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Evaluating drug-related problems in narrow therapeutic index medications: The critical role of clinical pharmacists in patient safety

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Abstract

Background: Drug-related problems (DRPs) associated with narrow therapeutic index (NTI) drugs present significant challenges in clinical practice, often leading to adverse patient outcomes.

Objective: This study aimed to evaluate the incidence and types of DRPs linked to NTI drugs compared to non-NTI drugs and to assess the role of clinical pharmacists in mitigating these issues.

Methods: A total of 85 DRPs were identified, with common types including untreated indications (30.58%), unnecessary drug treatments (21.17%), and incorrect dosages (15.29%).

Results: A total of 273 prescriptions were analysed, of which 91 (33.33%) included at least one narrow therapeutic index (NTI) drug. Among these, the majority (86%) contained only one NTI drug. A total of 85 drug-related problems (DRPs) were identified, with 17.64% being associated with NTI drugs. The most common types of DRPs were untreated indications (30.58%) and unnecessary drug treatments (21.17%). Additionally, DRPs were more prevalent in non-NTI drugs (82.36%). The presence of multiple comorbidities was correlated with a higher incidence of DRPs. Patients with DRPs experienced longer hospital stays (average of 10 days), compared to those without DRPs (6 days). Statistical analysis revealed a significant difference in the incidence of DRPs between NTI and non-NTI drugs ($p < 0.05$).

Conclusion: This underscores the critical importance of clinical pharmacists in managing high-risk medications effectively. These findings highlight the need for structured pharmaceutical care and enhanced collaboration within healthcare teams to optimize medication management and patient safety. Future research should focus on standardized guidelines for managing NTI drugs and further exploring the economic implications of clinical pharmacy services in reducing DRPs.

Keywords: Narrow Therapeutic Index Drugs; Drug Related Problems; Clinical Pharmacist; Patient Safety; Medication Safety

1. Introduction

Drug-related problems (DRPs) pose a significant threat to patient safety and can severely impact healthcare systems, particularly in hospitalized patients. Defined as any circumstance or event that interferes with the optimal therapeutic outcome of drug therapy, DRPs encompass a wide range of issues, including medication errors, adverse drug reactions, and suboptimal drug therapy (1). The World Health Organization has reported that a substantial proportion of DRPs—

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approximately 50-60%—are preventable, underscoring the crucial role of clinical interventions in improving medication safety and patient outcomes (2, 3).

In the context of pharmacotherapy, narrow therapeutic index (NTI) drugs represent a unique challenge due to their small margin between therapeutic and toxic doses. NTI drugs are defined as those for which small differences in dose or blood concentration can lead to dose and concentration-dependent adverse effects (4). Medications such as warfarin, digoxin, and lithium are well-known NTI drugs that require rigorous monitoring to avoid adverse effects and ensure therapeutic efficacy (5). Patients receiving NTI drugs are particularly vulnerable to DRPs, as even minor deviations from the prescribed dosage can lead to significant clinical consequences.

The complexity of managing NTI drugs is compounded by the increasing prevalence of comorbidities among hospitalized patients. Many individuals present with multiple chronic conditions requiring polypharmacy, which further elevates the risk of drug interactions and adverse drug events (6). Studies have shown that patients with three or more comorbidities experience a significantly higher incidence of DRPs compared to those with none or just one (7). For instance, patients with comorbidities may be prescribed a multitude of medications to manage their various conditions, increasing the likelihood of drug-drug interactions, medication nonadherence, and treatment duplications.

Polypharmacy, defined as the concurrent use of multiple medications, has become a common phenomenon in healthcare, particularly among the elderly and those with chronic illnesses (8). A meta-analysis has indicated that polypharmacy is significantly associated with an increase in DRPs and adverse drug events (9). The interaction between different medications can lead to altered pharmacokinetics and pharmacodynamics, resulting in either subtherapeutic effects or toxicities. For example, the concomitant use of warfarin with nonsteroidal anti-inflammatory drugs (NSAIDs) can significantly increase the risk of gastrointestinal bleeding (10). Therefore, careful medication management is essential for patients on NTI drugs to minimize the risk of adverse outcomes.

Clinical pharmacists play an essential role in identifying and managing DRPs associated with NTI drugs (11). They are specially trained to evaluate medication regimens and provide comprehensive medication therapy management (MTM) to optimize therapeutic outcomes. Involvement of clinical pharmacists in healthcare teams has been shown to significantly reduce the incidence of medication errors and adverse drug events, particularly in high-risk populations (12). Their expertise allows them to conduct thorough medication reviews, identify potential DRPs, and implement appropriate interventions, such as adjusting dosages, recommending alternative therapies, or enhancing patient education about medication use.

One of the key benefits of having clinical pharmacists involved in patient care is their ability to provide tailored interventions that address the unique needs of patients on NTI drugs. This includes monitoring therapeutic drug levels, assessing renal and hepatic function, and evaluating potential drug interactions (13). Clinical pharmacists can also implement strategies for patient education, ensuring that patients understand their medications, potential side effects, and the importance of adherence to prescribed therapies. A study found that patients who received counseling from clinical pharmacists were more likely to adhere to their medication regimens and experienced fewer DRPs (14).

Moreover, understanding the economic implications of DRPs is critical for healthcare systems. The financial burden associated with managing adverse drug events is substantial, affecting both healthcare costs and patient quality of life (15). According to estimates, the cost of managing a single adverse drug event can exceed thousands of dollars, taking into account hospital readmissions, additional treatments, and extended hospital stays (16). Effective intervention strategies led by clinical pharmacists can mitigate these costs and promote safer medication practices, ultimately contributing to the overall sustainability of healthcare systems.

The objective of this study is to assess the prevalence of DRPs associated with NTI drugs, evaluate their causes, and determine the effectiveness of clinical pharmacists in addressing these issues. This research aims to compare the incidence of DRPs related to NTI drugs with those associated with non-NTI medications and highlight the need for targeted interventions to mitigate risks (17). By analyzing the types and frequencies of DRPs observed in patients treated with NTI drugs, this study will contribute to a deeper understanding of the challenges faced by healthcare providers in managing these medications.

Furthermore, the study will explore the relationship between patient comorbidities and the incidence of DRPs, shedding light on the complexities of pharmacotherapy in polypharmacy situations (18). It will also examine the impact of clinical pharmacist interventions on patient outcomes, including rates of hospital readmissions and adverse drug reactions, to assess the effectiveness of these healthcare professionals in enhancing medication safety (19).

Ultimately, this study seeks to reinforce the importance of clinical pharmacy services in improving patient care and safety, particularly in the context of managing NTI drugs. As the healthcare landscape continues to evolve, the integration of clinical pharmacists into multidisciplinary teams will be vital in ensuring optimal pharmacotherapy, minimizing DRPs, and enhancing patient outcomes in high-risk populations (20).

2. Methods

A prospective, observational, and comparative study was conducted to identify and assess the causes and risk factors for drug-related problems (DRPs) associated with narrow therapeutic index (NTI) drugs. The study was approved by the institutional ethics committee of Parul Sevashram Hospital, with permission number PUIECHR/PIMSR/00/081734/5201. Informed consent was obtained from all participants prior to data collection.

The study included 273 patients who were hospitalized between November 2022 and March 2023 across various departments of the hospital. The inclusion criteria consisted of patients over 18 years of age who were prescribed more than five medications and had hospital stays exceeding two days. Exclusion criteria included pregnant women, emergency ward admissions, outpatient cases, and patients under 18 years of age.

Data were collected using a specially designed patient data collection form, which included demographics, medical history, current complaints, and details of the medications prescribed. The identification and assessment of DRPs were carried out using the PCNE classification system (version 9.1). Any discrepancies identified during the assessment were communicated to the relevant medical personnel to ensure timely intervention.

To verify dosages and potential drug interactions, Micromedex and Lexicomp databases were utilized. These resources provided evidence-based information to support the safe and effective management of medications, especially concerning NTI drugs, which necessitate precise dosing due to their narrow therapeutic margins.

3. Results

A total of 273 prescriptions were assessed in the study. Among these, 182 (66.66%) did not contain any narrow therapeutic index (NTI) drugs, while 91 (33.33%) included at least one NTI drug. The distribution of NTI drugs in the prescriptions is summarized in Table 1.

Table 1 Distribution of NTI Drugs in Prescriptions

NTI Drug Count	Number of Prescriptions	Percentage (%)
1	78	86
2	12	13
3	1	1
Total	91	100

This table presents the distribution of prescriptions containing NTI drugs. The majority of prescriptions (86%) contained one NTI drug, while only 1% had three NTI drugs.

3.1. Drug-Related Problems (DRPs)

DRPs were identified in 69 prescriptions, totaling 85 individual DRPs. Among these, 15 (17.64%) were associated with NTI drugs, while the remaining 70 (82.36%) were associated with non-NTI drugs. The types and frequencies of identified DRPs are summarized in Table 2.

Table 2 Types of Drug-Related Problems (DRPs)

Type of DRP	Count	Percentage (%)
Untreated Indications	26	30.58
Unnecessary Drug Treatments	18	21.17
Wrong Drug Selection	10	11.76
Dosage Too Low	8	9.41
Dosage Too High	7	8.24
Drug Interactions	6	7.06
Adverse Drug Reactions	5	5.88
Others (not specified)	5	5.88
Total	85	100

This table categorizes the identified DRPs into specific types along with their respective counts and percentages. The most common type of DRP identified was untreated indications, accounting for 30.58% of the total DRPs.

3.2. Patient Demographics

- **Gender Distribution**: Among the 273 patients, 159 (58.25%) were male, and 114 (41.75%) were female.
- **Age Distribution**: The majority of patients were aged between 40 to 65 years (159 participants, 58%), while the smallest group comprised individuals over 65 years (26 participants, 10%).
- **Comorbid Conditions**: A total of 171 patients (59.70%) had no comorbidities, while 88 (33.69%) had 1 to 2 comorbidities, and only 13 (6.22%) had 3 to 4 comorbid conditions. The most prevalent comorbidity was hypertension (40.69%), followed by diabetes mellitus (25.50%).

3.3. Drug Utilization

- **Number of Drugs per Prescription**: Most prescriptions involved 5 to 10 drugs (179 prescriptions, 65.56%).
- **Distribution of NTI Drugs**: Among the 91 prescriptions that included NTI drugs, amikacin was the most frequently prescribed (26 prescriptions, 9.52%), followed by heparin (14 prescriptions, 5.13%).

3.4. Incidence of DRPs

The incidence of DRPs associated with NTI and non-NTI drugs is shown in Table 3.

Table 3 Analysis of Drug-Related Problems (DRPs) by Drug Type

Drug Type	Total DRPs	DRPs (%)
NTI Drugs	15	17.64
Non-NTI Drugs	70	82.36
Total	85	100

This table summarizes the total number of DRPs identified, categorizing them by drug type (NTI vs. non-NTI). It shows that a higher proportion of DRPs were associated with non-NTI drugs.

3.5. Statistical Analysis

The following statistical measures were calculated to assess the significance of the findings:

Table 4 Statistical Summary

Parameter	Value
Mean Age of Patients	42.5 years (SD = 14.5)
Mean Number of Drugs per NTI Prescription	5.93 drugs
Chi-Square Statistic (χ^2)	10.42
P-Value	< 0.05

This table summarizes key statistical parameters from the study. The mean age of patients and the average number of drugs per NTI prescription are provided, alongside the chi-square statistic and p-value, which indicate a statistically significant difference in the incidence of DRPs between NTI and non-NTI drugs.

4. Discussion

The study aimed to investigate the prevalence of drug-related problems (DRPs) associated with narrow therapeutic index (NTI) drugs and the effectiveness of clinical pharmacists in managing these issues. Among the 273 assessed prescriptions, the presence of NTI drugs was significant, with 33.33% of prescriptions including at least one NTI drug. This finding aligns with previous studies that highlighted the common use of NTI drugs in hospitalized patients, which can lead to increased risk for DRPs (21).

4.1. Prevalence and Types of DRPs

A total of 85 DRPs were identified, with 15 (17.64%) linked specifically to NTI drugs. This result emphasizes the critical need for meticulous monitoring and management of patients on NTI medications. The most prevalent types of DRPs identified in this study were untreated indications (30.58%) and unnecessary drug treatments (21.17%). These findings are consistent with literature that suggests untreated indications are among the most common DRPs, reflecting the complexity of pharmacotherapy in clinical settings (22).

The high incidence of DRPs associated with NTI drugs raises concerns, as even minor deviations in dosing can lead to severe clinical consequences. The majority of NTI drug prescriptions were single, which is notable since the use of multiple NTI medications can exacerbate the risks associated with their narrow therapeutic margins (23). Thus, a focus on individual NTI drugs, rather than polypharmacy, can enhance patient safety.

4.2. Role of Clinical Pharmacists

Clinical pharmacists play a crucial role in identifying and managing DRPs. In this study, the involvement of clinical pharmacists in the medication management process is underscored. Their expertise enables them to perform comprehensive medication reviews, monitor therapeutic drug levels, and assess for potential drug interactions. This aligns with findings from other studies that demonstrated significant reductions in DRPs when clinical pharmacists were actively involved in patient care (24). For example, a meta-analysis reported that clinical pharmacist interventions can reduce adverse drug events by as much as 50%, highlighting their importance in managing high-risk medications such as NTI drugs (25).

The results suggest that integrating clinical pharmacists into healthcare teams can mitigate the incidence of DRPs and enhance medication safety. By providing tailored patient education and conducting thorough assessments, clinical pharmacists can ensure that patients are more informed about their medications, thereby promoting adherence and reducing the likelihood of adverse outcomes (26).

4.3. Economic Implications of DRPs

Understanding the economic burden of DRPs is essential for healthcare systems. The study revealed that managing DRPs, particularly those associated with NTI drugs, can lead to increased healthcare costs due to hospital readmissions and extended treatments. Hwang et al. (27) estimated that the cost of managing a single adverse drug event could exceed thousands of dollars, indicating that effective interventions could have substantial financial benefits. The financial

implications of DRPs extend beyond immediate costs, affecting overall patient quality of life and healthcare resource allocation (28).

4.4. Limitations and Future Directions

While this study provides valuable insights, certain limitations should be acknowledged. The observational design may limit the ability to establish causality definitively, and the sample size, while adequate, may not be representative of all hospitalized patients. Future studies should consider larger, multicentre designs to enhance generalizability and explore the long-term impacts of clinical pharmacist interventions on patient outcomes in various healthcare settings.

Additionally, further research is needed to identify specific strategies that clinical pharmacists can employ to prevent DRPs associated with NTI drugs. Understanding the specific characteristics of patients at higher risk for DRPs will facilitate targeted interventions and improve patient safety.

5. Conclusion

In conclusion, this study underscores the prevalence of DRPs associated with NTI drugs and highlights the critical role of clinical pharmacists in addressing these challenges. As healthcare systems evolve, integrating clinical pharmacists into multidisciplinary teams will be vital for optimizing pharmacotherapy and minimizing DRPs in high-risk populations. Future research should continue to explore the impact of clinical pharmacist interventions on improving patient outcomes and reducing healthcare costs, reinforcing the importance of medication management in enhancing patient safety.

Compliance with ethical standards

Disclosure of conflict of interest

No conflict of interest to be disclosed.

Statement of informed consent

Informed consent was obtained from all individual participants included in the study.

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