Prescribing information as a source for toxicology-related information

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Prescribing information, otherwise known as a package insert or drug label, has necessary information on a drug's safety and efficacy, but is limited when it comes to situations of overdose.[1] Package inserts are reliable and helpful in dosing drugs, but are not as useful when looking for toxicological information. As a package insert is approved by the US Food and Drug Administration (FDA), it is only applicable in situations where the drug is used as indicated. Package inserts are approved when the drug goes to market, but in that particular moment in time, there are only a few case studies of overdoses. The package insert is also not updated until required by the FDA or if the pharmaceutical company deems it is necessary.[2]

Pharmaceutical companies, the federal government, and professional organizations, do not provide sufficient updated poison and/or overdosage information to the physician.[3] The overdose sections found in package inserts are very general and often times contain very similar information to other drugs in the same class. Although an "overdose" section is required in a package insert, a toxicology section is only optional.[3] An overdose is when a person takes more than the medically recommended dose, while toxicology is the amount taken to cause damage or adverse effects to a living organism.[4,5] It is unethical to conduct clinical trials on humans to obtain primary literature on overdoses; therefore, most of the toxicological information in package inserts is from animal studies.

The information found in a package insert is not created to establish a medical standard of care but rather is required for a manufacturer to market, advertise, and promote the medication.[6] Among the drugs that cause the most fatalities in overdose, many do not have updated, or clear information in their package inserts on how to handle overdose situations. For example, some package inserts give insight on how to treat a patient but will say to contact a poison control center for additional information on the treatment of any overdose.[7]

While reviewing the package inserts of other classes of drugs, we can see some discrepancies between what the drug manufacturer recommends and what is done in practice. For example, a tricyclic antidepressant package insert states that large volume gastric lavage followed by activated charcoal is recommended.[8] In practice, gastric lavage is a method that has been abandoned and is rarely used. In benzodiazepine overdoses such as alprazolam, the package insert states to use flumazenil and immediate gastric lavage. The package insert does appropriately warn, however, against the use of flumazenil in benzodiazepine overdoses such as in chronic users and if a cyclic antidepressant is also on board.[9]

In conclusion, package inserts contain important information about a drug, but should not necessarily be the go to in overdose situations. In clinical practice the package insert is not considered the gold standard for management of drug toxicities.

In addition, it is important to know that pharmacokinetics, what the body does to a drug, does not equal toxicokinetics, what the body does to a drug in higher doses.[10] Package inserts are a good start to understanding overdoses and toxicology but certainly should not be replaced for primarily literature and expert understanding. Poison control centers and healthcare professionals who are experts in toxicology can provide a better and more thorough insight on dealing with overdoses and toxicities of medications.

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