Cross-sectional Study

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Assessment of frequency and types of drug interactions in intensive care units: a cross-sectional study

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Background: Drug interactions can cause adverse reactions, from treatment inefficiency to serious treatment complications in the patient. Due to the complexity of drug therapy and the simultaneous use of several drugs and different drug groups, patients hospitalized in intensive care units are exposed to more drug interactions. Therefore, this study was conducted to investigate the frequency of drug interactions in patients hospitalized in the ICU.

Methods: In this cross-sectional study, the files of 300 patients hospitalized in the ICU were examined. Drug interactions were determined using Lexicomp software and the book drug iteration facts. Data analysis was done using SPSS 21 software.

Findings: The findings showed that there were a total of 1121 cases of interference. Two hundred thirty-one (77%) patients had moderate interference, 94 (31.3%) patients had mild interference, and 67 patients (22.3%) had severe interference. One hundred eight patients had B-type interference, 223 C-type interference, 116 D-type interference, and 6 X-type interference, so most of the interactions are C-type interference. One hundred eighty-six patients had pharmacokinetic interference and 201 patients had pharmacodynamics interference. The highest interaction was between two drugs, heparin and aspirin with 58 cases.

Conclusion: This study highlights the alarming frequency and types of drug interactions observed in ICU. The high prevalence of drug interactions emphasizes the need for improved medication management and vigilance in these critical care settings. Polypharmacy and certain drug combinations were identified as major contributing factors to the occurrence of drug interactions, which calls for regular medication reviews and cautious prescribing practices.

Keywords: cross-sectional study, drug interactions, intensive care units, patient safety

Introduction

Drug interactions continue to be a significant concern in healthcare, particularly in ICUs where patients often receive multiple medications to manage their critical conditions[1]. These drug interactions can lead to adverse outcomes, including increased morbidity, prolonged hospital stays, and even mortality[2,3]. Therefore, a comprehensive understanding of the frequency and types of drug interactions in ICUs is vital to optimize patient care and enhance medication safety[3].

Several factors contribute to the high risk of drug interactions in ICUs. Firstly, critically ill patients frequently require multiple medications to address their complex medical needs, resulting in polypharmacy[4,5]. This exposes patients to a higher likelihood of drug interactions due to the simultaneous use of multiple drugs with varying pharmacological profiles[5].

Secondly, the severity of illness in these patients often necessitates the administration of medications with narrow therapeutic indices, such as anticoagulants, antiarrhythmics, and immunosuppressants[6]. Even minor interactions with these drugs could have profound consequences on patients' health outcomes and increase the risk of adverse drug events[7].

Additionally, the involvement of multiple healthcare professionals in the ICU, including physicians, pharmacists, and nurses, introduces the potential for miscommunication or lack of coordination in medication management[8]. This further contributes to the risk of drug interactions, as different healthcare providers may not have a complete overview of all medications administered to a patient[9].

Despite these well-recognized risk factors, there is limited comprehensive data on the frequency and types of drug interactions specifically in ICU settings[10]. Previous studies have focused

HIGHLIGHTS

- The high prevalence of interactions can be a warning.
- Polypharmacy was found to be a major contributing factor to the occurrence of drug interactions.
- The study findings underscore the importance of implementing electronic decision support systems and interdisciplinary collaboration in critical care settings to prevent and manage drug interactions effectively.

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more on specific drug combinations or narrow patient populations, making it difficult to fully understand the scope and magnitude of the problem[8–10].

Therefore, this cross-sectional study aims to assess the frequency and types of drug interactions in ICUs, providing valuable insights into the prevalence, patterns, and potential implications of these interactions on patient outcomes. By systematically evaluating the medication regimens of critically ill patients, we seek to identify common drug interactions, highlight potential areas of concern, and pave the way for targeted interventions to optimize medication safety within ICUs.

Such findings will not only enhance our understanding of the problem but also facilitate the implementation of evidence-based strategies to minimize drug interactions and improve patient care in ICU settings. Ultimately, the goal of this study is to determine the frequency and types of drug interactions in all patients admitted to the ICU.

Materials and methods

Study design and setting

This cross-sectional study was conducted in order to determine the frequency and types of drug interactions in all patients admitted to the intensive care units of Urmia University of Medical Sciences. Our work has been reported in line with the strengthening the reporting of cohort, cross-sectional and case–control studies in surgery (STROCSS) criteria[11].

Study participants and sampling

The study was carried out with the ethics code IR.UMSU.REC.1400.162 after the proposal was approved by the Research Council of the Faculty and the Ethics Committee of Urmia University of Medical Sciences. The working method was that the researcher, after obtaining permission from the relevant units in the relevant educational and medical centers (Imam Khomeini, Seyyed al-Shodha, and Motahari), went to the special departments of the relevant centers and proceeded to review the patients' files. It was collected from June 2021 to August 2021. In the first month, we tried to record the information of Imam Khomeini Hospital and Kausar Hospital, in the second month, Seyyed al-Shohda Hospital, and in the third month, Motahari Hospital, as well as Imam Khomeini Hospital, were examined again in the third month due to the large number of patients and special departments and new admissions. The exclusion criteria were being discharge before 24 h and transfer to other departments and death less than 24 h after hospitalization, and the inclusion criteria were at least 5 days of hospitalization in the ICU and receiving at least two drugs at the same time. The participants were both adult and pediatric patients of ICU. The information extracted from patient files was entered into the questionnaire by the researcher. A pharmacist researcher meticulously reviewed patient files, employing a predefined set of criteria to identify, and analyze drug-drug interactions in a comprehensive manner. All medication orders which were actually ongoing in the file have been recorded. The questionnaire prepared to collect the pharmaceutical and demographic information of this study included information related to age, sex, type of disease, time of diagnosis, comorbidities, and medications. The collection of demographic information and medications taken by the patient was obtained by referring to the medical record and asking the patient or the patient's companion.

Then, according to the information collected through the questionnaire, severe, moderate, and mild drug interactions were investigated by a pharmacist through Lexicomp drug interaction software. Also, the drug interaction fact book[12] was used as a reference to determine drug interactions. This book is a comprehensive drug information collection in which drugs are classified by therapeutic class, in a way that provides a wide range of drug information in terms of evaluating and comparing drugs. In pharmacology, drug interactions are categorized into four types based on their potential outcomes: Type A (pharmacokinetic interactions), Type B (pharmacodynamic interactions), Type C (combined pharmacokinetic and pharmacodynamic interactions), and Type D (delayed interactions) (also known as Type X).

Data analysis

The collected data was coded and entered in Microsoft Excel and was analyzed using Statistical Package for the Social Sciences (SPSS) version 21.0. Point estimate at 95% CI was calculated along with frequency, percentage, mean, SD, and mode. The patient was the unit, so the study had 1121/300 interactions = 3.7 interactions/patient.

Results

Three hundred patients participated in the study, 140 (46.6%) were female and 160 (53.4%) were male. And 52 (17.4%) were less than 1 year old, 19 (6.3%) were between 1 and 10 years old, 34 (11.3%) were between 10 and 40 years old, and 195 (65%) were older than 40 years. Of the 300 patients studied, 52 (17.3%) were from Seyed al-Shohda Hospital, 48 (16%) were from Kausar Hospital, 179 (59.7%) were from Imam Khomeini Hospital, and 21 (7%) were selected from Motahari Hospital were studied (Table 1).

Among all the patients in the study, 206 (68.7%) had no mild drug interactions, 90 (30%) had 1 or 2 mild drug interactions, four (1.3%) had 3 or 4 mild drug interactions. And of the 300 patients studied, 69 (23%) had no moderate drug interactions, 100 (33.4%) had 1 or 2 moderate drug interactions, 46 (15.3%) had 3 or 4 moderate drug interactions, and 85 (28.3%) had moderate interference in more than four cases. Also, among the

Table 1

Frequency distribution table of demographic variables.

Variables	Frequency	Percent
Sex		
Male	160	53/4
Female	140	46/6
Age		
Less than 1 year	52	17/4
1–10years	19	6/3
10–40 years	34	11/3
More than 40 years	195	65
Hospital		
Imam Khomeini	179	59/7
Seyyed al-Shodha	52	17/3
Motahari	21	7
Kausar	48	16

Table 2

Frequency distribution table of intensity variables.

Variables	Frequency	Percent
Mild drug interaction intensity		
No	206	68/7
1–2	90	30
3–4	4	1/3
Moderate drug interaction intensity		
No	69	23
1–2	100	33/4
3–4	46	15/3
More than 4	85	28/3
Severe drug interaction intensity		
No	233	77/7
1–2	61	20/3
3–4	6	2

patients in the study, 233 (77.7%) had no severe drug interactions, 61 (20.3%) had 1 or 2 severe drug interactions, six (2%) had 3 or 4 severe drug interactions (Table 2).

Of the patients in the study, 114 (38%) had no pharmacokinetic drug interactions, 103 (34.3%) had one or two pharmacokinetic drug interactions, 56 (18.7%) had three or four pharmacokinetic drug interactions, and 27 (9%) had percent) more than four cases have had pharmacokinetic interactions. Finally, out of 300 patients studied, 99 (33%) had no pharmacodynamic drug interactions, 106 (35.3%) had one or two pharmacodynamic drug interactions, 56 (18.7%) had three or four pharmacodynamic drug interactions, and 39 (13%) had more than four cases of pharmacodynamic interference (Table 3).

In the present study, 192 (64%) patients did not have type B interference, 67 (22.3%) had one type B interference, and 41 (13.7%) had more than one type B interference. And among all 300 patients present in the study, 77 (25.7%) patients had no type C interference, 64 (21.3%) had one type C interference, and 159 (53%) had more than one type C interference. Also, in these 184 (61.3%) patients did not have type D interference, 71 (23.7%) had one type D interference and 45 (15%) had more than one type D interference. Finally, in the above study, 294 (98%) patients did not have type X interference, 6 (2%) had one type X interference (Table 4).

Discussion

The present study investigated the frequency of drug interactions in patients admitted to the ICU of Urmia University of Medical Sciences. In this study, a total of 1121 interactions were reported.

Table 3

Type of interaction based on pharmacodynamics and pharmacokinetics.

Pharmacokinetic drug interaction		
No	114	38
1–2	103	34/3
3–4	56	18/7
More than 4	27	9
Pharmacodynamics drug interactions		
No	99	33
1–2	106	35/3
3–4	56	18/7
More than 4	39	13

Table 4

Assessment of drug interaction intensity based on A, B, C, and D interaction.

Type B interaction		
No	192	64
1	67	22/3
More than 1	41	13/7
Type C interaction		
No	77	25/7
1	64	21/3
More than 1	159	53
Type D interaction		
No	184	61/3
1	71	23/7
More than 1	45	15
Type X interaction		
No	294	98
1	6	2

The result showed that the most common drug-drug interaction was type C. In addition, the most patients of study had one or two moderate drug interactions. Also, among the patients in the study, only 2% had three or four severe drug interactions. Moreover, the result revealed the most patients of study had no pharmacokinetic drug interactions and only 9% had pharmacokinetic interactions.

In line with this study, Abideen *et al.*[13] in India showed that the percentage of drug interactions in the ICU was 90.3%, in the study by Rodrigues *et al.*[14] in Brazil the rate was reported as 89%, which is similar to the results of the present study, indicating the high incidence of drug interactions in the country's ICU.

In Turkashund *et al.*[15] study, out of 4318 interference cases, 2708 (62.7%) were related to moderate interferences and 1610 (37.3%) of those were severe interferences of replacement therapy. In the studies conducted in Pakistan[16] and India[13] also reported the most cases of drug interaction intensity at a medium level. In the study of Hosseini *et al.*[17], the intensity of drug interactions in most of the patients under study was mild and moderate. The most important reason for the difference in the results of the studies can be due to the difference in the methods of evaluating drug interactions in these studies.

Data analysis based on Lexicomp and drug interaction fact book showed that 108 (36%) patients had interaction B (an interaction in which two drugs may interfere with each other, but no study or evidence of a problem in the combination of these two drugs has been observed), 223 (74.3%) patients with C interference (in this type, there is an interference between two drugs, but the benefit of using this drug at the same time is greater than its harm), 116 (38.6%) patients with D interference (in this interference between two drugs) drugs have an interaction, but to check whether the benefits outweigh the harms, the patient's clinical condition should be evaluated) and six patients (2%) X interaction (there is a serious interaction between the two drugs). Most of the patients had C interference, followed by D-type interference. The results of the study are the same as the study of Mehrpoya *et al.*[18]. that most of the interferences in terms of the level of risk of interference are of type C (63.89%) and in the second place is interference of type D (21.98%). In the study of Acharya *et al.*[19]. in India, the most interactions in terms of risk

level of interaction were type C. In group C (treatment review), as mentioned, the benefits of taking these two drugs at the same time are usually more than the risks.

Based on the results of the study of 201 patients (67%) (Pharmacodynamics drug interactions are a type of drug interactions that occur in the combination of two drugs with a similar mechanism of action (which causes a cumulative and strengthening effect between two drugs) or electrolyte disturbances caused by a drug to change the effect of another drug) and 186 (62%) pharmacokinetic interactions (pharmacokinetic drug interactions are a type of drug interactions during which one drug affects the factors related to the pharmacokinetics (absorption, release and binding, and clearance of another drug) is identified. According to the results, pharmacodynamics interference is more than pharmacokinetic. The results are similar to Acharya *et al.*[19] study in India that the number of pharmacodynamics interactions is more than pharmacokinetic.

In the present study, drug interactions in none of the hospitals were significantly different between women and men and were almost the same between women and men. According to Turkashund *et al.*[15] study, the prevalence of interference was higher in women than in men. Some studies show no difference between the two sexes[20]. These nonaligned results show that the sex factor cannot be a definite and stable determining factor in predicting the risk of drug interactions. Therefore, it is necessary to pay attention to the patients hospitalized in the ICU, regardless of sex, in terms of the risk of drug interactions.

One effective strategy to address drug interactions in ICUs is the implementation of awareness campaigns. These campaigns aim to educate healthcare professionals, including physicians, nurses, and pharmacists, about the importance of identifying and managing drug interactions. By raising awareness about the potential risks associated with drug interactions, healthcare providers can improve their knowledge and vigilance when prescribing, administering, and monitoring medications in the ICU setting. The presence of a dedicated clinical pharmacist in the ICU has proven to be beneficial in preventing and managing drug interactions. These pharmacists possess specialized knowledge in medication management and are well-equipped to identify potential interactions during the medication reconciliation process. By actively participating in the healthcare team, they can provide valuable insights on optimizing medication regimens, adjusting dosages, and selecting alternative therapies to mitigate the risks of drug interactions and improve patient outcomes.

The utilization of drug information software, such as Lexicomp or similar programs, is a valuable tool for pharmacists and other healthcare professionals in managing drug interactions in ICUs. These software systems provide comprehensive and up-to-date information on drug-drug interactions, allowing pharmacists to quickly and accurately identify potential risks. By utilizing such software, healthcare providers can make informed decisions regarding medication selection, dosage adjustment, and timing of administration to minimize the likelihood of drug interactions.

While the mentioned strategies to address drug interactions in the ICU are valuable, it is important to acknowledge some limitations that may be associated with the study and their implementation:

1. Generalizability: The study may have been conducted in a specific healthcare setting, which may limit the generalizability of the findings to other ICUs with different demographics, patient populations, and institutional practices. Therefore, caution should be taken when applying these findings to other contexts.
2. Sample size: The study may have a limited sample size, reducing its statistical power and potentially limiting the ability to detect significant differences in outcomes between intervention and control groups or subgroups. A larger sample size would strengthen the study's validity and generalizability.
3. Bias: There could be inherent biases or confounders in the study design that might influence the results. For example, the study may not have accounted for potential differences in patient acuity, comorbidities, or severity of illness between the intervention and control groups. These factors could affect outcomes independent of the implemented interventions.
4. Compliance and adherence: The study assumes that healthcare providers consistently adhere to the implemented interventions, such as medication review by pharmacists or using CPOE systems. However, individual variations in compliance or adherence to these protocols may exist, which could affect the effectiveness of the interventions and overall outcomes.
5. External factors: The study might not account for external factors that could influence patient outcomes, such as changes in healthcare policies, variations in patient care across different shifts, or unmeasured confounders. These factors could potentially impact the results and conclusions drawn from the study. Moreover, the potential age-related differences in drug metabolism and pharmacokinetics were another limitation for this study.

Conclusions

This study highlights the alarming frequency and types of drug interactions observed in ICU. The high prevalence of drug interactions emphasizes the need for improved medication management and vigilance in these critical care settings. Polypharmacy and certain drug combinations were identified as major contributing factors to the occurrence of drug interactions, which calls for regular medication reviews and cautious prescribing practices. The findings underscore the importance of implementing electronic decision support systems and interdisciplinary collaboration to prevent and manage drug interactions effectively. Further research and interventions are warranted to address this critical issue and enhance patient safety in ICU.

Ethical approval

Ethical approval for this study (Ethical Committee IR.UMSU.REC.1400.162) was provided by the Ethical Committee of Urmia University of Medical Sciences, Iran on 10 November 2021.

Consent

Written informed consent was obtained from the patient for publication of this study. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request.

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Author contribution

R.B. and A.T.: study concept, data collection, writing the paper, and making the revision of the manuscript following the reviewer's instructions; H.S. and V.A.: study concept, reviewing, and validating the manuscript's credibility.

Conflicts of interest disclosure

The authors declare that they have no financial conflicts of interest with regard to the content of this report.

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Guarantor

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Data availability statement

The datasets generated during and/or analyzed during the current study are available upon reasonable request.

Provenance and peer review

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