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Educational Affairs
A Systematic Approach to Drug Interactions for Pharmacists

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Background

On December 15, 2016, the Chicago Tribune published an article titled, "Pharmacies Miss Half of Dangerous Drug Combinations."[1] This article contained results from an experiment that involved undercover investigators posing as patients. Investigators presented prescriptions with interacting drug combinations to 255 chain and independent community pharmacies in the Chicagoland area. The receiving pharmacist had to either contact the prescriber or inform the undercover reporter of the interaction in order to receive a passing score. To the average reader used to hearing that pharmacists are one of the most trusted healthcare professionals, the results were overwhelmingly impactful in a negative way. The article provides the statistic that 52% of the pharmacies dispensed the "dangerous" combinations without mentioning the interaction to the patient or prescriber. According to the author, these results offer "striking evidence of an industrywide failure that places millions of consumers at risk."[1]

Impact on Practice

Some pharmacists have questioned the clinical relevance of some of the drug-drug interactions (DDIs) in the experiment, and others have questioned some of the logistics of the study design. However, from a "big picture" standpoint, the release of this article leads us back to two questions – "What factors contribute to pharmacists dispensing drugs with documented interactions?" and "What can be done to prevent them?" There are many theories on this topic.

Speed vs. Safety

The Tribune article suggests that the errors may occur because of the emphasis on speed over safety. Such blame cannot be placed entirely on pharmacists, as several factors may be involved. Pharmacists in all settings face

intense pressures of minimal staffing, environmental stressors (e.g., impatient customers and fast-paced surroundings), and/or evaluation techniques utilized by the employer that place an overwhelming emphasis on timeliness.

Over-Reliance on Technology

While most view the use of technology as a safety net, it does not and cannot prevent all medication-safety issues. In fact, use of technology is creating new types of errors including selection of incorrect patient or incorrect drug from a drop-down menu, among others.[2,3] Users must also keep in mind that although DDI alerts are incredibly beneficial, they are not without flaws. Alerts are not designed to replace the knowledge, experience, and expertise of a pharmacist. In fact, a study performed on nine primary care clinical systems in Australia demonstrated that only two out of the nine systems provided sufficient information regarding the clinical effects of significant drug interactions.[4] With that in mind, users carry the responsibility of providing constant feedback to the information technology team at their facility regarding updates and clinical usefulness of the alerts they encounter. In addition, users must be aware of the strengths and shortcomings of the technology they are using and remember that the technology is only an aid. Regardless of which alerts fire, a thorough review of all patient information is required when ensuring the safety of the patient.

Alert Fatigue

An often mentioned concept related to technology errors is a phenomenon called "alert fatigue."[5] In an era of increasing dependence on technology, clinical decision support (CDS) has made it possible for pharmacists to receive real-time, patient-specific safety alerts. Unfortunately, too many alerts can lead to user desensitization and subsequent bypassing of such safety tools. In fact, a recent study suggests that 22% of general practitioners (GP) admitted to frequently or very frequently bypassing drug interaction alerts without thoroughly reviewing their contents, 35% admitted to doing this sometimes, and 42% to rarely or never doing this.[6] When asked about reasons for overriding DDI alerts, 97% of GPs surveyed indicated that the interaction for which they were provided an alert was not serious.[6]

Improving the specificity and quality of DDI alerts may help minimize alert fatigue.[7,8] In a recently published study, 55% of surveyed clinicians reported that a poor "signal-to-noise" ratio, (too many irrelevant or less important notifications mixed in with only a few important notifications), limited the usefulness of drug-drug interaction alerts embedded into a CPOE system.[8] A recent survey of community pharmacy managers identified that software that contained alerts that provided more detailed information or were customizable were perceived to be more useful.[7]

Many institutions and chains are trying to minimize alert fatigue by eliminating commonly overridden alerts or stratifying interactions to display only the more clinically relevant interactions.[1] With the knowledge that fired alerts have been carefully selected to display only the most important safety information, pharmacists are encouraged to focus on all alerts at all times with minimal bypassing.

Safety Approach to DDIs

Although there are no defined, systematic processes in the literature, there are techniques that pharmacists and pharmacies can apply to tackle drug-drug interaction (DDI) alerts. Many experienced clinicians may already be using some or all of these strategies, but the recent Tribune article suggests that there is room for improvement. Therefore, a brief refresher is provided for readers to help self-assess their current practice in approaching DDIs.

An important primary action that has been recommended is classification of the DDI with regard to pharmacokinetic or pharmacodynamic effects.[9,10,11] For example, medications that affect the absorption, distribution, metabolism, or excretion of another medication are pharmacokinetic in nature and can alter serum drug concentrations and consequently, clinical response.10 Medications with similar or competing pharmacodynamics can increase or reduce the effect of the other drug. Lastly, the ability for pharmacists to recognize drugs that have a narrow therapeutic index is essential, as DDIs can be much more frequent with these agents.[10]

If a pharmacist needs to explore an interaction further, most facilities subscribe to databases that can assist in the decision-making process. Alternatively, pharmacists can be encouraged to obtain their own references to expand their knowledge on fired alerts. A recently published study analyzed various resources and found that the following resources ranked highest in scope: Clinical Pharmacology, Drug Interaction Report, Lexicomp Interactions, and Micromedex Drug Interactions.[12] Micromedex and LexiComp ranked the highest among the list.[12] Attending continuing education programs on drug interactions may also be helpful. For those with a subscription, the Pharmacist's Letter offers DDI resources as well as a very detailed continuing education program on how to manage some of the most commonly encountered drug interaction alerts.[13,14]

Lastly, the pharmacist should evaluate patient-specific factors and formulate a plan that is reasonable based on the risk to the patient. This may include continuing, discontinuing, or substituting therapy on an individual basis.[9] Although it has been demonstrated that the most effective methods to prevent DDIs involve a team approach between physicians, nurses, and pharmacists, below is a proposed pharmacist-specific systematic method that can be used to ensure that they enter every shift prepared to encounter and successfully manage drug interactions. The strategies and descriptions are as follows:

1. **Improve Baseline knowledge**. Review your pharmacokinetics and pharmacodynamics principles, including p-glycoprotein and common CYP inhibitors, inducers, and substrates. Pay particular attention to narrow therapeutic index drugs and drugs known to be strong inhibitors/inducers. Review lists of QT prolonging agents, chelators, additive drug interactions (e.g., serotonin acting agents), and ototoxic agents. Identify populations more vulnerable to drug interactions. This may include elderly patients, patients on multiple medications, or patients presenting with a new prescription, dose change, or new medical condition.
2. **Know your resources.** Download credible and reliable mobile apps if you are not always at a computer during your shift. Know the online and print resources your site subscribes to. Keep up to date on new resources for certain disease states or patient populations. Attend book fairs or browse the bookstores for various pharmacy associations to assist with this. Recommend relevant titles to your supervisor or manager. Utilize only credible websites when searching for information on-line and remember to also consult secondary resources, like Pubmed when tertiary resources lack information.
3. **Approach alerts carefully and thoroughly.** Be aware of alert fatigue; try to consciously slow down and read the entire text of every alert. Look for the strength of the evidence used in the alert – is it based on published data or is it hypothetical? Consult at least two sources about the interaction, as interaction severity may be classified differently among various sources. Studies have shown that many databases have poor agreement when it comes to listing and classifying the severity of drug interactions.[15,16,17]
4. **Evaluate patient-specific risk.** Use data from the patient's chart to evaluate if the interaction is more or less severe based on allergies, labs, organ function, medical history, and other relevant data. Some alerts that fire may be referring to medications the patient is no longer taking.
5. **Formulate a recommendation.** Remember all of the components of an interaction (drug dose, duration, timing of administration, route, sequence of therapy, and indication). If you deem the interaction harmful, decide the best way to manage it (reduce/increase dose, change therapy, change administration times).
6. **Contact the physician.** Provide your findings and recommendation to the prescribing practitioner as well as to the patient. Document conversations and modifications to the treatment plan.

Conclusion

In summary, it is important for pharmacists to use the Tribune study to identify an opportunity for improvement and develop our field. The systematic approach presented above was designed to provide pharmacists with a technique for analyzing all interactions thoroughly. It is intended to evolve and become individualized for anyone wishing to incorporate it into their daily routine. We can work daily on amending our CDS systems, evaluation techniques, and environmental stressors. However, in the end we must also be willing to modify our behavior.

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