Fetal exposure to oral isotretinoin: failure to comply with the Pregnancy Prevention Program

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Oral isotretinoin (Accutane™), an effective treatment for cystic, recalcitrant acne, is a potent human teratogen.[1] To prevent fetal exposure to the drug, the Pregnancy Prevention Program was developed in 1988 by the manufacturer and the US Food and Drug Administration and has been used in Canada since then.[2,3]

As part of the program, printed material is distributed to prescribing physicians to be used in educating their female patients about the serious teratogenic effects,[4] it instructs physicians to have female patients undergo a pregnancy test and to prescribe the drug if the result is negative, and it instructs physicians to delay therapy until the second or third day of the patient's next normal menstrual period. The program also stresses to patients the importance of using 2 forms of contraception concurrently. Female patients are asked to sign a consent form acknowledging that they have been instructed through the program, are aware of the need to use 2 forms of contraception during isotretinoin therapy and agree to undergo pregnancy testing before, during and after the therapy.[2]

Despite these precautions, the Motherisk Program in Toronto continues to receive reports of fetal exposure to oral isotretinoin every year. We reviewed 4 recent cases to highlight the continuing problem in implementing the Pregnancy Prevention Program.

In all 4 cases the women were under 21 years of age and the pregnancies were unplanned. We found evidence of noncompliance with the Pregnancy Prevention Program on the part of both the women and their physicians (Table 1). Three of the women used contraception but only 1 form instead of 2. All of the women had been advised by their dermatologist not to conceive while taking the isotretinoin and, if they were sexually active, to use contraception. However, only one patient was provided with the program's printed material and signed the consent form. In one case the dermatologist did not wait for the pregnancy test results before prescribing the drug.

Fifty per cent of pregnancies in North America are unplanned and may result in inadvertent fetal drug exposure.[5] In a previous study we found that Canadian women who were prescribed oral synthetic retinoids and failed to use proper contraception tended to be younger than matched control subjects not prescribed such drugs and to seek counselling later in gestation.[2]

A recently published letter by a Canadian dermatologist substantiates our suspicion that pregnancies occurring during oral isotretinoin therapy stem from widespread noncompliance by dermatologists.[6]

Physicians prescribing oral isotretinoin should ensure that fetal exposure to the drug is prevented. The failure of implementing the Pregnancy Prevention Program, and in particular the difficulty in ensuring contraception, in the cases we have highlighted suggests that young women prescribed oral isotretinoin, especially adolescents, should be referred for professional contraception counselling. Very often young teenagers have little sexual experience and poor understanding of birth control methods, and thus they substantially increase the risk of fetal exposure to oral isotretinoin.[7] In addition, a renewed educational effort for physicians is warranted to heighten their awareness to this serious problem.

Table 1: Degree of compliance with the Pregnancy Prevention Program in 4 reported cases of fetal exposure to isotretinoin

Measure of compliance	Case 1	Case 2	Case 3	Case 4
Patient acknowledged knowing of teratogenic risk	Yes	Yes	Yes	Yes
Physician mentioned teratogenic risk	Yes	Yes	Yes	Yes
Pregnancy Prevention Program was discussed with patient	No	No	No	Yes
Physician advised patient to use 2 modes of contraception concurrently	No	No	No	No
Patient signed consent form	No	No	No	Yes
Patient used contraception during isotretinoin therapy	No*	Yes†	Yes‡	Yes§

*Patient did not intend to be sexually active.
†Oral contraceptive only; used on an irregular basis.
‡Oral contraceptive only; started before isotretinoin therapy but patient already pregnant (confirmed later by pregnancy test).
§Condom only.

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