasises the significant prevalence of clinically relevant drug-drug interactions (pDDIs) in post-stroke patients during rehabilitation treatment. The study found that both the total number of medications and the type of medication administered were statistically significant predictors of pDDIs. More attention should be paid to therapy assessment in ischaemic stroke patients, who had significantly higher exposure to clinically important pDDIs compared to haemorrhagic stroke patients. This association may be driven by differences in pharmacotherapy patterns, especially antithrombotic therapy. Moreover, comorbidities such as pneumonia or constipation could increase the odds of clinically relevant pDDIs, necessitating early identification and vigilant monitoring of pDDIs. The results highlight the need for comprehensive medication assessment in this vulnerable population to minimise avoidable medication-related harm and optimise rehabilitation outcomes.

Acknowledgement

Not applicable.

Funding

This research was funded by the Ministry of Science, Technological Development, and Innovation of the Republic of Serbia through two grant agreements with the University of Belgrade – Faculty of Pharmacy (Nos. 451-03-33/2026-03/200161 and 451-03-34/2026-03/200161).

Availability of data and materials

The data that support the findings of this study are available from the corresponding author upon reasonable request.

Ethics approval and consent to participate

The study was approved by the Ethics Committee of the Institute for Physical Medicine, Rehabilitation and Orthopaedic Surgery "Dr Miroslav Zotović" (Decision number: 116-16-10645/17, 12 Dec 2017).

AI use disclosure

Not applicable.

Conflict of interest

The authors declare no conflict of interest.

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