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Review Article

A REVIEW ON ADVERSE DRUG REACTION REPORTING IN WHO, CANADA AND AUSTRALIA

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ABSTRACT

The primary purpose of adverse drug reaction reporting is to provide early warnings or "signals" of previously unrecognized drug reaction. The method was developed in the 1960s in response to the thalidomide tragedy and is now well established throughout the developed world. Health professionals are the key original source of reports, the awareness of reporting the adverse reaction by the patient is not well practiced. Alternative methods for capturing clinical suspicions of adverse drug reactions should be investigated and could provide more systematic data. However much it can be improved, adverse drug reaction reporting is unlikely to identify all important unrecognized drug hazards. There is no guarantee for the complete safety of a medicine and adverse reactions are very common than expected. It is virtually impossible to determine the accurate number of adverse drug reactions experienced since it is difficult to assess causality and the fewer amounts of ADRs being reported. In the present work the adverse reaction reporting systems in WHO; Canada and Australia have been discussed. These systems have made it easier for the healthcare professionals and patients to report the adverse drug reactions. Complementary approaches therefore still need to be identified and developed. Imparting knowledge and awareness of ADR reporting among medical practitioners would bring the reporting culture among medical practitioners and increase the reporting rates of ADR.

Keywords: Adverse reaction, Thalidomide tragedy, adverse drug reaction reporting, Hazards, Healthcare

INTRODUCTION

Adverse Drug Reactions (ADRs) is a response to a medicinal product that is noxious or potentially harmful and unintended and which occurs at doses normally used in human for prophylaxis, diagnosis or therapy of a disease or for the modification of physiological function in which individual factors may play an important role.[1] Adverse event is an injury related to medical management, in contrast to complications of disease. Medical management includes diagnosis and treatment, failure to diagnose and treat and also includes the systems and equipment used to deliver care.[2] Adverse event not always occur due to drug it can also be caused by the incorrect user interaction.[3]

Apparently Health care systems fail to learn from their mistakes, this being one of the frustrating aspects for both patients and professionals. The health care providers and health care organizations fail to inform others about any mishaps that occur and what they have learned from the investigations that have been carried out, as a consequence, the same errors occur constantly and patients continue to be harmed. One solution to this problem is reporting: by the doctor, nurse, or other provider within the hospital or health-care organization, and by the organization to a broader audience through a system-wide, regional, or national reporting system. Adverse event reporting is the measure of progress toward achieving a safety culture.[2]

DISCUSSION

World Health Organization

In 1971, World Health Organization established an international system for monitoring the adverse reactions of drug by using the information derived from member states. WHO Headquarters is responsible for policy issues while the operational responsibility for the programme rests with the WHO Collaborating Centre for International Drug Monitoring, Uppsala Monitoring Centre, (UMC), in Sweden. The system started with 10 countries that had already established national systems for spontaneous adverse reaction reporting and who agreed to contribute data. For an effective international system to become operative, a common reporting form was developed, agreed guidelines for entering information formulated, common terminologies and classifications prepared and compatible systems for transmitting, storing and retrieving and disseminating data were created.[4]

The Uppsala Monitoring Centre (UMC) is the operational arm of the World Health Organization (WHO) drug monitoring programme, which maintains a global ADR database. The UMC was established in 1978, based on an agreement between the Swedish government and the WHO. The main purpose and activity of UMC is to collect global ADR data, especially from WHO International Drug Monitoring Programme member countries.[5]

After a patient has shared information about an adverse effect with their doctor or other health provider, it should be reported to the local or national pharmacovigilance centre (the great majority are not reported, which is a big problem). Here the likelihood of the medicine having caused the problem is further investigated. All possible causes are reviewed and the strength of the evidence is assessed, including other reports and material from reference works and journals.

Depending on the outcome, action may be taken - such as changing the way the drug is used, or even withdrawing it from the market. If the problem seems to be caused by sub-standard or counterfeit drugs, or there has been an interaction with another drug or substance, or the diagnosis or choice of drug was doubtful, other solutions are needed.

Reports of suspected adverse effects from member countries of the WHO Programme for International Drug Monitoring are sent to Vigi Base, the WHO international database, managed by the UMC. There they are reviewed and analysed and the bigger picture of worldwide evidence begins to emerge.[6]

Vigi Base is UMC's starting-point for the journey from data to wisdom about safer use of medicines and wise therapeutic decisions in clinical practice. It is the driving-force at the heart of the work of UMC and the WHO Programme. The purpose is to ensure that early signs of previously unknown medicines-related safety problems are identified as rapidly as possible.

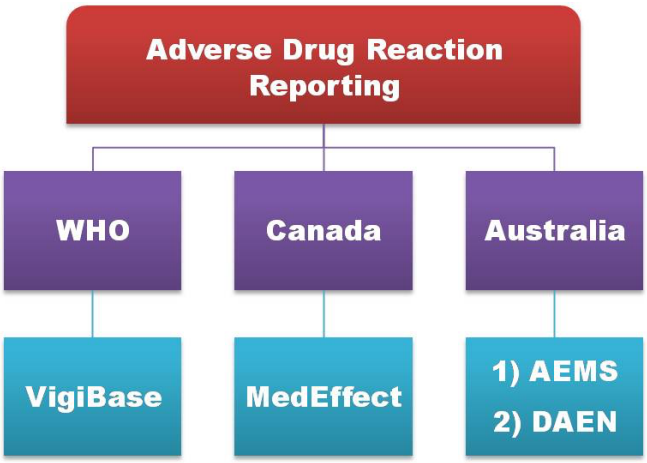
Vigi Base is the unique WHO global database of individual case safety reports (ICSRs). It is the largest database of its kind in the world, with over 16 million reports of suspected adverse effects of medicines, submitted, since 1968, by member countries of the WHO Programme for International Drug Monitoring.[7]

Origin of WHO programme

The formation of the WHO programme followed the thalidomide disaster of 1961 where many babies were born malformed to the mothers who consumed thalidomide during pregnancy for morning sickness. This ended an age of uncritical trust in medicine. It caused worldwide outrage. A proposal was made at Wold Health Assembly in the year 1962 to establish a system to monitor the adverse effects of medicine so as to prevent such tragedies happening again.[8]

It was in 1978 that the database which is now known as Vigi Base moved to Upsala and is being managed by UMC, together with the broader activities of the WHO Programme. The reports of suspected adverse effects of a particular medicinal product are send t Vigi Base by the members of the programme. These are known as individual case safety reports (ICSRs). UMC then reviews and analyses this international data and shares its results and conclusions with member countries.

The path taken by information about a patient's problem with medicine[6]



ADVERSE DRUG REACTION REPORTING FORM

Sr. No

REPORT ON SUSPECTED SERIOUS ADVERSE DRUG REACTION

For Report to
Drugs Controller
Pak Secretariat, Block C,
Ministry of Health,

1. PARTICULARS OF PATIENT

Name of patient

Age Weight (kg) Patient address

Sex ☐ Male Race
☐ Female

Pregnant ☐ Yes ☐ No ☐ Not applicable

Relevant Medical History

2. ADVERSE EVENT

Reason for reporting

☐ Requires or prolongs hospitalization ☐ Life threatening ☐ Death
☐ Permanently disabling or incapacitating ☐ Congenital anomaly ☐ Overdose
☐ Other (Please Specify)

3. SUSPECTED DRUG

Name of suspected Drug Generic Name
Name of manufacturer
Date of occurrence Duration of Event
Starting date of Medication
Route of administration
Discontinuation of Drug because of event ☐ No ☐ Yes Dated

4. REPORTING DOCTOR'S / PHARMACIST'S / NURSE'S SIGNATURE

Institution
Date

GUIDELINES TO FILL SERIOUS ADVERSE EVENT REPORT FORM

An adverse event is "Serious", if it

- Is life threatening
- Results in hospitalization
- Prolongation of hospitalization
- Causes malignancy
- Is an overdose resulting in clinically Relevant signs and / or symptoms
- Results in permanent disability
- Is associated with death
- Causes a birth defect
- Causes a relevant organ toxicity

An adverse drug event can be a manifestation of various etiologies such as

- Complication of an underlying disease
- Coincidental accident
- Concomitant medication
- Intercurrent disease
- Drug associated effect

Figure 1: WHO Adverse Drug Reaction Reporting Form[11]

The processes in the cycle may involve consultations among local, national or international colleagues and experts, manufacturers and members of the WHO Programme.[11]

Canada

Med Effect Canada provides consumers, patients, and health professionals with easy access to:

- Report an adverse reaction or side effect
- Obtain new safety information on drug and other health products
- Learn and better understand the importance of reporting side effects[9]

Med Effect is a part of the Therapeutic Access Strategy (TAS), a five-year strategy to improve the safety, effectiveness and access to therapeutic products available to the people in Canada. The Med Effect program includes a website, and a partnership initiative involving, for example, professional health care associations and consumer/patient groups. Connecting with other associations and groups will help to expand and maintain the community of networks knowledgeable about Med Effect. By making these connections, sharing information will be more effective.

The Med Effect program has been developed by Health Canada's Marketed Health Products Directorate (MHPD), with the following goals in mind:

- To offer centralized access to health products safety information which is appropriate and makes it in easy to find and easy to remember location. This includes access to Health Canada's advisories, warnings and recalls; the Canadian Adverse Reaction Newsletter (CARN); and the Canadian Adverse Drug Reaction Monitoring Program (CADRMP) Online Query and Data Extract.
- It helps the health care providers and consumers to file adverse reactions reports easily and effectively through web, phone, fax or mail.
- To build awareness about the importance of reporting adverse reaction reports to Health Canada, and how this information is used to identify and communicate potential risks.

Med Effect is being developed and designed in consultation with Canadian health professionals, consumers/patients and the general public.

Adverse Reactions to Health Products

Not all health care products are completely safe they carry both risk and benefits. Many of the risks observed are identified before marketing the product and are managed as "tolerable" side effects which are outweighed by the product benefits. It is only when the product enters the market unexpected or undesirable effects referred as adverse reactions are being discovered.

Adverse reactions may develop within few minutes of exposure to the product or may take years. This might occur even after the

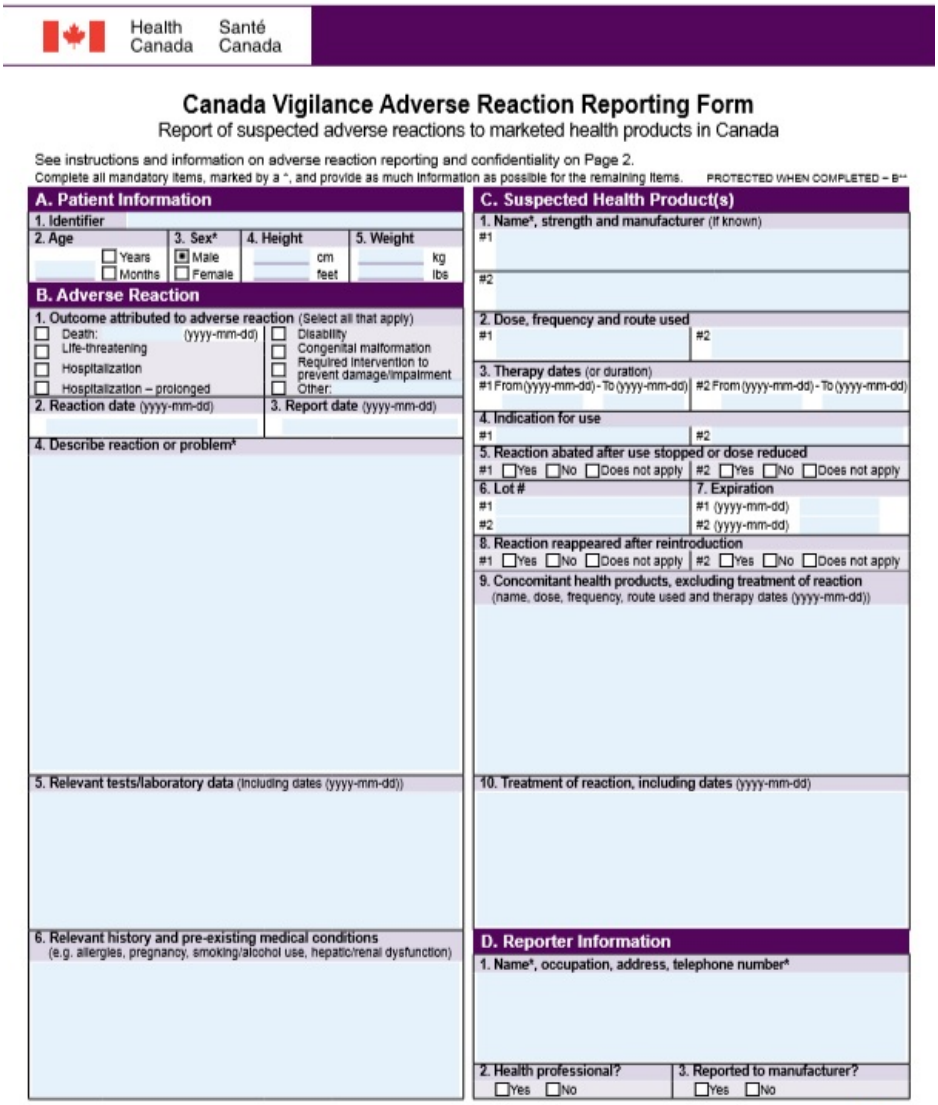
product is used as directed. Reactions can range from minor irritations, like a skin rash, to serious and life threatening reactions, such as a heart attack or liver damage.

- Certain adverse reactions are unexpected and may not necessarily be indicated on the product label or any other information provided with the product.

Proper tracking of adverse reactions helps in communicating the risks associated with various health products. The only way to achieve this is if Canadians - health professionals and patients/consumers alike -report adverse reactions to Health Canada.

By reporting an adverse reaction to Health Canada, Canadians will help the department to:

- Identify rare or serious adverse reactions that were previously unknown
- Make changes in product safety information or remove an unsafe product from the Canadian market
- Contribute to international data on the benefits, risks or effectiveness of health products
- Develop and disseminate new and better information to enhance Canadians' knowledge about the safety of health products



Health Canada Santé Canada

Canada Vigilance Adverse Reaction Reporting Form

Report of suspected adverse reactions to marketed health products in Canada

See instructions and information on adverse reaction reporting and confidentiality on Page 2.

Complete all mandatory items, marked by a *, and provide as much information as possible for the remaining items. PROTECTED WHEN COMPLETED – B**

A. Patient Information

1. Identifier

2. Age — Years / Months

3. Sex* — Male / Female

4. Height — cm / feet

5. Weight — kg / lbs

B. Adverse Reaction

1. Outcome attributed to adverse reaction (Select all that apply)

Death: (yyyy-mm-dd) / Life-threatening / Hospitalization / Hospitalization – prolonged / Disability / Congenital malformation / Required intervention to prevent damage/impairment / Other:

2. Reaction date (yyyy-mm-dd)

3. Report date (yyyy-mm-dd)

4. Describe reaction or problem*

5. Relevant tests/laboratory data (including dates (yyyy-mm-dd))

6. Relevant history and pre-existing medical conditions (e.g. allergies, pregnancy, smoking/alcohol use, hepatic/renal dysfunction)

C. Suspected Health Product(s)

1. Name*, strength and manufacturer (if known) #1 / #2

2. Dose, frequency and route used #1 / #2

3. Therapy dates (or duration) #1 From (yyyy-mm-dd) - To (yyyy-mm-dd) / #2 From (yyyy-mm-dd) - To (yyyy-mm-dd)

4. Indication for use #1 / #2

5. Reaction abated after use stopped or dose reduced #1 Yes No Does not apply / #2 Yes No Does not apply

6. Lot # #1 / #2

7. Expiration #1 (yyyy-mm-dd) / #2 (yyyy-mm-dd)

8. Reaction reappeared after reintroduction #1 Yes No Does not apply / #2 Yes No Does not apply

9. Concomitant health products, excluding treatment of reaction (name, dose, frequency, route used and therapy dates (yyyy-mm-dd))

10. Treatment of reaction, including dates (yyyy-mm-dd)

D. Reporter Information

1. Name*, occupation, address, telephone number*

2. Health professional? Yes No

3. Reported to manufacturer? Yes No

Figure 2: Canada Vigilance Adverse Reaction Reporting Form[12]

Australia

After the registration of a therapeutic good in Australia, the safety information and data on effectiveness are made available from clinical trials. The information provided by clinical trial related to the therapeutic good consists of the possible adverse events but not all adverse events are detected because they:

- Certain adverse events take long time to occur and the clinical trials do not take that long.
- Do not include enough patients to detect adverse events that occur rarely
- Do not include all of the different types of people who might eventually use the product and who might be more susceptible to some adverse events, such as older people, children, pregnant women or people with other medical conditions.[3]

When therapeutic goods are being used outside the controlled conditions like that of clinical trials, adverse events may be observed and these therapeutic goods are monitored for safety by TGA.

Certain important information in TGA's safety monitoring system is obtained from the reports submitted by the consumers and health professionals.

Information about the number of adverse event reports received each year by the TGA can be found at Adverse events: Australian statistics on medicines and Adverse events: Australian statistics on medical devices.

Most adverse event reports are made by sponsors (e.g. pharmaceutical companies and medical device suppliers), but many are also made by state and territory health departments, hospitals, health professionals and consumers.

TGA Adverse Event Management System (AEMS) consist of the adverse events reported for medicine and vaccine that TGA receives.

Along with the adverse events of the therapeutic good, their medical history, laboratory results and how the adverse event was treated are the information recorded in the database.

Entry of serious reports in AENS should be done within 2 working days, a letter of acknowledgement is then sent to the reporter. Reports are identified by unique ID number. Any additional information to be added to the existing case can be done by using the ID number.

Assessment and entry of adverse events into the database is done for future reference. The information is used by TGA staff to help identify safety signals. A safety signal is a 'flag' for a possible safety concern. When a signal is observed by TGA, a thorough evaluation is carried out to find the possible role of the therapeutic good in causing the adverse event.

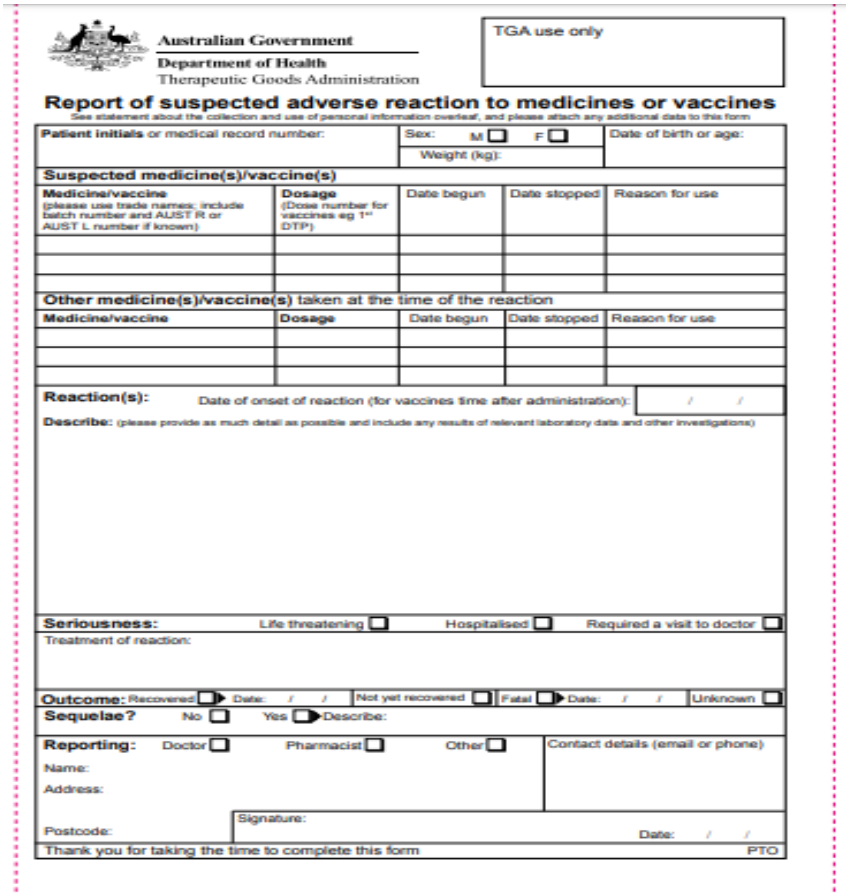
Three months after a report has been entered into the AEMS, information is transferred to the publicly accessible and searchable Database of Adverse Event Notifications. The three month time lag enables TGA staff to check and analyse the information in the report.

Database of Adverse Event Notifications (DAEN)

The Therapeutic Goods Administration (TGA) receives adverse event reports associated with medicines and medical devices. These reports come from a wide range of sources, including members of the public, general practitioners, nurses, other health professionals and the therapeutic goods industry.[10]

DAEN - medicines provides information about adverse events related to medicines and vaccines used in Australia.

Voluntary reports are made using a 'blue card', which can be submitted by health professionals, pharmaceutical companies and consumers. The Adverse Drug Reactions Advisory Committee (ADRAC), established in 1970, evaluates the submitted reports.[5]



Australian Government
Department of Health
Therapeutic Goods Administration

TGA use only

Report of suspected adverse reaction to medicines or vaccines

See statement about the collection and use of personal information overleaf, and please attach any additional data to this form

Patient initials or medical record number: | Sex: M ☐ F ☐ Weight (kg): | Date of birth or age:

Suspected medicine(s)/vaccine(s)

Medicine/vaccine (please use trade names; include batch number and AUST R or AUST L number if known)	Dosage (Dose number for vaccines eg 1st DTP)	Date begun	Date stopped	Reason for use

Other medicine(s)/vaccine(s) taken at the time of the reaction

Medicine/vaccine	Dosage	Date begun	Date stopped	Reason for use

Reaction(s): Date of onset of reaction (for vaccines time after administration): / /

Describe: (please provide as much detail as possible and include any results of relevant laboratory data and other investigations)

Seriousness: Life threatening ☐ Hospitalised ☐ Required a visit to doctor ☐

Treatment of reaction:

Outcome: Recovered ☐ Date: / / Not yet recovered ☐ Fatal ☐ Date: / / Unknown ☐

Sequelae? No ☐ Yes ☐ Describe:

Reporting: Doctor ☐ Pharmacist ☐ Other ☐ Contact details (email or phone)

Name:

Address:

Postcode:

Signature: Date: / /

Thank you for taking the time to complete this form PTO

Figure 3: Blue card –Report of suspected adverse reaction to medicines or vaccines[13]

CONCLUSION

The effectiveness of an ADR monitoring and reporting program depends on the awareness of all healthcare providers. The ADR's are generally reported by the healthcare professionals and the reporting system in the WHO countries, Australia and Canada are designed in such a way that the reports are received from patients also. There is a need for regular training and re- enforcement of regulations for ADR reporting among health care personnel. Attitudinal changes, whereby ADR reporting should be seen as an integral part of clinical activities of the doctors are very necessary for long term improvement of ADR reporting.

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