EDITORIAL

Reporting adverse drug events to the Therapeutic Goods Administration

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In Australia the Therapeutic Goods Administration (TGA) monitors the safety of medicines to improve the understanding of their possible adverse effects. Adverse events are the harmful and unintended consequences of medicine use. They are a leading cause of unplanned hospital admissions and deaths. Reporting adverse drug events to the TGA is therefore important for making the information known and widely available. Reports can come from health professionals, consumers and pharmaceutical companies. These reports are collected in the Database of Adverse Event Notifications (DAEN). This includes information about adverse events related to prescribed, over-the-counter and complementary medicines, and devices.

The TGA assesses potential signals and reports nationally and internationally to enable a clearer understanding of the risk of harm associated with a drug. It is important that health professionals report all suspected adverse events, including known adverse events (to monitor their frequency), for all drugs, no matter when they were registered. It is particularly important for detecting rare and potentially dangerous adverse effects, those occurring after prolonged exposure, and drug–drug and drug–disease interactions that may not have been observed in clinical trials.[1]

Although it is easy to send reports to the TGA, voluntary reporting is in decline. There are now less than 1000 reports by medical practitioners per year. Of the 11,662 reports in July–December 2019, only 4.6% were from medical practitioners. Although most prescribing is in general practice, few reports come from GPs. Reports from non-medical health practitioners comprised 15.3%, patients made 3.4% of notifications, pharmaceutical companies were responsible for 64.2% of reports and 12.5% were from other sources.[2]

It is unclear if the decline in reporting is because adverse events are truly declining, or there are behaviour changes regarding reporting. For example, health professionals used to receive printed copies of the publication Medicines Safety Update and the 'blue card'[3] reporting form. The blue card is now only available on the TGA website. If these hard copies, which are no longer printed, were visual cues for prescribers, perhaps raising expectations and awareness that adverse events are common and should be reported, their absence may have led to less reporting. Medicines Safety Update is now only published as relevant topics arise rather than in a bimonthly scheduled publication, as was previously the case, thereby reducing the profile of reporting.

Probably less than 5% of adverse reactions are reported, even in countries where reporting is mandatory.[4] A European systematic review found that the median rate of under-reporting by healthcare professionals was 94%.[5] Despite the limitations of voluntary adverse drug reaction reporting systems, they remain the most common and inexpensive method of collecting data to generate safety signals.

In Australia, it is mandatory for pharmaceutical companies to report all serious adverse events suspected of being related to their drugs, but reporting by health professionals has always been voluntary. Without robust reporting mechanisms supporting the detection of safety signals, rare adverse drug events may remain undetected for years, exposing patients to unanticipated risks. Examples of high-profile drug withdrawals include lumiracoxib (associated with severe hepatotoxicity), which only occurred after thousands of patients in Australia had been exposed.[6]

Neuropsychiatric adverse events associated with montelukast, and euglycaemic ketoacidosis associated with sodium-glucose co-transporter 2 inhibitors, are rare adverse effects detected only by careful pharmacovigilance analysis. The Australian pharmacovigilance system detected an outbreak of hyoscine hydrobromide toxicity due to wide variations in the concentration of the active ingredient.[7]

There is a need to understand the reasons for under-reporting. We need to consider the different motivators and barriers that influence the likelihood of completing and sending reports to the TGA. What has changed? For example, has the removal of the blue card reduced awareness of pharmacovigilance?

Recognising an adverse event is a key issue, however even when it is recognised it may not be reported. Definitions of medicine-related harm are multiple and varied[8] and this may make medical staff anxious if they are uncertain of the diagnosis. Available tools include the Naranjo Adverse Drug Reaction Probability Scale.[9] A possible solution is to have

standard descriptors adopted by practitioner groups and regulatory organisations to support better awareness, quality improvement and patient safety.[8]

Health professionals possibly report proportionally more serious adverse events, due to the impact on patient care, and because the TGA website stipulates particular interest in serious adverse events. However, this skews the reported data. This means that the DAEN may contain a higher ratio of serious to non-serious adverse event reports and also rare rather than common reactions. A further limitation is that a search of the DAEN will not provide information about the severity of adverse events, or the dose, strength or duration of use of a medicine. Reports for drugs accessed via the Special Access Scheme, Authorised Prescriber Scheme, Clinical Trial Notification Scheme or the Clinical Trial Exemption Scheme are not published in DAEN. This lack of publication may potentially be a disincentive to reporting.

Whereas publicity about a possible adverse event may increase reporting, there is a well-characterised progressive decline in adverse event reporting, following an initial peak, after a drug's regulatory approval. Other factors potentially contributing to low reporting rates by health professionals include a lack of time relative to other clinical priorities,[8] their awareness and perceived importance of pharmacovigilance,[8,10] and a lack of feedback about pharmacovigilance activities.[11] There may be limited awareness of adverse drug event reporting mechanisms and uncertainty about the cause of events, particularly when there is multimorbidity and polypharmacy.[10] An adverse event may cause misplaced concern regarding potential legal liability.[11]

To improve safety for patients, health professionals should be encouraged to report adverse drug events. We suggest education, starting at university, that any suspected adverse event related to a medicine should be reported, even if the reaction is already known. A lack of awareness of the need to report adverse drug reactions may have led to some clinical pharmacology departments specifically teaching about pharmacovigilance and the importance of reporting. Role modelling by more senior clinicians demonstrating reporting on ward rounds, in the early postgraduate years, might also encourage new graduates to report adverse events.

A longer term strategy to improve reporting is to consider adding successful aspects of an international pharmacovigilance system to the current Australian system. For example, a collaboration between the European Medicines Agency, the European Medicines Regulatory Network and academic research centres, provisionally termed the Regulatory Science and Innovation Programme for Europe (ReScIPE),[12] is an interesting model and broader than pharmacovigilance reporting. This model could be explored for more in-depth and clinically relevant approaches to reporting. Other jurisdictions such as New Zealand also have specific pharmacovigilance committees. An Australian committee could be reinstated to raise the profile of drug safety in Australia.

For the present, reports can be made online via the TGA website or via email. There is an online blue card reporting form which can be downloaded from the TGA website and emailed, faxed or posted to the TGA. Medical practices can download and install templates in their software to create adverse drug reaction reports. Health professionals can subscribe to the online version of Medicines Safety Update for advice on drug safety and information about emerging safety concerns.

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