Showing the blue card: reporting adverse reactions

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Summary

The primary function of an adverse reaction reporting system is to identify harmful effects associated with the use of medicines. Since 1964 the Australian system has contributed to the early recognition of many drug-related problems. Reports of suspected adverse drug reactions are sent to the Adverse Drug Reactions Unit of the Therapeutic Goods Administration by healthcare professionals, pharmaceutical companies and consumers. The reports are reviewed, coded and entered into a database before being analysed for patterns of adverse events. Selected reports are forwarded to the Adverse Drug Reactions Advisory Committee which can recommend actions ranging from no action to the withdrawal of a drug from the market. An important role of the Committee is to inform healthcare professionals about the adverse effects which emerge from their reports.

Key words: hyoscine, drug regulation.

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Introduction

In Australia, healthcare professionals, pharmaceutical companies and consumers can report suspected adverse drug reactions to the Adverse Drug Reactions Advisory Committee (ADRAC). Healthcare professionals usually submit reports on the 'blue card' which accompanies the Australian Adverse Drug Reactions Bulletin and the Schedule of Pharmaceutical Benefits. Reports can also be made by letter, fax or electronically to http://www.tga.gov.au/problem/index.htm#medicines

Constant review of reports

Suspected adverse drug reactions are generally reviewed within three working days by staff in the Adverse Drug Reactions Unit of the Therapeutic Goods Administration. Selected reports are further reviewed by the independent medical experts of ADRAC.

Reports are searched for signals that may indicate safety issues. Individual reports are reviewed and the proportional reporting ratio calculated for each reaction. This is the proportion of a specified reaction or group of reactions for a drug compared with the proportion for that reaction or group of reactions for all drugs in the database.[1]

Health professionals should not defer making a report because a suspected association between an adverse event and a medicine has not previously been noted or seems tenuous. This would limit the ability of the system to detect new associations. We are particularly interested in reports concerning newly marketed medicines because the safety information for these compounds is usually limited. We are also interested in reports concerning older medicines. The adverse event profile for these medicines may seem well-established, but new reactions, changes in the frequency of known adverse reactions, interactions or problems with generic forms of a medicine may occur and should be recognised to allow appropriate action to be taken. All reports are gratefully acknowledged.

Reports can be made by letter, fax or electronically

Analysis of aggregated reports

Reports are analysed for a possible causal relationship between an adverse event and a medicine. For signal detection, a cluster of reports is usually required, depending on the seriousness of the event and the information reported. International reports including literature reports are also considered in these analyses. Examples of the value of this type of analysis are shown in Boxes 1 and 2.

Over 200 000 reports have been received since the scheme commenced in 1964. In 2004, 9823 reports were received. Australia is a founding member of the WHO Collaborative Program for International Drug Monitoring and regularly contributes data to this program.

The most publicised recent contribution of the Australian spontaneous reporting system to the safety of medicines was the detection of an association between Travacalm and anticholinergic syndrome. Over a period of a few days in December 2002 and January 2003 reports were received of patients developing symptoms such as hallucinations, ataxia and visual disturbance after taking Travacalm, a motion sickness preventative containing hyoscine hydrobromide.

Box 1

Australian reports contributing to the early global recognition of a drug-related problem *

- Travacalm and anticholinergic syndrome
- Cerivastatin and rhabdomyolysis
- The 'Triple Whammy' – acute renal failure due to the combination of ACE inhibitor, diuretic and non-steroidal anti-inflammatory drug
- Tiaprofenic acid and cystitis
- Flucloxacillin and hepatitis
- Amoxycillin with potassium clavulanate and hepatitis
- Bismuth subgallate and neurotoxicity
- Mianserin and agranulocytosis
- Mebhydrolin and agranulocytosis
- Glucomannan and oesophageal obstruction
- Oxolamine citrate and hallucinations
- Coumarin and hepatitis
- Phenylpropanolamine and hypertension

* most recent first
(references available on request)

Box 2

Australian reports giving early notice of a drug-related problem in Australia *

- Pergolide and cardiac valvulopathy
- Atypical antipsychotics and hyperglycaemia
- Diptheria, tetanus, acellular pertussis vaccine and extensive limb swelling
- Leflunomide and pancytopenia and pulmonary toxicity
- Interactions with St John's wort
- Zanamivir and respiratory disorders
- Hypersensitivity reactions with echinacea
- Interferon and depression
- Ondansetron and chest pain
- Nefazodone and hepatic dysfunction and visual disturbances
- Isotretinoin and depression
- Ticlopidine and thrombotic thrombocytopenic purpura
- Kombucha tea and liver dysfunction
- Alendronate and oesophageal disorders
- Vigabatrin and visual field defects
- Clozapine, olanzapine and neuroleptic malignant syndrome
- Fluoroquinolones and Achilles tendinitis
- Selective serotonin reuptake inhibitors and withdrawal reaction, particularly in neonates
- Moclobemide and hypertension
- Cisapride and cardiac arrhythmias
- Minocycline and liver dysfunction
- ACE inhibitors and angioedema
- Cefaclor and serum sickness-like reactions
- Royal jelly and bronchospasm
- Clozapine and constipation
- Clozapine and myocarditis

* most recent first
(references available on request)

Prompt investigation by the Therapeutic Goods Administration Laboratories revealed that some individual tablets contained seven times the amount of hyoscine hydrobromide stated on the label.

Strengths of spontaneous reporting

Spontaneous reporting systems are most valuable for identifying potential medication-induced adverse events when they are rare events unlikely to be associated with other causes.[2] The Australian voluntary reporting system differs from some overseas systems in that it accepts reports from consumers as well as from healthcare professionals and pharmaceutical companies. This is particularly important for over-the-counter and complementary medicines as the consumer may not have consulted a healthcare professional about the suspected reaction.

Limitations of spontaneous reporting

Voluntary reporting systems have limitations and are complementary to other postmarketing safety assessment methods such as cohort and case-control studies. Spontaneous reporting systems generally do not allow for quantification of risk. Under-reporting of adverse events is likely and submission of reports is possible only when a potential connection between an adverse event and a specific medication is suspected.

Recognition and reporting are least likely to occur when adverse events happen after prolonged treatment with a drug, when the condition reported is common in the community (for example hypertension) or it has other plausible aetiologies (for example diabetes).[2] An association between those types of adverse event and a medicine is more likely to be detected in case-control or cohort studies. In Australia we are not usually able to determine the total amount of a medication consumed. The voluntary reporting systems therefore cannot calculate the prevalence of adverse reactions.

Communication

The primary function of Australia's voluntary reporting system is to identify the risk of harm from drugs. Following from this

the nature and extent of the risk must be communicated. The Australian Adverse Drug Reactions Bulletin is the main vehicle for communication of these risks. The Bulletin is distributed with *Australian Prescriber* to approximately 60 000 healthcare professionals and is also available online.* The database belongs to all Australians and anyone in Australia can contribute or request information. Currently searches can be requested via email to adrac@health.gov.au. An online facility for searching aggregated data is under development.

* http://www.tga.gov.au/adr/aadrb.htm

References

1. Evans SJ, Waller PC, Davis S. Use of proportional reporting ratios (PRRs) for signal generation from spontaneous adverse drug reaction reports. Pharmacoepidemiol Drug Saf 2001;10:483-6.
2. Gutterman EM. Pharmacoepidemiology in safety evaluations of newly approved medications. Drug Inf J 2004;38:61-7.

Conflict of interest: none declared

Report adverse drug reactions

Blue card

Fax: 02 6232 8392

Online at www.tga.gov.au/problem/index.htm#medicines

Dental notes

Prepared by Dr M. McCullough of the Australian Dental Association

Reporting adverse reactions

A large section of the public regularly visit their dentist, often much more frequently than they visit other health professionals. Dentists may well be in a unique position to be able to assess potential adverse reactions to the medication that we prescribe and that prescribed by our medical colleagues.

The Australian system of spontaneous reporting relies on both the public and health care professionals to have a high level of suspicion and to report potential adverse reactions. Such was the case with the recently observed association between the use of bisphosphonates and avascular necrosis of the jaw.[1] It is incumbent on dentists to be vigilant with regard to potential adverse reactions and be willing participants in the reporting of these events. Reactions can be reported to the Adverse Drug Reactions Advisory Committee using the blue card enclosed with this issue of *Australian Prescriber*.

Reference

1. Carter G, Goss AN, Doecke C. Bisphosphonates and avascular necrosis of the jaw: a possible association. Med J Aust 2005;182:413-5.