Pharmacovigilance and Patient Safety

Dr M. Roy Jobson
Chairperson: Pharmacovigilance Committee of the MCC
Outline

- Pharmacovigilance
- The South African Medicines Control Council (MCC)
- The National Adverse Drug Event Monitoring Centre
- (Clinical Trials)
- The ‘process’ and Patient Safety
- Media
- Conclusion
Pharmacovigilance

Pharmacovigilance is the science and activities relating to the:

• detection
• assessment
• understanding and
• prevention

of adverse effects or any other possible drug-related problems
Are drugs safer today? (1)

Lembit Rägo (WHO)

• During 1960-1999 there were 121 safety related withdrawals worldwide
  – Market life was known for 87 of those
  – Market life less than 2 years 31%
  – Market life less than 5 years 50%
  • *Fung et al. Drug Information Journal, 2001; 35:293-317*

• During 1972-1994, 583 new active substances were approved
  – Of these 59 were withdrawn later

• During 1990-2001 in UK 24 drugs were withdrawn due to safety reasons
Are drugs safer today? (2)

Lembit Rägo (WHO)

- In England and Wales the number of deaths related to ADRs has increased during last 10 years
  - Study of 3,277 Coroner’s Inquests in one UK district showed during 1986-1991 10 deaths due to prescribing errors and 36 due to ADRs
  - These 46 deaths made approximately 1 in 2000

- A meta-analysis of 39 prospective studies in USA
  - ADRs between fourth and sixth leading cause of death in USA; fatality rate as a result of ADRs was estimated 0.32% among hospitalised patients
  - The annual cost of ADR related hospital costs 1.6-4 billion US $

- Lazarou et al. JAMA, 1998;279:1200-1205
Regulation 1: Definitions
‘adverse drug reaction’ means a response in human or animal to a medicine which is harmful and unintended and which occurs at any dosage and can also result from lack of efficacy of a medicine, off-label use of a medicine, overdose, misuse or abuse of a medicine.
The MCC

• Statutory Council
• 24 members – appointed by Minister of Health
• Act 101 of 1965 – last amendment May 2003 to make MCC a ‘juristic person’
Section 1

In determining whether or not the registration or availability of a medicine is in the public interest, regard shall be had only to the safety, quality and therapeutic efficacy thereof in relation to its effect on the health of man or any animal, as the case may be.
Definition of a medicine

A *medicine* means any substance or mixture of substances used or purporting to be suitable for use or manufactured or sold for use in --

a) the diagnosis, treatment, mitigation, or prevention of disease, abnormal physical or mental state or the symptoms thereof in man; or

b) restoring, correcting or modifying any somatic or psychic or organic function in man.

and also includes veterinary medicines.
STRUCTURE & PROCESS
NADEMC

• The National Adverse Drug Event Monitoring Centre created in 1987
• It is a WHO collaborating centre – sends reports to ‘the Uppsala Monitoring Centre’ part of (?) Quality Assurance and Safety: Medicines Essential Drugs and Medicines Policy Health Technology and Pharmaceuticals Cluster

• Main conduit for spontaneous reporting of adverse drug reactions in South Africa (yellow form) [Patient reporting?]
• Based at UCT
• Interacts with Pharmaceutical Industry
• Reports to Pharmacovigilance Committee of MCC
South African issue?

• Adverse drug reactions are a sign that the medicine is working – medicines are meant to make you feel bad
• A rash interpreted to be a sign of the ‘disease’ coming out (logical!)
• Medicines a necessary part of life like food, air, water (e.g. vaseline???)
• Substitute one belief system for others:
  – ‘natural medicines are 100% safe and gentle’;
  – ‘we must sterilise our environments’
Annual ADR Reporting Rate: South Africa

Source: National Adverse Drug Event Monitoring Centre, 2003
Signals

A **signal** refers to ‘reported information on a possible causal relationship between an adverse event and a drug, the relationship being unknown or incompletely documented previously’.

Usually more than a single report is required to generate a signal, depending upon the seriousness of the event and the quality of the information.

Denominator unknown, so clinical trials / focused surveillance carried out
Clinical Trials

• Safety elements built into study design
• Pre-specified definitions of serious adverse events (SAEs) and adverse events (AEs)
• Blinding is a problem in terms of attribution
• Interim Analyses (independent DSMB)
• Can be very powerful – e.g. worldwide withdrawal of rofecoxib
Patient Safety

• Adverse drug reactions reported, collated, international picture (vigimed/other), (interaction with industry), presented to pharmacovigilance committee, may consult Clinical Committee i.t.o risk-benefit profile, recommendation to Council
• Dear Health Professional Letter (DDL)
• Medicines Safety Alert (DA)
• Council can:
  – instruct withdrawal of a medicine from market
  – cancel registration of a medicine
Media

• Sensational items (compare to ‘cars’)
• ‘ARVs are poison’ [toxicity vs benefit – ‘The drugs are toxic but the disease is toxicer’]
• Business/profit driven – ‘misleading advertising’ – ASA (refers to MRA!)
• Work with ‘sound bites’ and ‘headlines’
• ‘Talk shows’ barely scratch surface of issues (often just a vehicle for venting)
Conclusion

• Patient awareness of ADRs increasing but no concomitant communication / reporting to their health professionals?
• Health professionals not trained in recognising (and reporting) ADRs – challenge for our academics (esp. paediatrics and dermatology)
• ART requires sharp learning curve for all i.t.o. management of ADRs
• Pharmacovigilance (detect, assess, understand, prevent ADRs ‘+’) needs greater emphasis in improving patient safety