

MOTHERISK UPDATE

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Taking St John's wort during pregnancy

ABSTRACT

QUESTION A 23-year-old patient of mine has been taking St John's wort for postpartum depression for about 2 years. She is now planning her second pregnancy. Is she or her fetus at risk if she continues to take the herbal therapy?

ANSWER Despite the widespread availability and use of St John's wort and extensive research on the herb, there are almost no data on reproductive safety. At this stage, therefore, St John's wort cannot be recommended as safe therapy during pregnancy.

RÉSUMÉ

QUESTION Une de mes patientes âgée de 23 ans prend du millepertuis pour une dépression postpartale depuis environ 2 ans. Elle planifie maintenant sa deuxième grossesse. Est-ce qu'elle ou son fœtus courent des risques en continuant cette phytothérapie?

RÉPONSE En dépit de la disponibilité et de l'utilisation largement répandues du millepertuis ainsi que des recherches considérables sur cette herbe, il n'existe presque aucune donnée sur son innocuité dans le contexte de la procréation. Pour l'instant, le millepertuis ne peut pas être recommandé comme une thérapie sûre durant la grossesse.

St John's wort (*Hypericum perforatum*), named because it flowers around John the Baptist's day in June and "wort" is derived from the German word for plant, is the most common herbal therapy used for depression. In Germany, it accounted for a quarter of all antidepressant prescriptions in 1997.¹

In North America, St John's wort is a dietary supplement; in 1998, total retail sales in the United States totaled \$140 million.² St John's wort contains at least 10 different active substances; hypericin is considered the most active ingredient.³ The herbal extract displays the pharmacologic qualities of

several antidepressants by inhibiting the synaptic reuptake of serotonin, dopamine, and noradrenaline.⁴

Results of studies

Linde and Mulrow⁵ published a meta-analysis that included 2291 patients with "neurotic depression" or "mild to moderately severe

depressive disorders" from 27 trials. The reviewers concluded that the evidence indicated St John's wort was more effective than placebo for short-term treatment of mild-to-moderate depressive disorders. Although unable to conclude that St John's wort was better treatment than other antidepressants, they stated that it seemed comparable to maprotiline, imipramine, and amitriptyline.

In a recent double-blind, randomized placebo-controlled trial, the efficacy and safety of a well characterized *Hypericum perforatum* preparation was compared with placebo or sertraline for 8

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.

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weeks. Participants were adult outpatients with major depression. Neither St John's wort nor sertraline were significantly better than placebo.⁶

St John's wort is well tolerated and is perceived as safer than most antidepressants prescribed in Canada. It can, however, have adverse effects^{5,7-9} and interact with other drugs.² About 2% to 26% of patients using St John's wort report side effects that include nausea and restlessness (most common), delayed hypersensitivity, dizziness, dry mouth, and constipation. Photodermatitis is a rare, but well recognized, adverse effect. St John's wort's ability to induce the cytochrome P-450_{3A} metabolizing enzyme might put transplant patients receiving cyclosporine at risk of graft rejection.

St John's wort can be found at most pharmacies, natural food stores, and some grocery stores in Canada, and hence it is widely available to women of childbearing age. Whether recommended by a family physician or taken without recommendation, St John's wort could be harmful before pregnancy is diagnosed or during pregnancy.

Responses from a randomly selected group of Canadian physicians, medical students, naturopaths, and naturopathic students to a detailed questionnaire (242 respondents; 38% response rate) showed that St John's wort was the second most popular complementary medicine recommended by both medical doctors and naturopaths (*Echinacea* was first). Although only one physician recommended a herbal product to a pregnant patient, as many as 49% of the naturopaths felt comfortable recommending herbal products to pregnant women.⁹

To date, three animal studies have addressed use of St John's wort during the perinatal period. No reproductive toxic effects were found in

rats or dogs with oral doses of 900 and 2700 mg/kg.¹⁰ When a group of female mice receiving *Hypericum* from 2 weeks before conception and throughout gestation was compared with a group of female mice receiving placebo, one study¹¹ found that mouse offspring in both groups were similar in gestational age at delivery, litter size, perinatal outcome, body weight, body length, and head circumference growth through adulthood. Moreover, no differences were found in reaching physical milestones, in reproductive capability, or in growth and development of second-generation offspring. A similar study found lower birth weights among male offspring in the St John's wort group, but no long-term differences in early developmental tasks, locomotor activity, or exploratory behaviour throughout development.¹²

Self-treatment

Only two cases of women treating themselves with St John's wort during pregnancy are reported in the literature.¹³ In one case, where follow up was available, a woman took the herb from 24 weeks' gestation until delivery. Her neonate was reported to have normal results of physical examination and behavioural assessment during the first month of life.

Not enough data are available to conclude that St John's wort is safe for pregnant women or fetuses. Much more preclinical and clinical data must be accumulated before the herb can safely be regulated as an adjunct or alternative treatment to the antidepressant drugs currently prescribed for pregnant women. ❖

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