Prenatal Adverse Effects of Various Drugs and Chemicals
A Review of Substances of Frequent Concern to Mothers in the Community

Monica Bologa-Campeanu, Gideon Koren, Michael Rieder and Michael McGuigan

The Motherisk Program, Division of Clinical Pharmacology and Toxicology, Department of Pediatrics, and Research Institute, Hospital for Sick Children, and Departments of Pediatrics and Pharmacology, University of Toronto, Toronto, Canada

Contents

Summary .......................................................................................... 308
1. Drugs and Chemicals ................................................................. 309
   1.1 Ammonia ........................................................................... 309
   1.2 Analgesic/Anti-Inflammatory Medication ............................. 309
   1.3 Anthelmintics .................................................................... 309
   1.4 Antiasthmatics .................................................................. 311
   1.5 Antiemetics ....................................................................... 311
   1.6 Antifungals ...................................................................... 313
   1.7 Antimalarials ..................................................................... 313
   1.8 Antimicrobials ................................................................... 313
   1.9 Anxiolytics (Benzodiazepines) ............................................ 314
   1.10 Cold Medication ............................................................... 314
   1.11 Corticosteroids ................................................................. 314
   1.12 Environmental Pesticides .................................................. 315
   1.13 General Anaesthetics ......................................................... 315
   1.14 Histamine H$_2$-Receptor Antagonists ................................. 315
   1.15 Hair Care Products ............................................................ 316
   1.16 Laxatives ......................................................................... 317
   1.17 Local Anaesthesia ............................................................. 317
   1.18 Mercury Compounds ........................................................ 317
   1.19 Natural/Fuel Gases ............................................................ 317
   1.20 Oral Contraceptives .......................................................... 318
   1.21 Organic Solvents and Paints .............................................. 318
   1.22 Pediculocides .................................................................. 319
   1.23 Rubella Vaccine ............................................................... 319
   1.24 Sugar Substitutes .............................................................. 319
   1.25 Video Display Units and x-Rays ......................................... 320
2. Conclusion ............................................................................... 320
Summary

Using the number of calls to the Canadian Motherisk Program as an indicator of the drugs and chemicals frequently of concern to mothers during pregnancy, the risks to the fetus of exposure to these compounds have been reviewed.

The drugs which were of concern, and have been proven to be teratogenic, included alcohol, alkylating and antimetabolite agents, stilboestrol, disulfiram, heparin, lithium carbonate, phenytoin, tretinoin (retinoic acid), troxidone and valproic acid. For other compounds studied, there was either no data in the literature or no clear evidence of teratogenicity. The combination of doxylamine and pyridoxine, for example, has been associated with limb reduction defects in isolated case reports: cohort and case-control studies have failed to show a higher-than-baseline risk of malformations. In some cases of exposure to compounds with no known teratogenic potential, other adverse effects to the fetus are possible, and these effects are discussed in detail. In conclusion, when advising a pregnant woman about the potential teratogenic effect of a particular drug or chemical exposure, the health professional should also discuss other factors such as age, obstetric and medical history and the history of other exposures (including alcohol and smoking). In every pregnancy there is a 1 to 5% risk of major malformations, and even if the exposure does not appear to increase the teratogenic risk, such a risk still exists.

The thalidomide tragedy of the late 1950s resulted in medical practitioners often viewing every drug and chemical as a reproductive hazard to the pregnant woman. The reality is that only a few compounds have been proven to be teratogenic in humans (table 1), while the vast majority probably do not pose a threat to the fetus.

In a recent analysis, we demonstrated that pregnant women exposed to drugs and chemicals known not to be teratogenic assigned themselves an unrealistically high teratogenic risk of 25%. This assigned risk is comparable to the risk associated with thalidomide (Koren et al. 1987). There is a clear need for authoritative information and consultation services which can assist pregnant women and their physicians in understanding fetal risks. The advice provided should be based on unbiased, up-to-date information on the reproductive effects of drugs, chemicals and radiation.

In September 1985, we started a consultation programme for women concerned about antenatal exposure to drugs, chemicals and radiation, as well as exposure during lactation. A detailed description of the Motherisk Program appears elsewhere (Koren & MacLeod 1986; Koren et al. 1986). Initially, all the women who contacted us were seen in our weekly clinic. Subsequently, because of the increase in the number of women and families seeking advice and the repetition of some of the questions posed by women and their physicians, we started a telephone information service for certain drug and chemical exposures. Each call is answered by a staff physician or a postgraduate fellow from the Motherisk team. During the telephone interviews, data are collected on special forms which include the information deemed necessary for the study as well as a summary of the advice given.

As a rule, only simple requests for information are dealt with through the telephone. Multiple exposures, social, medical, legal and psychological problems are evaluated in the clinic. Appointments are also made for all women exposed to known or controversial teratogens, drugs of abuse, women who have a chronic medical condition and for any woman who prefers to be seen in the Motherisk clinic. Currently, we deal with 30 telephone inquiries daily from the province of Ontario (population 9 million) and consult 6 to 16 cases in our weekly clinic, mainly from the Greater Toronto area (population 4 million). In about 20% of cases the requests for information come from health professionals and it is hoped that as the public becomes more aware of the existence of Motherisk, a cumulative educational effect will become apparent. Although the data indicating the common exposures were obtained from a regional database, we believe that the information has wide applicability.