Scientific Research Publishing

Open Journal of Anesthesiology, 2026, 16(8), 145-156
https://www.scirp.org/journal/ojanes
ISSN Online: 2164-5558
ISSN Print: 2164-5531

Perioperative Pharmacologic Complexity and Potential Drug Interactions in Neurosurgical Patients: A Retrospective Cohort Study

Martínez Herrera Alvaro[1*], Galván Talamantes Yazmín[2], Riva-Palacio Reyes Alfonso[2]

[1]Department of Anesthesiology, Hospital Ángeles Lomas, Huixquilucan, Mexico
[2]Department of Intensive Care, Hospital Ángeles Lomas, Huixquilucan, Mexico
Email: *mherreraalvaro@outlook.com

How to cite this paper: Alvaro, M.H., Yazmín, G.T. and Alfonso, R.-P.R. (2026) Perioperative Pharmacologic Complexity and Potential Drug Interactions in Neurosurgical Patients: A Retrospective Cohort Study. *Open Journal of Anesthesiology*, **16**, 145-156.
https://doi.org/10.4236/ojanes.2026.168014

Received: June 27, 2026
Accepted: August 16, 2026
Published: August 19, 2026

Abstract

Introduction: Healthcare-associated harm represents a significant challenge, with an incidence of up to 6% across diverse healthcare settings. Medication-related events represent a leading contributor. This study aimed to characterize the frequency and severity of potential perioperative drug-drug interactions (pDDIs) in patients undergoing neurosurgical procedures. **Materials and Methods**: A retrospective observational study was conducted among patients undergoing neurosurgical procedures at Hospital Ángeles Lomas between January and June 2023. Data were collected from electronic medical records. All concomitant perioperative drug combinations recorded in the medical record were analyzed using Micromedex®, and potential drug-drug interactions (pDDIs) were identified and classified by severity as minor, moderate, or major. **Results:** Ninety-one patients were included in the final analysis, at least one pDDI was identified in all patients, with a median of 30 (IQR 20 - 43). A positive correlation was observed between the number of medications and total pDDIs ($r_s = 0.796$, $p < 0.001$). A higher pDDI burden was observed among patients aged ≥ 60 years and those with multiple comorbidities, although these differences were not statistically significant. Patients receiving baseline pharmacological treatment had significantly more pDDIs than those without baseline treatment ($p = 0.019$). Differences were also observed according to anesthetic technique ($p = 0.026$). Patients admitted to critical care settings showed a higher median number of pDDIs compared with those in general wards; however, these differences did not reach statistical significance ($p = 0.130$). Most patients (98.9%) were discharged with clinical improvement. **Conclusion**: Potential drug-drug interactions (pDDIs) were frequently identified among patients undergoing neurosurgical procedures and were associated with perioperative medication exposure, baseline pharmacological treat-

ment and anesthetic technique. These findings highlight the substantial pharmacological complexity of the perioperative neurosurgical setting and support the need for careful medication review during perioperative care.

Keywords

Drug-Drug Interactions, pDDI, Perioperative, Anesthesia, Neuroanesthesia

1. Introduction

Healthcare-associated harm represents a significant challenge, with an incidence of up to 6% across diverse healthcare settings [1] [2]. Among these events, medication-related harm is a leading contributor, accounting for up to 8%, with approximately one-third resulting in permanent disability or death [1]-[3].

Measuring harm and medication errors is essential to inform and guide preventive interventions and strategies [3]-[5]. The World Health Organization (WHO) has designated "Medication Without Harm" as the third Global Patient Safety Challenge, aligned with the International Patient Safety Goals (IPSG) developed by Joint Commission International, specifically Goal 3 [4] [6].

Medication-related harm occurs predominantly in specialized care settings [3] [7]. A perioperative incidence of 11.6% has been reported [7]-[9]. During the intraoperative phase, the administration of multiple drugs increases the risk of medication errors and drug-drug interactions, with the theoretical potential to compromise treatment efficacy, safety, and patient outcomes [8] [10].

Drug-drug interactions may be classified as pharmacodynamic, when two or more drugs act at the same site, resulting in synergism or antagonism, or pharmacokinetic, when alterations in absorption, distribution, metabolism, and/or excretion may increase toxicity or modify efficacy [8] [11]. They may also be classified by severity as minor, when they are tolerable and do not require medical intervention; moderate, when they require treatment; and major, when they lead to therapeutic failure, hospitalization, permanent harm, or death [12].

Characterizing potential perioperative drug-drug interactions is essential to prevent adverse events and guide decisions on discontinuation, dose adjustment, or drug selection, thereby ensuring safe anesthetic management and optimizing outcomes [11] [13] [14]. The main risk factors include polypharmacy, older age, the use of injectable medications, and drugs acting on the central nervous and cardiovascular systems, the latter classified as "high-risk" medications due to their potential to cause harm [3] [9] [15].

In this context, several recommendations have been issued, including the Royal College of Anaesthetists' Guidelines for the Provision of Anaesthetic Services (GPAS) [3] [9]. In addition, advances in knowledge have led to the development of analytical tools to assess potentially harmful drug-drug interactions using electronic databases [8].

2. Materials and Methods

The study was reviewed and approved by the Research Ethics Committee of Hospital Ángeles Lomas (protocol No. HAL 462/2023). The requirement for written informed consent was waived.

A retrospective observational study was conducted among patients undergoing neurosurgical procedures at Hospital Ángeles Lomas between January and June 2023. All patients who underwent neurosurgical procedures during the study period and were recorded in the central operating room database were included. Patients younger than 18 years, those with an ASA physical status of V - VI, incomplete medical records, or medicolegal cases were excluded. Data were collected from electronic medical records, including sociodemographic variables (age, sex, alcohol, tobacco, and other substance use) and clinical and pharmacological variables: comorbidities and baseline pharmacological treatment, allergies, ASA physical status and NYHA classification, preoperative and postoperative in-hospital medications, anesthetic technique and drugs administered (including anesthetics and adjuvants), diagnosis and surgical procedure, length of hospital stay, and discharge outcomes.

Baseline pharmacological treatment documented at hospital admission, intraoperative anesthetic and adjuvant medications, and postoperative in-hospital medications administered until hospital discharge were considered part of the perioperative medication exposure. All concomitant drug combinations recorded throughout this period were screened using Micromedex® to identify potential drug-drug interactions (pDDIs), defined as interactions that may occur based on concomitant drug exposure but are not necessarily clinically manifested. Each unique pDDI was counted only once per patient, regardless of repeated administration or occurrence across different phases of perioperative care. Severity classification (minor, moderate, or major) was assigned directly according to the Micromedex® database. No additional clinical adjudication was performed after database screening. Because the objective of the study was to characterize the overall perioperative pharmacological complexity, no temporal window for simultaneous drug administration was imposed; therefore, pDDIs were identified based on the complete perioperative medication profile rather than verified concurrent administration.

Statistical analyses were performed using IBM SPSS Statistics (version 32; IBM Corp., Armonk, NY, USA). Categorical variables were summarized as frequencies and proportions. Continuous variables were summarized as means with standard deviations (SD) or medians with interquartile ranges (IQR), as appropriate. Variables representing the number of potential drug-drug interactions (pDDIs) were summarized using medians and interquartile ranges. Group differences were assessed using the Mann-Whitney U test or Kruskal-Wallis H test, as appropriate. When the Kruskal-Wallis test was statistically significant, pairwise post hoc comparisons were performed using Bonferroni adjustment. In addition, associations between count variables were evaluated using Spearman's rank correlation coeffi-

cient. A p value < 0.05 was considered statistically significant.

This manuscript adheres to the applicable STROBE guidelines.

3. Results

3.1. Sociodemographic and Clinical Characteristics of the Study Population

A total of 94 patient records were identified during the study period; three were excluded—two due to incomplete medical records and one involving a patient under 18 years of age. The mean age was 58.16 ± 15.98 years, and 54.9% were female (Table 1).

Table 1. Sociodemographic and clinical characteristics.

	n = 91
Age, Mean ± SD	58.16 ± 15.984
Age group, No. (%)	
18 - 59 years	45 (49.5)
≥60 years	46 (50.5)
Female sex, No. (%)	50 (54.9)
Comorbidities, No. (%)	
Without comorbidities	29 (31.9)
At least one comorbidity	30 (33)
Two or more comorbidities	32 (35.2)
Comorbidities, No. (%)	
Systemic arterial hypertension	30 (33)
Thyroid disorders	20 (22)
Dyslipidemias	14 (15.4)
Diabetes mellitus	8 (8.8)
Heart diseases	6 (6.6)
Other comorbidities	25 (27.5)
ASA physical status, No. (%)	
ASA I	20 (22)
ASA II	57 (62.6)
ASA III	10 (11)
ASA IV	4 (4.4)
Preoperative diagnosis, No. (%)	
Spinal canal stenosis	34 (37.4)
Radiculopathies	30 (33)

Continued

Tumors	8 (8.8)
Hydrocephalus	4 (4.4)
Hematomas	3 (3.3)
Other diagnosis	12 (13.2)
Anesthesia technique, No. (%)	
Balanced general anesthesia	56 (61.5)
Total intravenous anesthesia	29 (31.9)
Sedation	3 (3.3)
Combined anesthesia	3 (3.3)
Hospital stay, No. (%)	
General wards	79 (86.8)
Intermediate care unit	4 (4.4)
Intensive care unit	8 (8.8)
Length of hospital stay, median [IQR]	3 [2 - 6]
General wards	3 [2 - 6]
Intermediate care unit	10 [2.25 - 21.75]
Intensive care unit	6.5 [1.5 - 16]
IMV, No. (%)	6 (6.6)
Length of IMV, median [IQR]	5 [2 - 12.25]
Discharged, No. (%)	
Clinical improvement	90 (98.9)
Transferred	1 (1.1)

Allergies were reported in 28.6% of patients; the most common were to NSAIDs and sulfonamides (6.6% each), followed by quinolones (3.3%) and beta-lactams (2.2%). Comorbidities were present in 68.2% of patients; 33% had at least one and 35.2% had two or more. The most common comorbidities were systemic arterial hypertension (33%), thyroid disorders (22%), dyslipidemia (15%), and diabetes mellitus (8.8%). Patients were classified according to the American Society of Anesthesiologists (ASA) physical status: 22% ASA I, 62.6% ASA II, 11% ASA III, and 4.4% ASA IV (Table 1).

The most common preoperative diagnosis was spinal canal stenosis (37.4%), followed by radiculopathies (33%), tumors (8.8%), and hydrocephalus and hematomas (4.4% and 3.3%, respectively) (Table 1). Surgical procedures included spine surgery (68.1%), cranial surgery (11%), and ventriculoperitoneal shunt (VPS) placement (4.4%).

Balanced general anesthesia was the most used technique (61.5%), followed by

total intravenous anesthesia (31.9%); sedation and combined general anesthesia with regional blockade were each used in 3.3%. Blood product transfusion was required in 15.4% of cases. A total of 86.8% were discharged to general wards, with a median length of stay of 3 days (IQR 2 - 6); 4.4% were admitted to the intermediate care unit (IMCU), with a median length of stay of 10 days (IQR 2.5 - 27.5); and 8.8% required admission to the intensive care unit (ICU), with a median length of stay of 6.5 days (IQR 1.5 - 16). Of those admitted to the ICU, 75% required invasive mechanical ventilation (IMV), representing 6.6% of the total cohort (Table 1).

3.2. Pharmacological Burden and Potential Drug-Drug Interactions

During the perioperative period, 14 - 48 medications were administered, with a median of 28 (IQR 23 - 32) and a mean of 28.3 ± 7.3. A positive correlation was observed between the number of medications and total pDDIs ($r_s = 0.796$, $p < 0.001$). During the hospital stay, up to 34 medications were used (median 10, IQR 8 - 13). In the intraoperative period, 2 - 10 anesthetic drugs were administered (median 7, IQR 5 - 7), along with up to 15 adjuvant drugs (median 8, IQR 5 - 10).

At least one pDDI was identified in all patients (Micromedex®), with a median of 30 (IQR 20 - 43). By severity, moderate and major pDDIs were observed in all patients, with medians of 6 (IQR 4 - 8) and 22 (IQR 14 - 35), respectively, whereas Mild pDDIs were identified in 25.2% of patients, ranging from 1 to 2 events per patient (Table 2).

Table 2. Pharmacological burden and potential drug-drug interactions.

n = 91	No. (%)	Min - Max	Median [IQR]	p-value
Baseline pharmacological treatment	67 (73.6)	1 - 13	3 [2 - 5]	
Hospital stay medications		4 - 34	10 [8 - 13]	
Intraoperative period medications (anesthetic drugs)		2 - 10	7 [5 - 7]	
Intraoperative period medications (adjuvant drugs)		0 - 15	8 [5 - 10]	
Perioperative period medications		14 - 48	28 [23 - 32]	
Potential drug-drug interactions				
Total	91	7 - 124	30 [20 - 43]	
Mild	23 (25.2)	1 - 2		
Moderate	91	1 - 40	6 [4 - 8]	
Major	91	5 - 101	22 [14 - 35]	

Continued

Age group			
18 - 59 years	9 - 106	28 [20 - 39]	0.201[a]
≥60 years	7 - 124	35 [22 - 44]	
Comorbidities			
Without comorbidities	9 - 106	27 [19 - 36]	0.145[b]
At least one comorbidity	7 - 87	30.5 [20 - 47]	
Two or more comorbidities	12 - 124	37.5 [23 - 43.5]	
Baseline pharmacological treatment			
Yes	7 - 124	33 [23 - 44]	0.019[a]
No	9 - 106	23 [17 - 34]	
Anesthesia technique			
Balanced general anesthesia	9 - 124	32 [22.5 - 45]	0.026[b]
Total intravenous anesthesia	7 - 104	26 [18 - 43]	
Sedation	8 - 17	9 [8.5 - 13]	
Combined anesthesia	28 - 36	33 [30.5 - 34.5]	
Hospital stay			
General wards	7 - 106	29 [20 - 42.5]	0.130[b]
Intermediate care unit	14 - 124	62 [17 - 114]	
Intensive care unit	25 - 87	40 [34.5 - 49.5]	

Comparison of the number of potential drug-drug interactions across groups. Statistical significance was set at $p < 0.05$. [a]Mann-Whitney U test; [b]Kruskal-Wallis H test.

3.3. Subgroup Analysis

Total pDDIs were analyzed by age group; patients aged 18 - 59 years had a median of 28 (IQR 20 - 39), compared with 35 (IQR 22 - 44) in those aged ≥ 60 years ($p = 0.201$). Median pDDIs were 27 (IQR 19 - 36) in patients without comorbidities, 30.5 (IQR 20 - 47) in those with at least one comorbidity, and 37.5 (IQR 23 - 43.5) in those with two or more comorbidities. Median pDDIs were 33 (IQR 23 - 44) in patients receiving baseline pharmacological treatment and 23 (IQR 17 - 34) in those without ($p = 0.019$). Median pDDIs were 32 (IQR 22.5 - 45) with balanced general anesthesia, 26 (IQR 18 - 43) with total intravenous anesthesia, 9 (IQR 8.5 - 13) with sedation, and 33 (IQR 30.5 - 34.5) with combined anesthesia ($p = 0.026$). By level of care, median pDDIs were 40 (IQR 34.5 - 49.5) in ICU patients, 62 (IQR 17 - 144) in IMCU patients, and 29 (IQR 20 - 42.5) in general wards ($p = 0.130$). A moderate positive correlation was observed between length of hospital stay and total pDDIs ($r_s = 0.478$, $p < 0.001$) (Table 2) (Figure 1). Overall, 98.9% of patients were discharged with clinical improvement, and one patient was transferred (Table 1).

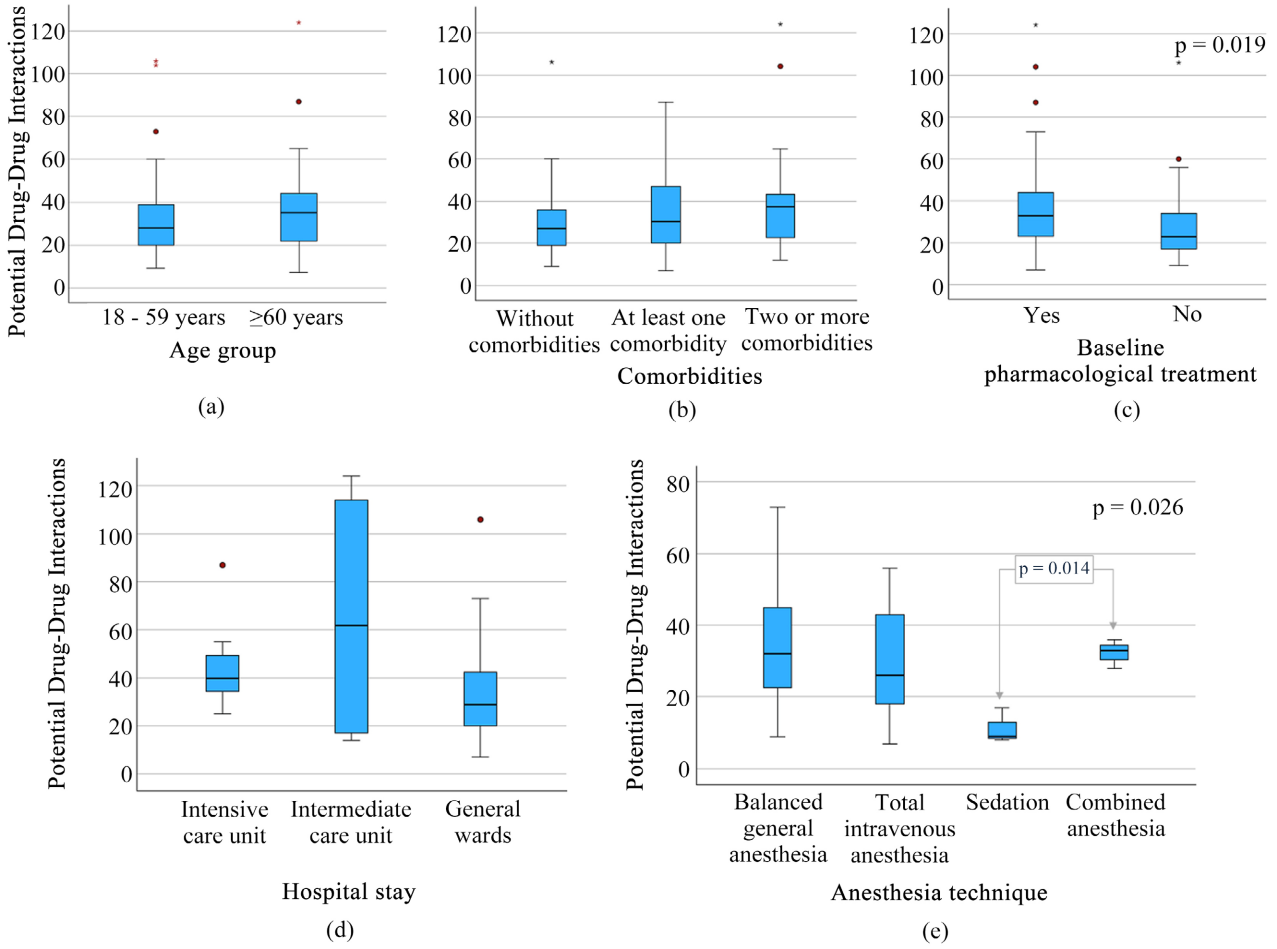

Figure 1. Potential drug-drug interactions. Comparison of the number of potential drug-drug interactions across groups. (a) Age group (p = 0.201). (b) Number of comorbidities (p = 0.145). (c) Baseline pharmacological treatment (p = 0.019). (d) Length of hospital stay (p = 0.130). (e) Anesthetic technique (p = 0.026): sedation vs combined anesthesia (p = 0.014) (Kruskal-Wallis H test; pairwise post hoc comparisons were performed using Bonferroni adjustment).

4. Discussion

This study demonstrated a high burden of potential drug-drug interactions (pDDIs), with universal exposure. The perioperative setting represents a highly complex pharmacological environment in which chronic therapies, anesthetic agents, adjuvants, and in-hospital treatments converge, creating an extensive network of potential interactions [8] [16]. These findings are consistent with the literature, which describes the perioperative setting as particularly vulnerable to medication-related problems. During anesthesia and perioperative management, multiple drugs with potent physiological effects are administered, thereby increasing the likelihood of pDDIs [8] [16] [17]. In addition, the complexity of the operating room environment—characterized by the rapid and simultaneous administration of medications—has been identified as a risk factor for medication errors and medication-related adverse events [16] [18].

The frequency of potential drug-drug interactions observed in this study appears higher than that reported in general surgical populations. Rabba *et al.* re-

ported a pDDI prevalence of 56% and a mean of 2.22 ± 3.76 interactions per hospitalized surgical patient [19]. Similarly, studies in hospitalized surgical patients have identified at least one potential drug-drug interaction in approximately 17% of patients [20]. Although these studies differ in design and population, the higher pDDI burden observed in our study may reflect substantial perioperative pharmacological complexity associated with neurosurgical care.

Compared with critical care populations, the pDDI burden observed in our cohort appears substantial. ICU-based studies have reported prevalences of 58% - 67%; however, direct comparisons are limited by differences in study design, patient populations, interaction detection methods, and definitions of pDDIs [21] [22]. Nevertheless, our findings highlight the extensive perioperative pharmacological exposure characteristic of neurosurgical patients.

The positive correlation between the number of perioperative medications and pDDIs observed in this study is consistent with previous reports identifying polypharmacy as an independent predictor of drug-drug interactions [18] [21]. From a probabilistic perspective, the number of potential drug combinations increases exponentially with the number of prescribed medications [18].

Patients receiving baseline pharmacological treatment had significantly more pDDIs than those without prior treatment. This finding is consistent with the available evidence, indicating that the coexistence of chronic medications with perioperative therapies increases the risk of drug-drug interactions and complicates medication reconciliation during hospitalization [8] [17] [18].

The findings observed in patients receiving sedation, combined anesthesia, or admitted to the intermediate care unit should be interpreted with caution because of the limited number of patients in these subgroups. Consequently, these estimates are exploratory and require confirmation in larger cohorts.

In contrast, the number of pDDIs did not differ significantly by age, comorbidity status, or length of hospital stay. Although previous studies have identified advanced age and multimorbidity as risk factors for medication-related problems, the lack of statistical significance in our study may be explained by the study design, sample size, or the total number of medications as the primary covariate [17] [23].

From a clinical perspective, it is important to recognize that not all drug-drug interactions have the same clinical relevance. In neuroanesthesia, certain drug combinations warrant particular attention given their pathophysiological plausibility. However, this study assessed potential drug-drug interactions (pDDIs), and thus not all necessarily translate into clinically manifest events.

Studies in hospital settings have shown that automated detection systems identify numerous potential interactions, although only a limited proportion are clinically relevant [21] [24]. The utility of these systems lies in identifying high-risk scenarios and guiding preventive strategies, rather than directly predicting adverse events. Strategies to improve medication safety in the perioperative setting include structured medication reconciliation, systematic medication review, and

clinical decision support systems to identify high-risk interactions in real time [16] [17] [25].

This study has several limitations, including its retrospective, single-center design, which may limit generalizability. In addition, drug-drug interaction identification relied on a single database, potentially introducing overestimation bias inherent to automated systems and variability depending on the database used. [26]. Finally, clinical adverse events attributable to the identified potential interactions were not assessed; thus, a direct causal relationship with specific clinical outcomes cannot be established.

Although the present study focused on the overall burden of potential drug-drug interactions, further analyses are underway to characterize the most frequent and clinically relevant interaction pairs and their potential implications for perioperative anesthetic management.

5. Conclusion

Potential drug-drug interactions (pDDIs) were frequently identified among patients undergoing neurosurgical procedures and were associated with perioperative medication exposure, baseline pharmacological treatment, and anesthetic technique. These findings highlight the substantial pharmacological complexity of the perioperative neurosurgical setting and support the need for careful medication review during perioperative care. Future prospective, multicenter studies are needed to determine the clinical relevance of these interactions and their association with adverse clinical outcomes in this population.

Author Contributions

1) Conceptualization, study design, methodology, statistical analysis, interpretation of results, supervision, manuscript drafting, and critical revision of the manuscript. 2) Yazmín Galván Talamantes: Methodological support, interpretation of results, manuscript drafting, and critical revision of the manuscript. 3) Alfonso Riva-Palacio Reyes: Data collection, interpretation of results, and critical revision of the manuscript.

All authors approved the final version of the manuscript and agree to be accountable for all aspects of the work.

Conflicts of Interest

No competing interests or funding declared.

Declaration of Generative AI and AI-Assisted Technologies in the Manuscript Preparation Process

During the preparation of this work the authors used ChatGPT (OpenAI) to assist with English translation and linguistic refinement of the manuscript. After using this tool/service, the authors reviewed and edited the content as needed and takes full responsibility for the content of the published article.

References

[1] World Health Organization (2021) Global Patient Safety Action Plan 2021-2030: Towards Eliminating Avoidable Harm in Health Care. World Health Organization.

[2] Panagioti, M., Khan, K., Keers, R.N., Abuzour, A., Phipps, D., Kontopantelis, E., *et al.* (2019) Prevalence, Severity, and Nature of Preventable Patient Harm across Medical Care Settings: Systematic Review and Meta-Analysis. *BMJ*, **366**, l4185. https://doi.org/10.1136/bmj.l4185

[3] Hodkinson, A., Tyler, N., Ashcroft, D.M., Keers, R.N., Khan, K., Phipps, D., *et al.* (2020) Preventable Medication Harm across Health Care Settings: A Systematic Review and Meta-Analysis. *BMC Medicine*, **18**, Article No. 313. https://doi.org/10.1186/s12916-020-01774-9

[4] World Health Organization (2017) Medication without Harm: WHO Global Patient Safety Challenge. World Health Organization.

[5] Koczmara, C.H. and Jelincic, V. (2007) Neuromuscular Blocking Agents: Enhancing Safety by Reducing the Risk of Accidental Administration. *ISMP Canada Safety Bulletin*, **18**, 28-32.

[6] Joint Commission International (2025) International Patient Safety Goals. Joint Commission. https://www.jointcommission.org/en/standards/international-patient-safety-goals

[7] Institute for Safe Medication Practices (2022) ISMP Guidelines for Safe Medication Use in Perioperative and Procedural Settings. Institute for Safe Medication Practices.

[8] Silva, A., Costa, B., Castro, I., Mourão, J. and Vale, N. (2023) New Perspective for Drug-Drug Interaction in Perioperative Period. *Journal of Clinical Medicine*, **12**, Article 4810. https://doi.org/10.3390/jcm12144810

[9] Mackay, E., Jennings, J. and Webber, S. (2019) Medicines Safety in Anaesthetic Practice. *BJA Education*, **19**, 151-157. https://doi.org/10.1016/j.bjae.2019.01.001

[10] Linares Borges, A., Alemán Aguilar, H., Rodríguez Muñiz, J.M., Martín García, L.M., Milián Vázquez, P.M., Betancourt Rodríguez, B.Y., *et al.* (2002) Interacciones Medicamentosas. *Acta Farmacéutica Bonaerense*, **21**, 139-148. http://sedici.unlp.edu.ar/handle/10915/6535

[11] Becker, D.E. (2011) Adverse Drug Interactions. *Anesthesia Progress*, **58**, 31-41. https://doi.org/10.2344/0003-3006-58.1.31

[12] Sahinovic, M.M., Struys, M.M.R.F. and Absalom, A.R. (2018) Clinical Pharmacokinetics and Pharmacodynamics of Propofol. *Clinical Pharmacokinetics*, **57**, 1539-1558. https://doi.org/10.1007/s40262-018-0672-3

[13] van den Berg, J.P., Vereecke, H.E.M., Proost, J.H., Eleveld, D.J., Wietasch, J.K.G., Absalom, A.R., *et al.* (2017) Pharmacokinetic and Pharmacodynamic Interactions in Anaesthesia. A Review of Current Knowledge and How It Can Be Used to Optimize Anaesthetic Drug Administration. *British Journal of Anaesthesia*, **118**, 44-57. https://doi.org/10.1093/bja/aew312

[14] Pass, S.E. and Simpson, R.W. (2004) Discontinuation and Reinstitution of Medications during the Perioperative Period. *American Journal of Health-System Pharmacy*, **61**, 899-912. https://doi.org/10.1093/ajhp/61.9.899

[15] Gibb, D. (1984) Drug Interactions in Anaesthesia. *Clinics in Anaesthesiology*, **2**, 485-512. https://doi.org/10.1016/s0261-9881(21)00157-9

[16] Wahr, J.A., Abernathy, J.H., Lazarra, E.H., Keebler, J.R., Wall, M.H., Lynch, I., *et al.* (2017) Medication Safety in the Operating Room: Literature and Expert-Based Rec-

ommendations. *British Journal of Anaesthesia*, **118**, 32-43. https://doi.org/10.1093/bja/aew379

[17] Perks, A., Cheema, S. and Mohanraj, R. (2012) Anaesthesia and Epilepsy. *British Journal of Anaesthesia*, **108**, 562-571. https://doi.org/10.1093/bja/aes027

[18] Lee, Y., Liew, Y., Sim, M.H. and Sim, X.L.J. (2025) Association of Polypharmacy and Perioperative Outcomes: Systematic Review and Meta-Analysis. *Journal of Perioperative Practice*, **36**, 29-41. https://doi.org/10.1177/17504589251320818

[19] Rabba, A.K., Abu Hussein, A.M., Abu Sbeih, B.K. and Nasser, S.I. (2020) Assessing Drug-drug Interaction Potential among Patients Admitted to Surgery Departments in Three Palestinian Hospitals. *BioMed Research International*, **8**, Article 429. https://doi.org/10.1155/2020/9634934

[20] Durrence 3rd, C.W. and Hume, A.L. (1985) Potential Drug Interactions in Surgical Patients. *Drug Intelligence & Clinical Pharmacy*, **42**, 1553-1556.

[21] Bakker, T., Abu-Hanna, A., Dongelmans, D.A., Vermeijden, W.J., Bosman, R.J., de Lange, D.W., *et al.* (2021) Clinically Relevant Potential Drug-Drug Interactions in Intensive Care Patients: A Large Retrospective Observational Multicenter Study. *Journal of Critical Care*, **62**, 124-130. https://doi.org/10.1016/j.jcrc.2020.11.020

[22] Hammes, J.A., Pfuetzenreiter, F., Silveira, F.D., Koenig, Á. and Westphal, G.A. (2008) Prevalência de potenciais interações medicamentosas droga-droga em unidades de terapia intensiva. *Revista Brasileira de Terapia Intensiva*, **20**, 349-354. https://doi.org/10.1590/s0103-507x2008000400006

[23] Kashiwazaki, D., Tomita, T., Hori, E., Akioka, N., Akai, T., Noguchi, K., *et al.* (2024) Frequency, Characteristics, and Preventability of Adverse Drug Reactions in Perioperative Neurosurgery: Analysis over 11 Years. *World Neurosurgery*, **189**, e624-e631. https://doi.org/10.1016/j.wneu.2024.06.136

[24] Choi, Y.H., Lee, I.H., Yang, M., Cho, Y.S., Jo, Y.H., Bae, H.J., *et al.* (2021) Clinical Significance of Potential Drug-Drug Interactions in a Pediatric Intensive Care Unit: A Single-Center Retrospective Study. *PLOS ONE*, **16**, e0246754. https://doi.org/10.1371/journal.pone.0246754

[25] McLean, A.L., Schlattl, A., Senft, C., Hartmann, M. and Schwarz, F. (2025) Reducing Medication Errors in Neurosurgery through Clinical Pharmacy Interventions: A Prospective Observational Study. *Neurosurgical Review*, **48**, Article No. 687. https://doi.org/10.1007/s10143-025-03849-8

[26] Riera, P., Rigo-Bonnin, R., Ribas Sala, J., *et al.* (2022) Drug-Drug Interactions in an Intensive Care Unit and Comparison of Two Databases: Does Knowledge of Clinically Relevant Interactions Matter? *Farmacia Hospitalaria*, **46**, 290-295.