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Original Research

Identifying high risk medications causing potential drug–drug interactions in outpatients: A prescription database study based on an online surveillance system

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Abstract

Background: Drug–drug interactions (DDIs) are a significant cause for adverse drug events (ADEs). DDIs are often predictable and preventable, but their prevention and management require systematic service development. Most DDI studies focus on interaction rates in hospitalized patients. Less is known of DDIs in outpatients, particularly how community pharmacists could contribute to DDI management by applying their surveillance systems for identifying high-risk medications.
Objectives: The study was related to the implementation of the first online DDI surveillance system in Finnish community pharmacies. The goal was to demonstrate how community pharmacies can utilize their prospective surveillance system 1) for identifying high risk medications causing potential DDIs in outpatients, 2) for collaborative service development with local physicians, and 3) for academic risk management research purposes.
Methods: All DDI alerts given by the online surveillance system were collected during a one-month period in 16 out of 17 University Pharmacy outlets in Finland, covering approximately 10% of the national outpatient prescription volume. The surveillance system was based on the FASS database, which categorizes DDIs into four classes (A–D) according to their clinical significance.
Results: Potential drug–drug DDIs were analyzed for 276,891 dispensed community pharmacy prescriptions. Potential DDIs were associated with 10.8%, or 31,110 of these prescriptions. Clinically significant interaction alerts categorized as FASS classes D (most severe, should be avoided) and C (clinically significant but controllable) were associated with 0.5% and 7.0% of the prescriptions, respectively.

Conflict of interest: Terhi Toivo, no conflict of interest. Kari Laine, M.D. is the CEO and a shareholder of Medbase Ltd, co-owner to the immaterial rights of the SFINX drug interaction database. Dr. Janne Mikkola worked at the time of the study at the University Pharmacy. Prof. Marja Airaksinen has been a board member of the University Pharmacy since 2007. No external funding was used to conduct this study.

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Methotrexate and warfarin had the highest risk of causing potentially serious (class D) interactions. These interaction alerts were most frequently between methotrexate and NSAIDs and warfarin and NSAIDs. In general, NSAIDs were the most commonly interacting drugs in this study.
Conclusions: This study demonstrates that community pharmacies can actively contribute to DDI risk management and systematically use their surveillance systems for identifying patients having clinically significant DDIs. The findings also indicate that the majority of potentially serious interactions in outpatients involve a limited number of drugs, particularly NSAIDs, warfarin and methotrexate. Further research should focus on community pharmacists' involvement in DDI risk management in collaboration with local health care providers.

Keywords: Drug–drug interaction; Community pharmacy; Prescription; Outpatient; Service development; Risk management

Introduction

Drug–drug interactions (DDIs) have shown to be a significant cause for adverse drug events (ADEs).[1–4] The estimates of hospital admissions caused by DDIs vary from 0.1% to 2.6%.[5–7] ADEs related to drug–drug interactions increase the length of stay in the hospital, add costs, and result in adverse consequences for patients.[8] Many drugs have even been withdrawn from the market due to their potential to cause fatal drug–drug interactions.[9,10]

Drug–drug interactions are more often predictable and preventable than other causes for adverse drug events, and therefore, they are an important medication safety issue. Most of the existing studies on DDI incidence focus on interactions in hospitalized patients,[11,12] with fewer concerning the incidence of DDIs in primary care outpatients. These studies have focused on certain patient groups, e.g., aged people or cancer patients[13–18] or on certain medicine groups, such as HIV drugs.[19,20] Patient's age, number of prescribers involved and polypharmacy significantly increase the risk for drug–drug interactions.[13,21–25]

DDI incidence estimates vary markedly across studies from different countries since the health care environments and systems vary. Drugs that are approved and marketed vary by country, and so do prescribing patterns. There are also big differences between drug interaction screening programs and databases with regard to inclusion, severity classification, and documentation level of DDIs.[26] Even widely used interaction screening programs differ in detecting interacting drug–drug pairs.[26,27] These differences produce markedly varying results across the DDI incidence studies.[28–30]

In addition to contextual differences in DDI studies, research methods used in DDI incidence studies vary. Retrospective methods are most frequently used, cross-sectional studies from health care databases or prescription registers occurring frequently.[25,28,29] Few studies have used online surveillance systems in community pharmacies to detect DDIs.[22,31–33] Swedish and Finnish studies have used FASS or SFINX interaction databases which classify interactions according to their clinical significance.[25,28,30,31,34] Our systematic literature review on previous DDI studies revealed that only few studies (4 out of 21) were conducted in community pharmacy settings, none of them using large datasets. The existing studies were primarily focused on describing the rate of DDIs, but not service development for community pharmacists' involvement in systematic management of clinically significant DDIs in collaboration with local physicians.

Objectives

The objective of this study was to investigate the rate and types of clinically significant, potentially harmful DDIs occurring in a national sample of primary care outpatients and how community pharmacists can prospectively contribute to their identification. The study was related to the implementation of the first online DDI surveillance system in Finnish community pharmacies. The goal was to demonstrate how community pharmacies can utilize their surveillance system 1) for prospectively identifying high risk medications causing potential DDIs in outpatients, 2) for collaborative service development with local physicians, and 3) for academic risk management research purposes.