Case Report

Disseminating Drug Prescribing Information: The Cox-2 Inhibitors Withdrawals

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Abstract

This case study examined the recent withdrawal of valdecoxib to determine the timeliness of updates in commonly used information sources used by healthcare professionals. The method included assembling a purposive sample of 15 drug reference and warning systems that were then systematically monitored for several months after the withdrawal of valdecoxib to determine the time to update this information. These information sources were classified and described qualitatively. A time to diffusion curve was plotted and the average number of days to report the drug withdrawal or update reference databases was calculated. Only 2 of 15 information systems reported the drug withdrawal on the actual date of the FDA announcement. Institutional electronic textbooks took an average of 109.8 days (±14 days) to report the withdrawal. In addition, one pharma-sponsored dissemination source (Peerview Press) had not updated their information as of this publication.


Introduction

On April 7, 2005, the popular cox-2 inhibitor valdecoxib (Bextra®) was withdrawn from worldwide markets at the request of the Food and Drug Administration. This action followed the withdrawal of rofecoxib (Vioxx®), a similar drug, in the Fall of 2004.

We were interested in determining the timeliness of frequently used drug reference databases and warning systems that healthcare professionals might consult for this type of information. Although drug manufacturers are mandated to send notification letters to healthcare professionals, busy clinicians are frequently overwhelmed with information about new indications for drugs, new black box warnings, new direct-to-consumer marketing campaigns, letters from insurance companies asking to switch drugs within classes due to formulary issues and many other things. It is often difficult to keep all this information organized in one’s mind to provide safe and efficient clinical care and improve the safety of prescribing.

Although the pharmacy would be unable to dispense a withdrawn medication, unknowingly prescribing a withdrawn medication might, at the very least, cause apprehension among patients. In addition, the efficiency of the health care system is further strained by callbacks from pharmacists. More important, if current medical information systems used to keep up with changes in medicine don’t include drug withdrawals, it is possible that other important information could be missing such as new drug-drug interactions and newly reported adverse reactions and contraindications. For example, cerivastatin was prescribed in conjunction with gemfibrozil after the label listed them as contraindicated in 1999, resulting in 12 fatalities due to rhabdomyolysis. Additionally, rofecoxib was prescribed for several years after evidence of increased cardiovascular risk was known. Between 1997 and 2001, 14 drugs were pulled from the market potentially affecting millions of patients.

Health care professionals need a “warning” system about new medical information such as drug withdrawals and black box warnings, and they need a reference system to look this information up when needed. Without both, healthcare professionals may not know when new information is available and probably won’t be able to find it when they need it. This has been shown in studies that have demonstrated lengthy times to translate new evidence into clinical practice, poor dissemination of new information and by the high percentage of unanswered clinical questions that physicians have.

Case Description

We examined various widely available medical information tools potentially used to find out new drug information and identified several examples of each type (warning systems and reference databases) that provide drug information. These different medical information sources were searched and monitored in the weeks following the withdrawal of valdecoxib and a time to diffusion analysis was conducted to assess the timeliness of these systems.
Methods

We assembled a convenience sample of commonly used medical information systems that were available before the withdrawal of valdecoxib from the market. This was a purposive sample designed to be representative of different types of tools including electronic textbooks (MicroMedex, Lippincott’s Nursing Drug Guide, Mosby’s Drug Consult, USP DI® Drug Information for the Health Care Professional, and Up-To-Date), web-based sources (Medscape, MD Consult, Web MD, The Food and Drug Administration’s Center for Drug Evaluation and Research website [FDA CDER] and The Physicians’ Desk Reference website [PDR.net]), pharmassponsored dissemination sources (MD Linx and Peerview Press), and handheld-internet databases (Epocrates, Lexi-Comp and Tarascon).

The reference database tools MicroMedex, Lippincott’s Nursing Drug Guide, Mosby’s Drug Consult, USP DI® Drug Information for the Health Care Professional, and Up-To-Date are large subscription electronic textbooks or reference books that include information on therapeutics and specific drug information. Medscape, MD Consult, Web MD, The Food and Drug Administration’s Center for Drug Evaluation and Research website (FDA CDER) and PDR.net are internet news and reference sources. Medscape represents an example of a coordinated reference tool (web-based database with search engine) and warning tool (e-mail notification). MD Linx and Peerview Press are two free e-mail services that provide information to physicians that is written or sponsored by pharmaceutical companies. A handful of relatively new drug databases (Epocrates, Lexi-Comp Drug Database and Tarascon Electronic Database) display drug prescribing information on a handheld computer and this information can be updated via the Internet each time the handheld computer is synchronized with a desktop computer.

The subscription-based sources (e.g., MicroMedex, Lippincott’s, etc.) were chosen as representative of the types of sources commonly available at large academic medical centers, while other sources were selected based on applicable tools from recent searches for reference tools and an unpublished study of warning tools that included searching various medical websites, evidence-based databases, monitoring and posting to list-serves and consulting practicing physicians and experts. All of these sources were monitored (after the withdrawal of valdecoxib) by one of the authors (SS) and independently validated by a second (DS). In all cases results were equally reported by both authors. They were monitored daily for the first 2 weeks after the withdrawal, weekly for the next month, and then every 2 weeks until the publication of this manuscript (time to diffusion analysis). This monitoring included accessing the sites at the prescribed time and reading the drug abstracts thoroughly in order to determine when the update of the withdrawal was posted. For sources that send out daily e-mail notifications, these were monitored for news of the drug update on a daily basis until the publication of this manuscript. Electronic copies of each monograph and e-mail update were saved on the designated dates and were re-checked by the two authors independently prior to publication, to ensure the withdrawal notification did not appear earlier than the reported update date. Agreement on the date of withdrawal notifications was present for all information systems monitored.

Examples: Performance of Drug Information Sources

Electronic Textbooks

None of these sources contained information of the drug withdrawal within the two weeks following the withdrawal of valdecoxib. On average, it took these sources 109.8 (± 14) days to be updated (see Figure 1). None of these sources has a coordinated warning tool for immediate notification of physicians of changes.

Web-based Sources

Medscape presented the information of the valdecoxib withdrawal on the day of the announcement and also sent out an e-mail notifying clinicians. MD Consult, Web MD and FDA’s CDER website presented the news within several days of the announcement. It took PDR.net 268 days to update their information on the valdecoxib withdrawal.
Pharma-sponsored Dissemination Sources
MDLinx provided coverage of the withdrawal four days after the announcement via e-mail (warning tool) and in their web-based database (reference database). Peerview press, which previously had covered news about rofecoxib, did not mention the withdrawal to its readers.

Handheld-Internet Databases
Physicians synchronizing their handheld computer with Epocrates, a handheld warning and reference database tool, would have received notification of the valdecoxib withdrawal and the updated information would be in the database if the drug was looked up on the same day of the withdrawal. The Lexi-Comp Drug Database and the Tarascon Electronic Database updated their databases within a few days of the withdrawal, although neither of these databases has a warning tool for notifying users of changes.

Time to Diffusion Analysis
Only two sources reported the withdrawal on the day of its occurrence (Epocrates and MedScape Drug Reference, see Figure 1). Several other sources updated this information within four days. As of this writing, PeerView Press had not been updated.

Discussion: The Importance of a Coordinated Warning and Reference Database Tool for Prescription Drug Awareness
The overwhelming growth of prescription medicines coupled with information that changes on a daily basis are powerful arguments for the need of coordinated information warning and reference database tools for practicing medicine. These tools may be specific for drug prescribing information or incorporated into more comprehensive medical information systems. Clinicians need both types of tools so that they can be notified of new information, including drug information, as it becomes available, and also have a place to find the information when it is needed in practice. Although we used a major drug withdrawal as a proxy for the quality of drug information in commonly used medical information systems, it could serve as an appropriate measurement for the usefulness of these systems as it applies to disseminating drug-prescribing information. A black-box warning will be added to about 8% of drugs after they are first marketed and another 3% will be withdrawn from the market due to side effects.14

While only two tools had the drug withdrawal information at the time that it occurred, there was another set of tools that reported it within 4 days. However, the average length of time it took to update several major electronic textbooks was lengthy (109.8 days). Our survey of these institutional resources found that they are static databases, updated periodically. Additionally, one web-based source (PDR.net) took 268 days to update and a Pharma-dissemination source (Peerview Press) was still not updated as of this writing.

Until integrated information systems, including computer physician order entry and e-prescribing, are widely deployed that provide updated valid and relevant information to clinicians, are specialty-specific, and couple this with prescribing and administration information in centrally accessed databases, we suggest applying the described methodology to evaluate drug information tools in clinical settings. The best systems will update valid and relevant information daily and will have a coordinated warning and reference database component.

References