Drug Safety News: Current Problems and Future Solutions

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"The future belongs to those who believe in the beauty of their dreams." - Eleanor Roosevelt

What dreams can we imagine for drug safety? Perhaps, in an idealized future, patients would experience only benefit, never harm, from their medications. This overview presents current problems in drug safety and glimpses of possible solutions, based on the three main categories of adverse drug reactions (ADRs): medication errors/drug misuse; adulteration; and inherent toxicity.

Mediation Errors/Drug Misuse
Much energy has been focused on the first type of ADR; medication errors. These are essentially problems in the way in which drugs are used. Problems range from obvious errors in drug administration to more complex societal concerns, as demonstrated by these examples:

- Wrong drug: EPINEPHrine 1:1000 for topical use was injected in error instead of Lidocaine 1 per cent with EPINEPHrine 1:100,000; the patient died.[1]
- Prescribing: Despite warnings concerning the safety of antidepressant drugs in children, and the need for monitoring for suicidal ideation, prescribing patterns show less than ideal prescribing and no improvements in monitoring.[2]
- Prescription drug addiction: Approximately 1-3% of Canadians misuse prescription opiate drugs due to addiction. Resultant fatalities are on the rise.[3]

In theory, these types of problems are all preventable by using the drugs properly. Current solutions mandate improvements at every step of the medication pathway: prescribing, monitoring, labelling, storage and verification procedures. A good resource for these details exists at ISMP-Canada. For the future, experts on medication errors place improving undergraduate education of medical students high on their list of ways to increase awareness

of drug safety issues.[4] These experts also recommend using bar codes to ensure that the right drug is always given to the right patient. Electronic prescribing will reduce illegibility and rule-based errors.[5] In 2009, only 27 percent of Canadian general practitioners were able to prescribe electronically.[6] Public health issues also need to be addressed, such as providing more resources for the treatment of drug addiction.

Adulteration of Drug Products

A second cause of adverse drug reactions is adulteration of the drug product; the presence of an impurity which can be harmful. Adulteration can occur intentionally or unintentionally, as in these examples:

- Counterfeit products discovered recently in North America include counterfeit "Alli", which contained sibutramine rather than orlistat.[7]
- Dietary supplements containing selenium poisoned 201 people in the US and were found to contain 200 times the dose stated on the label. Symptoms of selenium poisoning are diarrhoea, fatigue, hair loss and fingernail discolouration and brittleness.[8]
- Conventional products: nabilone capsules were accidentally labelled as trazodone.[9]

This type of ADR is also preventable. It can occur with conventional medicines, as in the nabilone example, but usually occurs with health supplements that lack adequate regulation, especially those purchased over the internet. Possible solutions in the future require increased regulation of dietary supplements, and increased staffing of government inspectors. For now, be suspicious if a patient describes unusual effects from a product, or if there is a change in the physical characteristics of a product that might suggest counterfeiting. The globalization of the pharmaceutical industry due to cost pressures has resulted in a high percentage of drugs that are imported. In the US, it has been estimated that 80 per cent of active ingredients and 40 per cent of the final drug products are imported. Quality control is harder to enforce.[10]

Inherent Toxicity of Drug Chemicals

Even if no medication error occurs or impurity exists, ADRs can still happen because of an inherent chemical property of the drug molecule. The common inherent toxicities of a drug may be revealed in pre-marketing studies, and post-marketing surveillance adds to our knowledge of less common reactions.

- Recent safety warnings from Health Canada include fentanyl transdermal conversion guideline changes; rituximab and progressive multifocal leukoencephalopathy; zanamivir and a fatality resulting from its unapproved use as a solution; decreased potency of new heparin products due to a change in USP standards; deferasirox and new contraindications to reduce the risk of kidney damage and GI haemorrhage; mycophenolate and pure red cell aplasia; isotretinoin and sever, potentially fatal skin reactions; and zinc-containing denture adhesives and excessive zinc levels leading to myeloneuropathy and blood dyscrasias.[11]
- New safety information from the FDA; a new risk management strategy for long-acting beta agonist drugs restricts their use due to reports of severe asthma exacerbations.[12]
- Warnings from the European Medicines Agency: sibutramine has been removed from the market in Europe due to the risk of myocardial infarction and stroke; finasteride and

possible increased risk of male breast cancer; statins and sleep disturbances, memory loss, sexual dysfunction, depression and interstitial lung disease leading to breathing problems.[13]

The third type of ADR is not as easily preventable. In the future, some degree of prevention might be attained though an increased understanding of the genetics of drug-induced injury. By identifying specific individuals at risk, we can avoid giving them a potentially toxic drug. Leveraging the current voluntary reporting system for ADRs with systems such as the FDA's proposed Sentinel Initiative will help to identify new ADRs. Sentinal will link existing healthcare databases, such as those already used for administration and insurance, to create a national monitoring process that is continuous and operates in real time.[14] For now, increased use of the existing Health Canada reporting system for ADRs will add to the available knowledge.

Conclusion

The problems are multifaceted and thus require a wide variety of solutions. Technology will help, but education, reallocated funding, improved staffing, increased attention to safety issues, and wider us of existing processes will all play a role in making drug safety a reality.

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