Pharmacovigilance Analysis of Drug-Drug Interactions in the FDA Adverse Event Reporting System: A Retrospective Study

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Introduction

As healthcare systems advance globally, the complexity of healthcare becomes a challenge and affects healthcare professionals and patients.[1] Every year, the number of patients suffer from adverse events due to health-related risks that are not appropriately accounted for and affects the quality and safety of patient care.[2] Any practice that involves patient safety should carefully analyze and manage for life-threatening situations including medication errors, healthcare-associated infections, unsafe medical practices and procedures, diagnostic errors, etc.

According to the National Coordinating Council for Medication Error Reporting and Prevention (NCCMERP), a medication error is a preventable event that involves medication use that may result in patient harm at any point of the medication use process including ordering medications to monitoring patients.[3] The Food and Drug Administration (FDA) has developed the FDA Adverse Event Reporting System (FAERS), which is a web-based database used by healthcare professionals, patients, and manufacturers to publicly review and report medication or biologic related adverse events (FDA), to minimize medication error risks. Another strategy used to prevent drug interactions is the use of health information technology (HIT), which includes clinical decision support systems or electronic health records, to double check the patient's high-risk medications and medication history.[4]

With secondary data collected from FAERS, this study focuses on medication error, more specifically drug-drug interactions. The investigator will analyze and assess drug interaction labeled reports sent through the FAERS database to determine correlations between the interactions, demographics, and prevalence of incorporated drug classes to estimate the prevalence of this medication error worldwide. The hypothesis is that if the medication error reported to FAERS happened in the years of 2017 to 2019 and is labeled as a potential drug-drug interaction, then the use of pharmacovigilance can estimate the prevalence rates of drug-drug interactions globally.

The aim is by doing so, the study creates awareness of the negative impact that drug-drug interactions have on patient care to healthcare professionals, patients, and manufacturers. Prevention is key in handling medication errors and is a high priority worldwide in the healthcare system risk mitigation plans.[5] Thus, the objective of the study will be to analyze and assess drug-drug interactions in the FAERS database to determine trends and correlations in prevalence by demographic characteristics and risk factors and drug classes and frequencies.

Methods

Study Design and Population
The study design was correlational descriptive research, retrospectively assessing drug-drug interaction cases over a period of 3 years, from 2017 to 2019 populated in the FDA Adverse Event Reporting System (FAERS). The study population was composed of patients involved in the case listing from the FAERS for the determined study period.

Literature Review
For the literature review, the investigator searched Google Scholar and PubMed databases using the terms "drug-drug interactions", "assessment", "pharmacovigilance", and "medication errors." The collected 32 articles were screened with the abstracts, and 15 articles were excluded because the aims and objectives of the studies were not similar to the investigator's research. The investigator read the remaining 15 articles' full text and decided to include 10 out of the 15 articles for the final study.

Data Collection
The investigator initially searched by the reaction terms "labeled drug-drug interactions" in the database. In the listing of cases, the reported event dates are limited to the years of 2017, 2018, and 2019. For this study, only cases labeled as "serious" were included in the assessment. A total of 54 serious cases were produced and exported into a Microsoft Excel spreadsheet. Duplicated cases, which were determined based on similar variables, and cases with only one suspected medication provided were removed, and the finalized total cases was 38. The analyzed data from the FAERS report includes the suspect product name, drug class, event date, and patient's sex and age.

The investigator searched for known interaction and severity of the interaction between the suspected products for each case from the following databases: LexiComp and Micromedex. With each found interaction, the investigator included the data into the previously exported Microsoft Excel spreadsheet. For each suspected product, the investigator used LexiComp and Micromedex databases to determine the respective drug class.

Statistical Analysis
Microsoft Excel was used to create charts and tables and to analyze the data from the FAERS database to determine correlations between different aspects of the cases including the products, established interaction severity, drug classes, and patient's sex and age.

Results

From the FAERS, a total of 38 severe cases including 44 drug-drug interactions were evaluated. There are 5 cases that involved more than one interaction. Discrepancies between the proprietary databases including Lexicomp and Micromedex were reviewed. Of the 44 interactions, Lexicomp has identified 11 contraindicated interactions, while Micromedex has only classified 4 interactions as contraindicated. From the 33 interactions that both databases can classify, there is a 52% difference in the severity rating between the two databases.

The demographic of the cases includes 60.5% females and 36.8% males. There is 2.6% of the cases that did not specify the sex of the patient. Between the selected three years of reported case events, 45% of cases occurred in the year 2017, 42% of cases occurred in the year 2018, and 13% of the cases occurred in the year 2019. Half of the reported cases occurred in the United States. Of the 33 reported cases, 55% of the cases involve patients equal to or greater than 65 years of age, 24% were less than 65 years of age, and 21% were not specified.

The drug classes that are commonly identified among the 38 drug interactions include antineoplastic agents (n=9, 12%), antiplatelets (n=8, 10%), antihypertensive agents (n=8, 10%), and anticoagulants (n=7, 9%). Agents in other drug classes that are involved in the reported cases are noted. Most commonly involved drug in these cases is aspirin, which appeared in 9 out of 44 interactions (20%).

Table 1. Drug Classes of Medication Involved in the Reported FAERS Drug-Drug Interaction Cases

Drug Class	Percentage
Antineoplastic	12%
Antihypertensive	10%
Antiplatelets	10%
Anticoagulant	9%
Antiarrhythmic	6%
Antianginal	6%
Antibiotic	5%
B2 Agonist	5%
Antilipemic	4%
Antifungal	4%
Anticholinergic	4%
Corticosteroid	3%
Immunosuppressant	3%
Opioid analgesic	3%

Discussion

Overall, the study has assessed drug-drug interaction labeled cases from the FDA Adverse Event Reporting System (FAERS). The comparison between the Micromedex and Lexicomp databases show that although both resources are evidence-based, there are conflicting results in the analyzed drug-drug interactions. Factors observed in the study included age and sex of the patients and the drug classes involved in the cases. The results have provided baseline information about the prevalence and correlational relationship of drug-drug interactions between age groups, sexes, and therapeutic drug classes.

This study supports the idea of pharmacovigilance in improving or enhancing information and technology incorporated into the healthcare workflow such as clinical decision support systems (CDSS) or electronic health record (EHR) alerts. The study focuses on the aspect of improving patient care by optimization of drugs and medication for the treatment and avoiding undesirable effects including medication errors. The data obtained from this study will bring awareness to the prevalence of drug-drug interactions globally and will be useful in the development of future and extensive adverse drug reactions (ADR) monitoring and alerting programs in clinical settings.

References

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