

Anti-inflammatory drugs taken in early pregnancy more than double risk of miscarriage

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The risk of miscarriage is 2.4 times greater for women who took any type and dosage of nonaspirin nonsteroidal anti-inflammatory drugs (NSAIDs) in early pregnancy, according to a study in *CMAJ* (*Canadian Medical Association Journal*).

Nonaspirin NSAIDs are a class of drugs that include <u>naproxen</u>, ibuprofen, <u>diclofenac</u>, and celecoxib, and are one of the most common medications used during pregnancy. However, there are concerns about use of these drugs in pregnancy, although studies on the risks have been inconsistent.

Researchers from the University of Montreal, CHU Ste-Justine, Quebec, and Ecole Nationale de la Statistique et de l'Analyse de l'Information, Rennes, France, undertook a study to determine the risk of miscarriage associated with the types and dosages of nonaspirin NSAIDs. They looked at a total of 4705 cases of miscarriage up to the 20th week of gestation, 352 (7.5%) of whom took nonaspirin NSAIDs. Of the 47 050 women in the control group who did not miscarry, 1213 (2.6%) had been exposed to nonaspirin NSAIDs. The data came from the Quebec Pregnancy Registry, which provides information on filled prescriptions, physician visits and diagnoses, and hospitalisations during pregnancy.

Women ranged in age from 15 to 45 years old on the first day of gestation and were insured by the Régie de l'Assurance Maladie du



Québec (RAMQ) for their medications for at least one year prior to and during pregnancy. Exposure to nonaspirin NSAIDs was defined as having filled at least one prescription for any type of the drug during the first 20 weeks of pregnancy or in the two weeks prior to the start of the pregnancy.

Ibuprofen is the only nonaspirin NSAID available over the counter in Quebec, and women in the RAMQ drug plan can have that prescribed as a prescription. Naproxen was the most commonly used nonaspirin NSAID followed by ibuprofen.

"The use of nonaspirin NSAIDs during <u>early pregnancy</u> is associated with statistically significant risk (2.4-fold increase) of having a spontaneous abortion," writes Dr. Anick Bérard, from the University of Montreal and the Director of the Research Unit on Medications and Pregnancy at CHU Ste-Justine. "We consistently saw that the risk of having a spontaneous abortion was associated with gestational use of diclofenac, naproxen, <u>celecoxib</u>, ibuprofen and rofecoxib alone or in combination, suggesting a class effect."

The highest risk was associated with diclofenac alone and the lowest risk was in users of rofecoxib alone. However, dosage of nonaspirin NSAIDs did not appear to affect risk.

These findings are consistent with other studies but are novel with regards to the nonaspirin NSAIDs types and dosages.

"Given that the use of nonaspirin NSAIDs during early pregnancy has been shown to increase the risk of major congenital malformations1 and that our results suggest a class effect on the risk of clinically detected spontaneous abortion, nonaspirin NSAIDs should be used with caution during pregnancy.," the authors conclude.



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