



Drugs Indicated for Use During Pregnancy

Pregmedic Symposium : Clinically Relevant
Pharmacokinetic Changes in Pregnancy

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THE SOCIETY OF OBSTETRICIANS AND GYNAECOLOGISTS OF CANADA

Objectives

- Discussion on appropriate testing of drugs for use in men and women in Canada
- Advocate for testing of drugs used during pregnancy exclusively in women



Bioequivalence

- Health Canada and the FDA recognize that bioequivalence studies demonstrate significant variability between men and women.
- More than 30% of the studies reviewed would not have passed bioequivalence criteria for one sex when it did for the other.



Intra-subject Variability in Men vs. Women

INTRA-SUBJECT VARIABILITY IN MEN VS. WOMEN

DRUG	MEN	WOMEN
Alprazolam	29.4%	4.9%
Cimetidine	9.9%	15.8%
Erythromycin	25.7%	18.1%
Naproxen (at low dose)	9.1%	5.1%
Nitroglycerine	39.5%	21.3%
NAPA (N-Acetylprocainamide - Class III antiarrhythmic agent)	4.4%	9%



Drugs Approved for Testing in Either Males or Females

DRUG	USE	TESTING GROUP
Ethinyl Estradiol; Levonorgestrel	Oral contraception	Healthy non-pregnant females
Synthetic Conjugated Estrogens	Vaginal estrogen	Healthy physiologically or operatively post-menopausal females
Ethinyl Estradiol; Norgestimat	Oral contraception	Healthy non-pregnant females
Desogestrel; Ethinyl Estradiol	Oral contraception	Healthy non-pregnant females
Mestranol; Norethindrone	Oral contraception	Healthy non-pregnant females
Ondansetron Hydrochloride	Anti-nausea	Normal healthy males and females
Alosetron Hydrochloride	Anti-diarrhoea	Normal healthy females
Sildenafil Citrate	Erectile dysfunction	Normal healthy males
Tadalafil	Erectile dysfunction	Normal healthy males



Regulation

- Need for Canada to develop guidelines and specific requirements for vulnerable special populations, such as pregnant women



SOGC Opinion

- Drugs that are to be used exclusively in men or women should not be tested in a small number of men and women; but should be tested in an adequate number of men only or women only, depending in which sex the drug is being used/intended.



Drug Substitution

- The SOGC does not believe that drugs should be substituted without the patient and the physician both agreeing to such a change.
- Substituting for price only is not acceptable; especially for drugs that have been tested in very few subjects, sometimes as little as 15-20 patients, most often in both males and females.



Conclusion

- Call on Health Canada to review its guideline on testing of drugs for vulnerable populations, especially pregnant women.
- Testing standards should be set at a minimum of 100+ patients to detect inter-personal variability and eliminate errors that can happen when transposing tests between males and females, especially for diseases/conditions that affect exclusively one sex or the other.



Conclusion

Call to Action:

Healthcare professionals and women's groups to advocate the Government of Canada to establish an ad-hoc committee to develop recommendations to change the way drugs for exclusive use in pregnancy are tested.





Thank You

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