Hydroxychloroquine 'Probably Safe' in Pregnancy

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DÜSSELDORF, GERMANY — The anti-inflammatory compound hydroxychloroquine appears to be relatively safe during pregnancy, according to a small number of studies totaling about 250 patients.

But these studies have not provided overwhelming evidence proving the safety of this agent in pregnancy, Jean-Charles Piette, M.D., said at an international conference on cutaneous lupus erythematosus. Until 1995, nearly all physicians stopped hydroxychloroquine (Plaquenil) when a patient with lupus erythematosus (LE) became pregnant because there were no data on whether the drug was safe during pregnancy, said Dr. Piette of Hôpital Pitié-Salpétrière, Paris.

Now, many physicians who treat about four to five pregnant women with connective tissue disorder each year regularly prescribe antimalarials to such patients despite a lack of evidence officially establishing the safety of the drugs during pregnancy.

In fact, 69% of 52 physicians who responded to a survey about the use of antimalarials during pregnancy said they continued antimalarials in pregnancy sometimes, often, or always (J. Rheumatol. 2002;29:700-6).

Hydroxychloroquine (HCQ) is known to cross the placenta and is present in similar concentrations in blood from the umbilical cord and the mother (Arthritis Rheum. 2002;46:1123-4).

In one study, 33 women with LE who were exposed to HCQ during 36 pregnancies had similar obstetric outcomes and levels of lupus activity, compared with 53 unexposed pregnant women with LE from the same lupus pregnancy center (Ann. Rheum. Dis. 1996;55:486-8). The investigators in the trial concluded that the continuation of HCQ "is probably safe during pregnancy," Dr. Piette noted.

In a separate study, HCQ did not cause any disease flares in a group of eight women with systemic LE and two with discoid LE, whereas three patients had flare-ups in a placebo group of nine patients with systemic LE and one with discoid LE. None of the infants born to women taking HCQ had congenital abnormalities, and all of them had normal auditory and neuroophthalmologic evaluations at 1.5-3 years of age (Lupus 2001;10:401-4).

A small number of studies suggest the drug is relatively safe in pregnancy, but the studies have not offered overwhelming evidence of safety.

The drug also was not linked to any unusual side effects in another series of 53 pregnancies in women with LE that resulted in live births.

A study conducted by Dr. Piette and his colleagues compared 133 consecutive pregnancies in 90 women with connective tissue disease who took HCQ with 70 consecutive pregnancies in 53 control women with similar disorders who did not take HCQ. Of the pregnancies in women who received HCQ, 122 were exposed to 400 mg/day, and the remaining 11 received 200 mg/day.

Three malformations occurred in exposed infants, while four developed in the infants of control women. One child died as a result of prematurity in each group.

After the last follow-up of children at a mean age of 26 months (age ranging from 12 to 108 months), none of the children exposed to HCQ had visual, hearing, growth, or developmental abnormalities (Arthritis Rheum. 2003;48:3207-11).

Despite data that show no teratogenicity with HCQ, the Physicians' Desk Reference Web site for patients advises pregnant patients to avoid HCQ except in the suppression or treatment of malaria when the benefit outweighs any possible hazards.

HCQ exists at low levels in breast milk—344 ng/mL and 1,424 ng/mL in a report on two mothers—and is delivered in extremely low levels to breast-feeding children. "I think we can ensure that at such a low level there is no risk," Dr. Piette said.

Some reports have noted teratogenicity with high-dose chloroquine; one case occurred in a pregnant woman with lupus. These have included a few cases of ear or eye toxicity. Dr. Piette said that he recommends contraception in patients who receive chloroquine. ■