Triptans May Not Raise Risk of Fetal Defects

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PHILADELPHIA — Sumatriptan and naratriptan do not appear to significantly raise the risk of major congenital malformations in fetuses that are exposed to the drugs in utero, according to the latest analysis of an international pregnancy registry.

Established in 1996, the GlaxoSmithKline registry has accumulated data on 849 pregnancies exposed to the drugs. Birth defects occurred in 4.5% of infants exposed in the first trimester or during all of their gestation, which was not significantly higher than that previously identified for women with migraines. Major congenital malformations are known to occur in the offspring of women with migraines at a slightly higher rate than in the general population (3.4% vs. 2%-3%, respectively), Marianne C. Cunnington, Ph.D., and her colleague Sara A. Ephross, Ph.D., reported in a poster at the International Headache Congress. Both are employees of GlaxoSmithKline.

The registry relies on a voluntary reporting strategy that encourages healthcare providers to submit information on exposed pregnancies as early as possible. Retrospective case reporting also is accepted. Pregnancy outcome is ascertained by medical records that the provider forwards after birth, or by medical records confirming other outcomes, including fetal demise or abortion.

At the outset, the registry collects data on the timing, dosage, duration, indication, and administration of the drugs; maternal demographics; expected date of delivery; and any prenatal testing. At follow-up, there is a review of the pregnancy outcome, drug exposure during the pregnancy, and the women's headache history during pregnancy.

So far, the registry has amassed information on 761 pregnancies exposed to sumatriptan and 88 exposed to naratriptan. Outcomes are known for 570 of the sumatriptan-exposed pregnancies and 57 of the naratriptan-exposed pregnancies. Twenty-one sumatriptan-exposed pregnancies and 31 naratriptan-exposed pregnancies are pending delivery. The rest have been lost to follow-up, the investigators noted in their poster at the congress, which was sponsored by the International Headache Society and the American Headache Society.

Among the sumatriptan-exposed pregnancies, there were 23 birth defects, 4 fetal deaths, 32 spontaneous fetal losses, and 11 induced abortions.

The malformations that occurred in infants who were exposed to sumatriptan in the first trimester included abnormal head circumference, single palmar crease and systolic murmur; moderate craniosynostosis; cerebral abnormality with developmental delay; partial cleft lip; ventricular septal defects (4); biliary atresia; diaphragmatic hernia; pyloric stenosis (3); anterior displacement of anus; hip dysplasia; polydactyly; malformation of left hand; and Down syndrome (3). No data were available for the three birth defects that occurred in infants who were exposed to sumatriptan after the first trimester.

Among fetuses exposed to naratriptan, there were five spontaneous losses, one induced abortion, and one live infant with a 2.5-mm ventricular septal defect that was expected to close spontaneously.

The pregnancy registry did not contain any data on the exposure to the combination of sumatriptan and naproxen.

Dr. Cunnington noted that five additional independent studies, including a Swedish study of more than 2,000 sumatriptan recipients, have failed to find an increase in birth defects associated with in utero exposure.

"While its use in pregnancy cannot be encouraged," she wrote, "there is consistent evidence that sumatriptan is not associated with a substantial increase in the risk of major congenital malformations following exposure."

To report pregnancies exposed to sumatriptan, naratriptan, or the sumatriptan/naproxen combination, North American physicians can call 800-336-2176, and international physicians can call 910-256-0549.

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