Improving the drug withdrawal process could reduce number of deaths

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The number of deaths associated with drugs that were subsequently withdrawn from the market could have been reduced had there been fewer delays in the withdrawal process, according to research published in the open access journal *BMC Medicine*. This situation could be improved by better reporting of these deaths and quicker action from manufacturers and regulators.

For a drug to be approved by regulators it must be considered to have more potential benefits than potential harmful side effects. In some instances, side effects are only noted after the drug has been approved and is on the market. When this is the case, drug regulatory authorities can take several actions, which can include the addition of the side effect to the label as an "undesirable effect", the inclusion of a warning label, or allowing the patient to choose whether or not to take the drug. The final regulatory action is to suspend the drug's license, and it is withdrawn from the market.

Researchers from Oxford University searched several databases, including the WHO's records on medicinal products, the US FDA's website, the European Medicines Agency's drug database, and PubMed. Between 1957 and 2011, more than 400 drugs were withdrawn from the market; of these, 95 were identified as withdrawn because deaths were attributed to the drug. Most of the drugs were used in the treatment of neurological or psychiatric disorders, followed by painkillers and anti-inflammatories.

The time between the first death being reported and the drug being withdrawn has not changed since 1957. The average time for withdrawal was four years. Yet the researchers found that the more recent the launch date, the sooner deaths were reported. The gap between the launch of a drug and its withdrawal from the market has also shortened over time.

First author, Igho Onakpoya, says: "Better international co-ordination among regulatory authorities is needed and should lead to speedier and more uniform decision-making processes when drugs are suspected of causing deaths."

It was found that 40% of the drugs were withdrawn in more than one country, but only 27% were withdrawn from all countries they were sold in. There were fewer drug withdrawals in African and Asian countries than in Europe and the USA. There are several reasons why a drug may be withdrawn in one country and not others. For example, the number of reported harmful side effects can be different between countries, or the drug could be cheaper than the alternatives.

The researchers conclude that changes in the withdrawal process are needed to avoid needless deaths. They say: "What we need is early formal studies when deaths are suspected to have been due to a drug. Increased transparency in the reporting of adverse events in clinical trials would also help with quicker identification of potentially dangerous drugs, and greater efforts should be made to strengthen drug monitoring systems in low- to middle-income economies."

More information: Delays in the post-marketing withdrawal of drugs to which deaths have been attributed: a systematic investigation and analysis, Igho J Onakpoya, Carl J Heneghan and Jeffrey K Aronson, *BMC Medicine*, DOI: 10.1186/s12916-014-0262-7

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