

MOTHERISK UPDATE

Meena Pole, MD Gideon Koren, MD, FRCPC

Finasteride

Does it affect spermatogenesis and pregnancy?

ABSTRACT

QUESTION A few women have asked me whether finasteride, taken by their partners for male pattern baldness, will affect their pregnancies. The product monograph is very alarming: it sounds as if even handling the medication could cause harm, especially to a male fetus. Should a man stop taking finasteride if his partner is planning pregnancy or is pregnant? What is the risk to the fetus if its mother accidentally handles crushed or broken tablets?

ANSWER To date, there are no reports of adverse pregnancy outcomes among women exposed to finasteride. Taking 1 mg of finasteride daily did not have any clinically significant effect on men's semen. Absorption through the skin while handling tablets is extremely unlikely to cause fetal exposure or harm. There is no reason to discontinue the drug. Motherisk is currently following up women who are pregnant or planning pregnancy and whose partners are taking finasteride.

RÉSUMÉ

QUESTION Quelques patientes m'ont posé des questions concernant les effets possibles sur leur grossesse du finastéride pris par leur partenaire pour l'alopécie typiquement masculine. La monographie du produit est très alarmante: elle laisse entendre que la simple manipulation du médicament pourrait être dommageable, en particulier pour les fœtus mâles. Les hommes devraient-ils cesser de prendre du finastéride quand leur partenaire prévoit une grossesse ou est enceinte? Quel risque court le fœtus si la mère manipule accidentellement des comprimés écrasés ou brisés?

RÉPONSE Jusqu'à présent, il n'existe aucun rapport signalant des issues défavorables de grossesse chez les femmes exposées au finastéride. Le fait de prendre 1 mg de finastéride par jour n'avait aucun effet cliniquement significatif sur le sperme. Il est extrêmement improbable que l'absorption par voie cutanée en manipulant les comprimés expose le fœtus ou lui nuise. Il n'y a pas de raison de cesser la médication. Motherisk exerce présentement le suivi de femmes enceintes ou qui prévoient une grossesse dont le partenaire prend du finastéride.

Finasteride, an oral type II 5 α -reductase inhibitor, selectively blocks androgen activity in the prostate and skin and hence is potentially useful for treating male pattern baldness, hirsutism, and acne.¹ Hirsute women's skin shows heightened 5 α -reductase activity,² so finasteride could be used to treat them also.

Finasteride, a potent competitive 5 α -reductase inhibitor, reduces testosterone metabolism to dihydrotestosterone (DHT).^{1,3} This is an important step because baldness is not known to occur

unless testosterone is converted to dihydrotestosterone. Finasteride decreases circulating DHT without decreasing testosterone.³

Dihydrotestosterone is responsible for acne, increases of body and

facial hair during puberty, prostate gland growth, and development of male genitalia in utero. Use of finasteride is, therefore, contraindicated for pregnant women or women trying to become pregnant.¹

Do you have questions about the safety of drugs, chemicals, radiation, or infections in women who are pregnant or breastfeeding? We invite you to submit them to the Motherisk Program by fax at (416) 813-7562; they will be addressed in future Motherisk Updates. Published Motherisk Updates are available on the College of Family Physicians of Canada website (www.cfpc.ca). Some articles are published in *The Motherisk Newsletter* and on the Motherisk website (www.motherisk.org) also.

Risk of exposure

Finasteride is absorbed mainly from the gastrointestinal tract, is not affected by food, and has a bioavailability ranging from 60% to 80%. It is highly bound to protein and undergoes extensive metabolism by hepatic cytochrome P-450 enzymes.

Motherisk questions are prepared by the **Motherisk Team** at the Hospital for Sick Children in Toronto, Ont. **Dr Pole** was a member and **Dr Koren** is Director of the Motherisk Program.

It is mainly eliminated through bile and feces (60% to 80%) with minimal renal excretion (no dose adjustment is needed for elderly patients or patients with renal impairment). Its mean serum half-life ranges from 4.7 to 7.1 h but, because its biologic half-life is much longer, DHT might be suppressed for nearly 2 weeks after discontinuing it.³

In one study, semen levels were measured in 35 men taking 1 mg of finasteride daily for 6 weeks.⁴ Highest level measured was 1.52 ng/mL; mean level was 0.26 ng/mL. Assuming a 100% vaginal absorption through a 5-mL ejaculate per day, women would be exposed to 7.6 ng/d, a negligible amount. This level is 750 times lower than the "no effect" level for developmental abnormalities in rhesus monkeys.⁴

Consequences of exposure

Similarly, animal studies conducted by the drug's manufacturer of giving 800 ng/d of finasteride intravenously (750 times the highest estimated exposure of pregnant women from semen of men taking 1 mg/d) to monkeys found no abnormalities among male fetuses.⁴ To confirm the relevance of results in rhesus monkeys for human fetal development, pregnant monkeys were administered high oral doses of finasteride (2 mg/kg/d, which is equivalent to 100 times the recommended human dose of 1 mg/d, or 12 million times the highest estimated exposure from semen of men taking 1 mg/d). Results showed abnormalities in male external genitalia, but no other abnormalities and no effect on female fetuses.

In 1999, a double-blind, randomized placebo-controlled multicentre study was conducted on 181 men between 19 and 41 years old. These men received 1 mg/d of finasteride or placebo for 48 weeks (4 spermatogenic cycles) and no drugs for the following 60 weeks. Among these

181 men, 79 were included in a subset for collection and analysis of sequential semen samples. Results showed that 1 mg/d of finasteride did not have any significant effect on sperm concentration, total sperm per ejaculate, or sperm motility or morphology.⁵

The absence of clinically significant effects of 1 mg/d of finasteride on semen parameters supports the hypothesis that testosterone and not DHT is the primary androgen regulating spermatogenesis, sperm maturation, and seminal fluid production.^{4,5} Similarly, men with 5 α -reductase deficiency have life-long (including in utero) suppression of DHT formation, with low serum DHT levels and mildly elevated testosterone levels. Their other morphologic features include rudimentary prostates, small seminal vesicles, normal epididymal size, and markedly diminished volume of ejaculate.^{6,7}

The notable decrease in volume of ejaculate in these men was attributed to in utero reduction of DHT, which led to development of a rudimentary prostate gland. In the absence of any other anatomic abnormalities, these men have been shown to have normal spermatogenesis and healthy progeny.^{6,9} Side effects reported with finasteride were mainly related to sexual dysfunction; effects were mild and disappeared after treatment was discontinued.³

Women also become alarmed after reading finasteride's label or product monograph. They are afraid to handle crushed or broken tablets, especially during pregnancy.⁴ Tablets, however, are coated with film, so risk of absorption of finasteride through the skin is negligible and is unlikely to cause harm to a fetus.

No drug interactions have been reported with finasteride. Hirsute women taking oral contraceptives who were treated with finasteride

showed a marked elevation in serum cholesterol levels. Finasteride alone did not produce this effect.¹⁰

In the future, finasteride could be used to treat acne and hirsutism in women.^{10,11} Women using finasteride should be advised to use contraception to avoid pregnancy and hence the risk of feminization of male fetuses' external genitalia. To date, no study has explored the effect of 5 α -reductase inhibitors on hirsute patients. ❖

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