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Optimizing Pharmacy Drug Alert Systems to Prevent Significant Drug-Drug Interactions

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The prescribing of safe and effective drug therapy is becoming increasingly complex. More and more patients are receiving multiple drug therapies for acute and chronic conditions or diseases. As the number of medications taken by the individual patient increases, the potential for drug-drug interactions (DDI) that have clinically important consequences increases. A DDI is defined as concomitantly administered medications which interfere with the efficacy or safety profile of each other. In the early 1990s, patients experienced serious cardiac toxicity after taking antihistamine drugs in combination with macrolide antibiotics. Subsequently, the antihistamines terfenadine and astemizole were withdrawn from the marketplace, in part, due to safety concerns about drug interactions.[1] More recent evidence through the 2003 Tennessee Medicare database suggest that drug combinations with similar DDI continue to de dispensed and increase the risk of sudden death by five-fold.[2]

Systems that can prevent DDI can theoretically reduce the morbidity, mortality and cost to patients that experience significant DDI. Computerized algorithms to identify DDI have been available for over three decades.[3] Current computerized software tools have relied on release of DDI-alerts that "pop-up" on the screen to alert the individual entering the drug order. As can be expected, the reliability and effectiveness of such DDI-alert systems is dependant on several variables such as workload, education, and provider perceptions. The purpose of the current review is to describe limitations of current pharmacy DDI-alert systems and potential solutions to optimize their use.

Methods

A literature search was performed on September 10th using the MeSH Database in PubMed. The MeSH term 'drug interactions' was combined with several MeSH terms related to 'pharmacy' as outlined in Table 1 below. The MeSH term 'drug interactions' was ultimately combined with the text word' [tw] 'alert' and limited to articles that were available as full text, in English, in humans, and published in the

last five years. The thirty-one articles were reviewed and original research articles pertaining to use of

DDI-alert systems in pharmacies were included.

Table 1. Summary of search strategy utilized to identify articles related to drug-drug interactions

alerts.

Search	Most Recent Queries	Time	Result
#14 Search **"alert"[tw] AND "Drug Interactions"[Mesh]** Limits: **published in the last 5 years, only items with links to full text, Humans, English**		11:50:55	31
#13 Search **"Community Pharmacy Services"[Mesh] AND "Drug Interactions"[Mesh]** Limits: **published in the last 5 years, only items with links to full text, Humans, English**		11:49:30	17
#9 Search **"Community Pharmacy Services"[Mesh] AND "Drug Interactions"[Mesh]**		11:48:51	39
#12 Search **"Drug Interactions"[Mesh] AND "Pharmacies"[Mesh]**		11:47:58	36
#11 Search **"Drug Interactions"[Mesh] AND "Pharmacies"[Mesh] OR "Pharmacy"[Mesh]**		11:47:42	7067
#5 Search **"Drug Interactions"[Mesh] and "alert"[tw]**		11:42:07	125
#4 Search **"Drug Interactions"[Mesh]and "alert"[tw]**		11:41:56	125
#3 Search **"Drug Interactions"[Mesh]and "alert"**		11:41:44	126

<u>Probability of severe DDI in Pharmacies</u>

The incidence and response to severe DDI is easier to quantify in certain Nordic countries

secondary to nationalized healthcare delivery systems. The Swedish drug interaction database is a system

that has been incorporated into pharmacies in both Sweden and Finland.[4, 5] The system categorizes

DDI-alerts into classes A-D, where A represents 'not clinically significant' while D represents 'serious

clinical effects'. A review of 39,539 prescriptions was performed between September and November

2004 in southern Finland.[5] These data indicated that 9.8% of all prescriptions generated a DDI-alert,

however only 0.4% of all prescriptions were categorized as significant (class D). A longer-term study

conducted in northwest Sweden reviewed 8,214 patients who had filled two or more prescriptions

(~119,920 prescriptions).[4] A class D interaction was detected among 2% of patients. Overall, these data

suggest that incidence of significant DDI to be low in Nordic countries. The applicability of this data set

to the US population may be limited given that US patients can use multiple pharmacies and can have multiple prescribers. Despite these limitations, one could argue that focusing DDI-alert systems on severe DDI could improve pharmacy workload and response to these alerts.

Pharmacist response to DDI-alert systems

The response of community pharmacists to DDI-alerts was collected through a 7 day prospective observational design from a single US chain community pharmacy.[6] This observational period was followed by a questionnaire directed at a panel of nine community pharmacists to quantify the proportion of time spent dealing with and overriding DDI-alerts. A total of 51 (11 major) DDI alerts were observed and all (100%) alerts were overridden by the pharmacists. The time spent on review and override was less that one minute per DDI-alert. A majority (7 of 9)of the independent panelists indicated that they spent less that 12.5% of their daily shift attending to DDI-alerts but that $80 \pm 14\%$ was spent on DDI that were not clinically significant. The panelists deemed the large number of DDI alerts to be desensitizing to pharmacists. The panelists argued that software sensitivity must be adjustable by the pharmacist and that previous overrides should be documented to reduce duplication of DDI-alerts from patient to patient.[6]

Indermitte and colleagues performed a larger prospective observational study of pharmacist responses to DDI-alerts from 15 community pharmacies operating in Switzerland.[7] All participating pharmacies used a common DDI management system known as Pharmavista®. This software permitted individual pharmacies to adjust the sensitivity of the DDI system to permit automatic overrides. A total of 787 potential DDI-alerts were recognized and 35.3% automatically overridden by the software settings. Of the remaining 510 DDI-alerts, 36.7% were overridden by the pharmacist without evaluation. Direct analysis such as literature consultation, prescriber or patient consultation was performed with only 87 (11.1%) of the DDI-alerts. However only 10 DDI-alerts were defined as severe and in all cases pharmacists intervened. Patient outcomes related to automatic and pharmacist directed DDI-alert overrides were not captured.[7]

Barriers to Pharmacist response to DDI-alerts

A stratified random sample of 3000 community pharmacies was selected to collect data from a 34-item survey of 4 issues: 1) workload, 2) use of technology to process prescriptions, 3) response to DDI-alerts.[8] The survey was to be completed by pharmacy managers and an overall response rate of 25% was achieved. The respondents were mangers of busy pharmacies with mean ± SD of 1375 ± 691 prescriptions per week, with a 14.1 ± 4.9 prescriptions filled per pharmacist hour. Only, 56.1% of pharmacies had a computer software package with detailed DDI alerts and 29.9% were customizable by the pharmacist. Interestingly, pharmacies with computer systems that provided detailed DDI were more likely to dispense drugs with potential DDI than pharmacies than pharmacies without this system (p=0.008). A comparison of 90th and 10th percentile of pharmacies to identify risk-factors for dispensing drugs with DDI was made. The number of prescription/pharmacist hour and pharmacies that customize DDI-alerts directly correlated with increased risk for dispensing drugs with potential DDI.[8]

Although the sophistication and use computerized DDI systems may be beneficial. Pharmacist attitudes to such systems are also vital to their implementation and utility. Pharmacist views on DDI-alert systems were captured through a survey of employees of the Veteran Administration system.[9] This study included the response of 84 pharmacists, half of whom indicated that the DDI-alert system gave them information that they all ready knew. Only two percent perceived the system to be a 'waste of time'. Over 80% felt that more detailed information should be provided and management alternatives should be included.[9]

Summary

The rising number of prescriptions dispensed over time increases the probability of DDI. Computerized DDI-alert systems have been in use in pharmacies to prevent DDI. Current data suggest that a majority of DDI-alerts in community pharmacies are not significant and substantial time is spent in response to DDI-alerts. Several barriers exist to the optimization of DDI-alert systems and stem primarily from the customizability and pharmacy workloads. Limited data exist regarding the rate of adverse events

due to significant DDI resulting from drugs dispensed due to pharmacist overrides of DDI-alerts.

Although DDI-alert systems are a logical technology to utilize in pharmacies, systematic evidence supporting their clinical impact is lacking.

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