A28: Patient Safety and Adverse Event reporting

Encouraging AE reporting for non-pharmacovigilance professionals

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What do they have in common?

All deaths related to pharmaceutical drugs/medicines
HISTORY OF MEDICINES AND MONITORING?

- 1848: Hannah’s Death - Chloroform
- 1938: GIT Toxicity of ASA was proved
- 1955: Yellow Card - UK
- 1961: McBride’s Letter
- 1964: WHO drug monitoring
- 1968: EMA established
- 1989: New EU PV Legislation
- 1995: TGA established
- 2012: New EudraVigilance Format
- 2017: AUS - PV Inspection
- 2020: Federal food, drug and cosmetics Act

https://www.youtube.com/watch?v=41n3mDoVbk&t=605s
WHAT IS PHARMACOVIGILANCE AND WHY IS IT SO IMPORTANT

Pharmacovigilance (PV) is the process and science of monitoring the safety of medicines and taking action to reduce risks and increase benefits from medicines.

PV comprises of:

• Collecting, managing and analysing data (including Adverse Event data) on the safety of medicines
• Looking at data to detect ‘signals’ or safety issues.
• Communicating with stakeholders such as healthcare professionals (HCPs) or regulatory authorities (TGA, FDA, MHRA, HSA)
• Acting to protect patients and public health

An activity with shared responsibility and mandatory character, in which the entire health system incl. HCPs, health institutions, the Pharmaceutical Industry, distributors, marketers and patients participate.
PHARMACOVIGILANCE THROUGHOUT PRODUCT LIFE

CLINICAL TRIAL
Investigators, Sponsors, Nurse coordinators, CRA’s

Registration

POST REGISTRATION/POST MARKETING
SPONTANEOUS
Patients, Doctors, Pharmacists, Nurses, and all others

SOLICITED PROGRAMS
Staff in Non-interventional Research, Patient Support, Disease Management, Compassionate Use, Market Research Programs and Investigator Initiated Trials (IITs).

Ensure those exposed to drug safety reporting before and after product approval are thoroughly educated.
What is an ADVERSE EVENT?

An *Adverse Event* (AE) is any untoward medical occurrence in a patient or clinical trial subject administered a medicinal product and which does not necessarily have a causal relationship with this treatment.

This can include (but is not limited to):

- Side effects from medicines (e.g. rash, swelling at infusion site)
- Disease (e.g. contracting hepatitis after infusion of a medicine)
- Worsening of a pre-existing condition (e.g. bleeding event after administration of a prothrombic medicine)

May or may not be related to the medicinal product.

If an AE is related to the product = Adverse Drug Reaction (ADR)

SPECIAL SITUATIONS

In addition reporting of the following situations (regardless of whether or not an adverse event has occurred), is also required.

- Lack of efficacy – i.e. instances where a product hasn’t worked
- Overdose
- Maladministration or medication error (e.g. patient given expired product)
- Misuse/abuse
- Off-label use (use of a product other than for its intended use, e.g. Paediatric use)
- Occupational exposure (nurse developing rash from using a cream applied to patients)
- Unexpected therapeutic benefit (improvement of erectile dysfunction after antihypertensive)
- Transmission of an infectious agent (for example a virus) via a product
- Reports of the use of fake products
- Drug exposure via mother/father (including follow-up for infant outcome)
- Pregnant or breastfeeding woman using product
- Exposure to a product during conception/childbirth
WHO NEEDS TO REPORT ADVERSE EVENTS?

All HCPs regardless of position or title, have a responsibility to report all adverse events associated with products, including reports of special situations. *Primum non nocere - First do no harm.* HCPs are encouraged to report to the TGA as well as to the Sponsor (Owner or Marketing Authorisation Holder) of the product in Australia.

"Pharmacovigilance is a continuous obligation and responsibility of all HCPs"
HEALTH CARE STANDARDS AND CODES THAT SUPPORT AE REPORTING

1. Healthcare facilities and providers

The National Safety and Quality Health Service (NSQHS) Standards were developed and are governed by the Australian Commission on Safety and Quality in Health Care (the Commission) as part of the Australian Health Service Safety and Quality Accreditation (AHSSQA) Scheme. Standard 4 – Medication Safety Standard


Competency standards describe the skills, attitudes and other attributes (including values and beliefs) attained by an individual based on their knowledge and experience which together enable the individual to practise effectively as a pharmacist.

3. APHRA - Code of conduct for all registered healthcare providers

Sec 3.10 and Sec 6 - Reporting adverse events to the relevant authority, as necessary and participating in systems for surveillance and monitoring of adverse events
Origin of medicine and vaccine adverse events received by the TGA (2013-17)
2015–16, $20.8 billion was spent on medicines. 777 000 prescriptions are filled under the PBS.
ADVERSE EVENTS IN HEALTHCARE

These large international reviews of patient charts estimate that between 4% and 17% of hospital admissions are associated with an adverse event and a significant proportion of these (one- to two-thirds) are preventable.

A systematic review of eight chart review studies (from the USA, Australia, the UK, New Zealand and Canada) found a median overall incidence of adverse events of 9.2% (of which approximately 43% were preventable), with over half being operation (40%) or drug (15%) related.

Australian literature: the proportion of all hospital admissions that are medication-related is between 2-3%. In 2011-2012: Medication hospital admission rate of 230,000 annually. Average cost per separation in 2011-12 of $5,204.

The costs of adverse drug events in Australian hospitals amounted to AUD 1.2 billion in 2011, or 3.95% of the public hospital spending.

WHAT HAPPENS TO THE AE INFORMATION AFTER IT IS REPORTED

Sponsors and Health Authorities collect the AE information that HCPs and others report. They analyse the reports to identify trends or signals.

Signal Detection:
- Size?
- Qualitative
- Quantitative
• Inform HCPs and consumers through alerts and articles in publications (Medicines Safety Update and Medical Devices Safety Update)

• Propose changes to product labelling, or adding warnings, precautions and AE information to the PI and CMI

• Request the sponsor to undertake post-marketing studies to investigate the safety concern before further action is taken.

• Cancel the registration of the product, or limiting the population in which it can be used
# DRUGS WITHDRAWN FROM THE MARKET

<table>
<thead>
<tr>
<th>Drug</th>
<th>Year</th>
<th>Adverse Reaction</th>
</tr>
</thead>
<tbody>
<tr>
<td>Thalidomide</td>
<td>1961</td>
<td>Congenital Limb Defects (Risk of teratogenicity). Current use Leprosy and Multiple myeloma</td>
</tr>
<tr>
<td>Zimelidine</td>
<td>1983</td>
<td>Risk of Guillain–Barré syndrome, hypersensitivity reaction, hepatotoxicity</td>
</tr>
<tr>
<td>Fenfluramine</td>
<td>1982</td>
<td>Lactic Acidosis</td>
</tr>
<tr>
<td>Astemizole</td>
<td>1999</td>
<td>Fatal arrhythmia; Torsades De Pointes</td>
</tr>
<tr>
<td>Phenylpropanolamine</td>
<td>2000</td>
<td>Haemorragic stroke</td>
</tr>
<tr>
<td>Rofecoxib</td>
<td>2004</td>
<td>Cardiovascular Event (MI and stroke)</td>
</tr>
<tr>
<td>Valdecoxib</td>
<td>2005</td>
<td>Cardiovascular Disorders</td>
</tr>
<tr>
<td>Lumiracoxib</td>
<td>2008</td>
<td>Liver damage</td>
</tr>
<tr>
<td>Rosiglitazone</td>
<td>2010</td>
<td>Cardiovascular Disorder (CHF; MI and stroke)</td>
</tr>
</tbody>
</table>
WHAT IS THE IMPACT OF AE REPORTING?

**Sponsor**
- Improved/earlier signal detection
- Updates to PI/CMI/other educational material
- Earlier communications to HCPs and Authorities

**HCP**
- Improved/prompt awareness of risk
- Better management of AE’s/compliance
- Better patient outcomes

**Consumer**
- Better awareness of AE’s
- Reduction in AE’s
- Improved/safer experience
CHALLENGES

1. Fear of litigation / unfavorable outcome (fear of getting involved in a lawsuit)
2. Guilt for having been responsible for damage observed in the patient;
3. Insecurity about reporting suspicions of AE (belief that notification only required if certainty that the damage was caused by drug);
4. Lack of interest, time or other excuses related to postponing the notification AE
5. Lack of knowledge or awareness (When, What and how to report)
6. Unavailability of reporting tools or solutions (blocked websites on pharmacy computers)
7. Don’t have all the information for reporting purposes
8. Complacency (believing that AE is well known therefore no need to report)
9. Little/no perceived incentive

WHAT IS THE TGA DOING TO MAKE AE REPORTING EASIER?

• Black triangle - This product is subject to additional monitoring
• Black box - highlight special warning statements (public health impact)
• Section 4.8 of AU PI – TGA now have mandatory wording Reporting suspected adverse reactions after registration of the medicinal product is important. It allows continued monitoring of the benefit-risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions at http://www.tga.gov.au/reporting-problems
• TGA are now recommending adding company contact details to the Section 8 of the AU PI to assist users with communicating with sponsors
• On-line AEMS reporting
• Updating the CMI
• Consumer focused tools on the TGA website
WHAT IS INDUSTRY DOING TO MAKE AE REPORTING EASIER?

• Asking for consent
• Explaining importance of providing follow up
• Designing QR codes/Apps to record/collect AEs
• Using template emails
• Creating videos/Training on AE reporting
• Including AE reporting wording in contracts/HCP materials
• Preparing Risk Minimisation Materials for specific risks (patient alert cards, HCP guides, information booklets, on-line materials, training modules)
• Making simple acronyms to remember min info (RADIO, PERD, PPRA)
WHAT TO REPORT (MIN. INFO) – THINK PIRATE!

Product (batch, expiry, model #, manufacturer...)

Identifiers (Pt initials, DOB, age, gender, Aboriginal/TSI...)

Reporter details (HCP, your name, email, phone, address...)

Adverse Event (or special situation)

Telephone or

Email the Sponsor and report to TGA

The TGA particularly needs to know:

• all suspected AEs to therapeutic goods (relatedness)
• serious AEs, such as those suspected of causing:

➢ Death/life threatening
➢ admission to hospital
➢ Incapacity/disability
➢ prolongation of hospitalisation
➢ birth defects
➢ Other important medical event

You don't need to be certain that the product caused the AE, just suspicious!

See which events should be reported: https://www.tga.gov.au/reporting-adverse-events
TGA AND INDUSTRY – WORKING TOGETHER ON IMPROVING AE REPORTING

• PV education needs to start early
• May be not that early!
• TGA and Industry identified that we need to work together on educating upcoming HCP’s
• We are working on a Lecture/Seminar face-face and online to go out to students in their final year of tertiary education
• Why is it so important for Industry to work together with the TGA?
• United front to ensure patient safety and improve patient outcomes
WHAT CAN WE DO TO CONTINUE TO IMPROVE AE REPORTING

• Make educational materials interesting, engaging and impactful (Reminders such as letters, emails or posters)
• Effectively educate company representative/liaisons
• Effectively educate and provide training to HCPs
• Work as a team to improve patient outcomes
• Leverage training resources already available (Share)
  • TGA - Website content developed specifically for consumers
• Modification of the AE reporting form or process (simplification of reporting)
• Incentives such as provision of educational credits and Chocolate bribery
• Enhancing availability of reporting forms;
• Increasing feedback to AE reporters
ADVERSE EVENT – REPORTING RESPONSIBILITIES

REMEMBER – PHARMACOVIGILANCE IS EVERYONE’S RESPONSIBILITY

Collection of AE data enables the TGA and Sponsors to assess the safety of their products, maintain Benefit/Risk balance and save patient lives!

Do Not Delay, Report it today!

http://www.cfhi-fcass.ca/SearchResultsNews/2010/10/01/fca3fcb9aa-e4cb-a64c-af52bbadda8d.aspx
RESOURCES

- https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6074778/
- https://www.who.int/hiv/topics/pharmacovigilance/2a_why_pv.pdf?ua=1
Questions?

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