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Commentary: Triptan Use during Pregnancy: A Safe Choice?

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Abstract and Introduction

Introduction

Up to one-fifth of the female population suffers from migraine headache and the prevalence peeks during their late 20s through their 40s.[1] The influence of pregnancy and the puerperium on migraine is versatile, as these events can trigger migraine attacks or influence frequency and severity.[2–4] Many but not all pregnant women experience a reduction in migraine burden, still leaving a substantial number of patients with a treatment indication. While some women manage to find options to treat their migraine, such as reduction in work, sufficient hydration, biofeedback or other relaxation techniques,[2,5] many still require drug treatment to acutely abort a migraine attack. As with many other treatments, the safety of triptans during pregnancy is largely unknown and the choice of drugs to treat a migraine attack is limited.

In this issue of *Headache*, Nezvalová-Henriksen et al add new data on the safety of triptan use during pregnancy.[6] In this study among 69,929 pregnant women participating in the population-based Norwegian Mother and Child Cohort, information on migraine headache and on triptan use before as well as during pregnancy was collected via standardized questionnaires. Data on congenital malformation and other severe pregnancy-related outcomes were obtained from the Norwegian Medical Birth Registry. Reported triptan use (yes or no) was categorized according to the time of use (during entire pregnancy, during the first trimester, and during the second or third trimester). The authors used 2 control populations: (1) the group of pregnant women who reported triptan use at least 6 months prior to the pregnancy but not closer to or during the pregnancy and (2) pregnant women who never reported triptan use or migraine. Outcome events included congenital malformations, survival, low birth weight, prematurity, low Apgar score, atonic uterus, prolonged labor, and perinatal/postpartum blood loss of >500 mL.

A total of 2.2% of women used a triptan (about half of them used sumartriptan) during pregnancy. These women were more likely to be overweight or obese, to suffer from obstetric complications (ie, preeclampsia, high blood pressure, hospitalization, vaginal bleeding, folate-deficiency anemia, and others) and were also more likely to use other pain medications and medications with potential teratogenic or detrimental effects when compared with the nonmigraine control group.

The results of the study indicate no association between triptan use during pregnancy and congenital malformations overall when compared with the nonmigraine group. The adjusted odds ratios (95% confidence intervals) were 0.9 (0.7–1.2) for any and 1.0 (0.7–1.3) for major congenital malformation. Use of triptans during the second/third trimester of pregnancy was associated with an increased likelihood of an atonic uterus (OR = 1.4, 1.1–1.8) and blood loss >500 mL during labor (OR = 1.3, 1.1–1.5). The group of women with migraine who only used triptans before but not during the pregnancy had quite similar incidence of adverse pregnancy-related outcomes as the nonmigraine group.

The data from this large registry are consistent with previous reports of little risk for infant-related outcomes when using a triptan during pregnancy.[7,8] However, several aspects of the study should be considered. The data provided by Nezvalová-Henriksen et al do not include information on the frequency and dose of triptan use and do not present results for specific triptans. Any association with a particular triptan could be diluted in a "class effect." Similarly, malformation overall was used as an outcome, potentially missing associations with specific malformations. Further, no data were presented on the frequency of miscarriages and elective abortions, which could have been different among triptan users. From a methodological point of view, adjustment for factors potentially affected by triptan use can hide effects mediated through these factors and could have introduced bias.[9] For example, an effect of triptans on prematurity might be explained by the previously reported association between migraine and preeclampsia, which is a major cause of preterm delivery.

However, all these potential sources of bias might be negligible compared with the potential harmful effects of triptans for the women, including hypertension, preeclampsia, hospitalization, vaginal bleeding, and folate-deficiency anemia as clearly suggested in the paper by Nezvalová-Henriksen et al.[6] Whether these associations, however, are due to the actual triptan exposure or to shared

causes with the underlying indication (ie, migraine) would have to be discerned. Further, the authors present only data on overall of triptan use during pregnancy rather than use in the first trimester (ie, before a specific diagnosis such as preeclampsia). Thus, exposure could have in theory begun after the event. In any case, if women on triptans have a higher frequency of these obstetrics complications, they may have to be monitored more closely during pregnancy. Furthermore, a recent study linked migraine during pregnancy with substantially increased risk of ischemic and hemorrhagic vascular events,[10] outcomes that were not evaluated in this study.

While available data support low risk of malformations in general as a consequence of triptan use during pregnancy, many important questions remain regarding their safety for the pregnant woman. Future studies could evaluate the comparative safety of different therapeutic approaches to treat migraine during pregnancy, including but not limited to triptans, while assessing the role of migraine severity and the timing of drug intake in relation to specific outcome events.

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