The Pharmacovigilance of Complementary Medicines (CAMs)

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Historical Perspective

Thalidomide tragedy

• It was an effective *tranquilizer* & *painkiller* & was declared a "*wonder drug*" for *insomnia, coughs, colds* & *headaches* --- morning sickness.

• Deformation called Phocomelia, shortened limbs etc
Introduction

- Pharmacovigilance began with thalidomide.
- Do not need “CAM Thalidomide” to wake the Pharmacovigilance stakeholders.
- Policy makers, “Pharmaceutical Co”, Physicians, Pharmacists, Patients -- allow for the successful safety monitoring of CAM
- More than 100 countries have regulations for CAM
Key facts

• Use for thousands of years.
• Myth that natural = safe
• Use of CAMs is growing.
• Poor accessibility to modern drugs
• Shortage of physicians
• Cost of drugs
• Many depends on CAM for primary health care.
• CAM generating billions of dollars.
Key facts

- Don't think that these are also drugs
- Availability- Over the counter/ internet
- False but attractive claims by prescriber and manufacturers
- Health tonics and food supplements
- Lack of Good Manufacturing Practices (GMPs)
Monitoring of CAM

• The worldwide use is enormous, - imp. to identify the risks associated with their use.
• used in conjunction with other medicines, interaction of combination.
• Regulatory status consequently determines the access
• Safety influenced
  – Regulated/ not regulated
  – Prescription/ non-prescription
  – Regulate / un-regulated providers and distributors
  – Qualified / unqualified providers
Monitoring of CAM vs Drugs

- Drugs - clinical trials and spontaneous reports - physicians, dentists, pharmacists, and nurses
- CAM - all providers of traditional, complementary, and alternative medicine - involvement of consumers.
- non-prescription medicines - substantial proportion
- come directly without pre or postmarketing safety monitoring.
Reporting of ADRs

- Routine Clinic visit
- Suspicion of ADR
- Possible ADR documented and reported
- MCC

Possible ADR reported to PV Committee

Suspicion of ADR

Possible ADR documented and reported
Unique Challenges

• lack of uniformity in identification
• lack of information on adverse effects
• inadequate studies of ADRs, such as frequency and causes,
• “Natural” = safe. % of ADRs to CAM in our database is small
Quality control

Quality control - more complex than pharmaceuticals.

• quality of the raw material/product
• agricultural practices
• collection practices - plant selection and cultivation
Quality

Poor quality control may result in a high incidence of adverse reactions

- Quality of the product itself
- adulteration - potent substances
- contamination – other substances.
Remember

‘“You need not be certain...

Just be suspicious”
St. John’s Wort ( Hypericum perforatum )

- Eg of Adverse Effects: Photosensitivity, Insomnia, vivid dreams, headache, dizziness
- Drug Interactions: (through induction of the Cytochrome P450 enzyme CYP3A4, but also CYP2C9 and induction of the P-glycoprotein (P-gp) efflux transporter
- Examples of interaction
  Decreased levels Warfarin : Decreased Oral contraceptives or hormone replacement therapy, Decreased levels of PI protease inhibitors (ARV)
Kava Kava (Piper methysticum)

- Anxiolytic, assist with insomnia
- Hepatotoxicity: liver failure
- withdrawn from the market from SA (Feb 2004)
Information Flow in NPC

- Regulatory changes
- Medicine alerts
- DHCPL

MCC

Cohort
Request for cohort studies on specific problems (CEM)

Programmes
- Rational use of drugs in programmes
- Evaluate the impact of programmes
- Inform guidelines
- Re-education/training of staff

Analysis
CONCLUSION

• CAM are widely used in health care.
• Pharmacovigilance for CAM, in its infancy - essential
• monitoring the safety - presents unique challenges
• Reporting ADRs for must be encourage
- benefits >>> risks
- greatest achievable margin
- the individual patient
- population as a whole

Thank you for your attention!


• Dr. R. K. Dixit, MD Professor Pharmacology & Therapeutics King George’s Medical University, Lucknow. November 2012 43 "Herbal DrugsImportance of Regulatory Affairs"

• Ushma Mehta, Mukesh Dheda, Gavin Steel, Marc Blockman, Augustin Ntilivamunda, Gary Maartens, Yogan Pillay, Karen Cohen. Strengthening Pharmacovigilance in South Africa. *SAMJ pending publication*