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Safety and Efficacy of Drugs in Pregnancy

CANADIAN SOCIETY OF PHARMACOLOGY AND THERAPEUTICS CONFERENCE
Montreal
May 27, 2011

OUTLINE

- Background
- Current situation in Canada
- What is happening in other countries
- What we would like to see for Canada

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OUR MISSION

To advocate for the safe and effective use of medications in pregnancy and lactation.

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GOALS

- Increase awareness of pregnancy issues at government level (Health Canada)

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- Require standard labelling of medicines for use in pregnancy and lactation

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- Require standard labelling of medicines for use in pregnancy and lactation
- Provide practitioners and patients access to current and reliable information for decisions making
- Advocate for the development of patient registries or surveillance programs for medications used during pregnancy and breastfeeding

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Pharmacokinetic Changes in Pregnancy

- Changes in total body weight and body fat

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- Delayed gastric emptying and prolonged GI transit

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- Increased extracellular fluid and total body water

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- Delayed gastric emptying and prolonged GI transit
- Increased extracellular fluid and total body water
- Increased cardiac output
  - Increased stroke volume and maternal HR

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Pharmacokinetic Changes in Pregnancy

- Changes in total body weight and body fat;
- Delayed gastric emptying and prolonged GI transit;
- Increased extracellular fluid and total body water;
- Increased cardiac output
  - Increased stroke volume and maternal HR
- Increased blood flow to organs
  - Increased glomerular filtration rate

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- Decreased albumin concentration with reduced protein binding

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  - Increased stroke volume and maternal HR
- Increased blood flow to organs
  - Increased glomerular filtration rate
- Decreased albumin concentration with reduced protein binding
- Altered hepatic enzyme activity

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Odd but True

- MOST drugs are used in pregnancy / lactation to treat chronic or pregnancy induced conditions
  - Most are used 'off label'
- Very FEW drugs are studied for use during pregnancy / lactation
  - little guidance is available to physicians/patients
- MOST product monographs advise that drugs should NOT be used during pregnancy / breastfeeding

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Odd but True

- For reasons related to litigation, most pharmaceutical companies do not address the use of drugs during pregnancy
- Information is usually obtained post-approval
  - Pregnancy exposure/retrospective birth defect registries
  - Case series

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Odd but True

- Significant difference in pharmacokinetics exist between men and women
- Bioequivalence studies include both men and women
  - Results are based on average of both genders

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Odd but True

- No requirements exist to disclose the exact population used in bioequivalence trials
- Generic drugs for a vulnerable population such as pregnant women may be approved based on results obtained using men

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HEALTHCARE PROFESSIONALS ARE LEFT WITH THE BURDEN OF EVALUATING THE RISK/BENEFIT OF USING A MEDICATION DURING PREGNANCY/BREASTFEEDING

WHAT IS HAPPENING IN OTHER COUNTRIES ?

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UNITED STATES

- FDA requires labeling according to preset categories
- Most drugs are labeled Pregnancy Category "C"
- Pregnancy Categories are
  - A: Controlled studies in humans
  - B: Human data is reassuring (animal positive) or animal studies show no risk
  - **C: Human data is lacking - animal studies positive or not done**
  - D: Human data show risk, benefit may outweigh risk
  - X: Animal or human data positive

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UNITED STATES

- In 2008, FDA proposal to amend labeling regulations
  - Pregnancy information to move from the "***Contraindication***" section to the section "***Use in Specific Populations***"

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FDA PROPOSED PREGNANCY LABELLING

- prescription drug labeling would require:
  - pregnancy exposure registry information (if applicable)
  - a general statement about the background risk of fetal developmental abnormalities
  - clinical considerations
  - a data component

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- On Dec. 30, 2009, FDA announced collaboration with researchers, "*Medication Exposure in Pregnancy Risk Evaluation Program*"
- Data will be used from 11 health plan-affiliated research sites

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EUROPE

- *The European Medicines Agency Evaluation (EMEA) has:*
  - *Guideline on the Exposure to Medicinal Products During Pregnancy: Need for Post-authorisation Data*
  - *Guideline on Risk Assessment of Medicinal Products on Human Reproduction and Lactation: From Data to Labelling* ***effective January 2009***

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EUROPEAN LABELLING REQUIREMENTS (EMEA)

Examples of acceptable statements for use in section PREGNANCY of product monograph

Based on human experience (specify), Drug X is suspected to cause congenital malformation (specify) when administered during pregnancy.

Drug X should not be used during pregnancy (specify trimester) unless the clinical condition of the woman requires treatment with Drug X.

A moderate amount of data on pregnant women (between 300-1000 pregnancy outcome) indicate no malformative or feto toxicity for Drug X.

No effects during pregnancy are anticipated, since systemic exposure to Drug X is negligible.

Canada - DSEN

- Drug Safety and Effectiveness Network
- Bill C51
- CIHR
- SPECIAL POPULATIONS
  - Efficacy and safety in pregnancy

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PREGMEDIC PRIORITIES

- Draft Guideline for Inclusion of Pregnant Women in Pharmacokinetic studies was presented to Health Canada in June 2009
- Advocate for the adoption of the European Labelling Requirements for Pregnancy and Lactation (EMEA) by Health Canada
- Request creation of registries for women who need to take drugs during pregnancy and post market surveillance studies;
- Ensure that drugs indicated for women are studied in women

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SYMPOSIUM SPEAKERS

- David Knoppert, Pregmedic Chair
- André Lalonde, SOGC
- Iain McGilveray, McGilveray Pharmacon Inc.
- Gideon Koren, Hospital for Sick Children
- David Knoppert, St Joseph's Hospital
- Offie Soldin, Georgetown University
- Janine Hutson, University of Toronto