Pharmacovigilance: New Challenges for WHO

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Safety and Vigilance: Medicines
Thanks to Dr S Pal, Dr D Tanaka
Contents

Pharmacovigilance and WHO Programme for International Drug Monitoring (PIDM)

Future of WHO PIDM

Challenges
WHO Programme for International Drug Monitoring
WHO Programme for International Drug Monitoring

How it started

Thalidomide 1961

WHO Programme for International Drug Monitoring (PIDM) 1968

• World Health Assembly Resolution 16.36

• INVITES Member States to arrange for a systematic collection of information on serious adverse drug reactions observed during the development of a drug and, in particular, after its release for general use.
Could we have reliably predicted phocomelia ahead of market authorization?

Clinical development of medicines

**Phase I**
20 – 50 healthy volunteers to gather preliminary data

Animal experiments for acute toxicity, organ damage, dose dependence, metabolism, kinetics, carcinogenicity, mutagenicity/teratogenicity

**Phase II**
150 – 350 subjects with disease - to determine safety and dosage recommendations

**Phase III**
250 – 4000 more varied patient groups – to determine short-term safety and efficacy

**Phase IV**
Post-approval studies to determine specific safety issues

Preclinical Animal Experiments

Development

Post Registration

Phase IV

Spontaneous Reporting
WHO definition of pharmacovigilance (PV)

The science and activities relating to the detection, assessment, understanding and prevention of adverse effects or any other possible drug-related problems

The importance of pharmacovigilance, WHO, 2002
WHO Programme for International Drug Monitoring

Why?

What next?

PIDM

Who?

What?
Quiz

1) How many countries founded the WHO Programme for International Drug Monitoring in 1968?
   - 10

2) How many countries are members of the WHO PIDM now?
   - 150 (122 full, 28 associate)

1) How many of these countries are from low and middle income settings?
   - 94 (63%)
Members of the WHO Programme for International Drug Monitoring
1968-2015
Capacity building: Africa focused
Public health programmes
Tool kits
Advocacy

ATC DDD

International platform, policies, Intergovernmental, norms, guidance, donor liaison, resources

WHO CC Accra (2009)
WHO CC Oslo >30 years
WHO HQ Geneva >50 years
WHO CC Rabat (2010)
UMC WHO CC Uppsala >40 years
WHO CC Lareb 2012

Implement, collect ADRs, share globally, make national safety regulatory decisions

Capacity: Francophone & Arabic countries
Integrated vigilance systems, Strengthening of pharmacovigilance practices, medication errors

Technical support, capacity building database, tools, signal detection, research

PV in academia
Patient reporting

National Pharmacovigilance Centres

Capacity: Francophone & Arabic countries
Integrated vigilance systems, Strengthening of pharmacovigilance practices, medication errors

Technical support, capacity building database, tools, signal detection, research

PV in academia
Patient reporting
WHO Programme for International Drug Monitoring

- Why?
- Who?
- What next?
- What?
The WHO global ICSR database  VigiBase®

The oldest and largest Individual Case Safety Reports (ICSRs) database

Freely accessible to National Centres

Global + country-specific signal detection
WHO Programme for International Drug Monitoring

**Provide leadership on matters critical to health**
- Lead strategic development
- Advocate and integrate, standard of care, platform and framework

**Shape the health research agenda**
- Develop and promote PV policies
- Convene regular meetings of the Member States and other stakeholders,

**Define norms and standards for health**
- Expert committees & working groups: develop, adapt norms, guidelines, standards, best practices
- Classification: medicinal products and drug utilization research

**Articulate policy options for health**
- Communicate safety globally, to influence regulatory decisions and policies
- Drive the integration of PV in public health programmes.

**Provide technical support and build capacity**
- Establish and co-ordinate a network to provide technical support in PV
- Contribute to building strengthening, capacity, infrastructure to achieve international standards

**Monitor health trends**
- Develop indices and metrics to monitor PV systems and practice
- Guide countries in the monitoring and evaluation of PV systems and
WHO Advisory Committee on Safety of Medicinal Products: norms and standards for PV

ACSoMP

- Constituted in 2003
- High level group of experts
- Composed of 12 members from all 6 WHO regions

12th WHO Safety Advisory Committee meeting, 2015, Geneva
Quiz

• What is the name of the WHO global database for spontaneous adverse reaction reports?

  VigiBase

• Who maintains the database?

  WHO Collaborating Centre of International Drug Monitoring, Uppsala Monitoring Centre (UMC)
WHO Programme for International Drug Monitoring

Why?

What next?

What?

Who?
Priorities for the future

- Signal detection using other data sources (electronic health records, social media)
- Integration of PV into Public Health programmes
- Pro-active and active surveillance methods for new medicines
- Making use of technology for reporting
- Patient reporting
- Medication errors
- Emergency response (e.g. Ebola)
- Regulatory framework
- Integrated vigilance systems
What is the urgency for PV in LMIC?

- More than 300 products in the pipeline for neglected diseases, HIV AIDS, TB and malaria
- At least half of them will be launched in the coming years in those very settings where there is little or no capacity for post approval monitoring
PV is at the heart of Public Health Programmes (PHPs)

PV contributes to:

- prevent unnecessary harm
- improve clinical practice
- promote rational use of drugs
- support research and education
However…

In most settings PV and PHPs operate in isolation, as independent vertical programmes.

• PV could often remain to be incorrectly perceived as a luxury discipline.
• PHPs would not be neither aware of or trained in the need to detect and report AE.
• PHPs would not always collaborate with PV centres, sometime even not be aware of PV centres.
• Still in general, PV might not be seen as a component of PHP.
Integration of PV into Public Health Programme

Pharmacovigilance is effective / sustained if integrated with Regulatory Function. PV centres and PHPs need to collaborate better.
WHO Strategies for integrating PV in PHPs

A Medicinal Product is registered / approved

Cohort event monitoring (CEM)

Product Life

Spontaneous reporting

TSR: Targeted Spontaneous Reports

Daisuke Tanaka
14 September 2015
PV in LMIC: Challenges Remain

- Lack of resources, political support
- Lack of competence
- Lack of PV systems and/or inadequate function
- Lack of communication and information exchange

WHO survey of PV systems in 55 countries
Solutions

- Improve resources and political support by introducing PV through Public Health Programs
  - Building functional PV systems
  - PV methods to monitor new products
  - Improve accessibility
  - Improve competence

- Improve information exchange, communication and decision making, by overcoming technical barriers and capacity building
Overcome technical barriers to PV in LMIC

VigiFlow

- for receiving and storing ADR reports.
- the entered reports can be extracted as XML files
- can be transferred to other (E2b) databases
- a search and statistics module is built into the system
- Easy to use and error-checking ensures accuracy.
Dedicated resources

WHO solutions for pharmacovigilance in public health programmes

WHO Advisory Committee on Safety of Medicinal Products (ACSoMP)

ACSoMP was established in 2003 to provide advice to WHO, including its Collaborating Centre for International Drug Monitoring (the UMC), and through it to the Member States of WHO, on safety issues relating to medicinal products.