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Hydroxychloroquine

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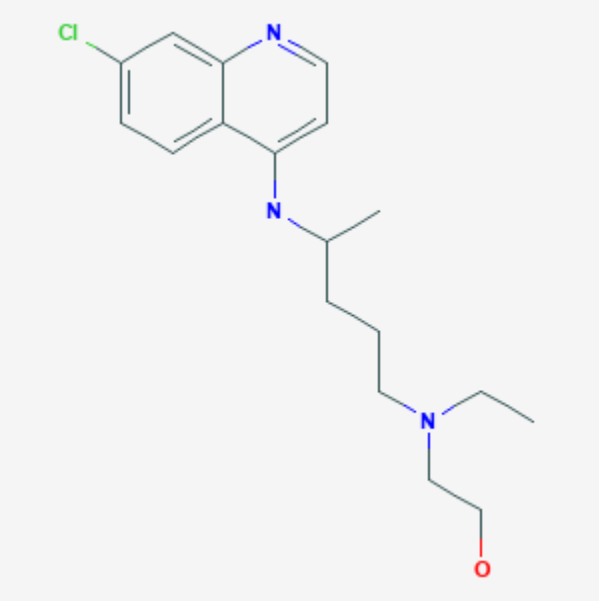

Drug Levels and Effects

Summary of Use during Lactation

Infants exposed to hydroxychloroquine during breastfeeding receive only small amounts of the drug in breastmilk. In infants up to at least 1 year of age, careful follow-up found no adverse effects on growth, vision or hearing.[1-3] International experts indicate that hydroxychloroquine is acceptable during breastfeeding.[4-7]

When given once weekly for malaria prophylaxis, the amount of drug is not sufficient to harm the infant nor is the quantity sufficient to protect the child from malaria. Breastfeeding infants should receive the recommended dosages of hydroxychloroquine for malaria prophylaxis.[8]

Drug Levels

Hydroxychloroquine is usually available as the sulfate salt with hydroxychloroquine constituting about 75% of the labeled dose of hydroxychloroquine sulfate. It has a half-life of over a month. Some studies have not been clear about the salt form and dosage of the products being taken and others have sampled milk after only a few doses before steady state was reached. These flaws make interpretation of some of the data difficult.

Maternal Levels. In a patient beginning therapy with 200 mg of hydroxychloroquine (salt unspecified) twice daily, the highest milk level detected was 10.6 mcg/L from 3 to 12 hours after the fourth dose. After the first 48 hours of treatment with a total dosage of 800 mg, a total of 3.2 mcg was excreted into her breastmilk. This amounted to 0.0003% of the mother's total dosage.[9] However, it is unlikely that steady state had been reached at this time.

A woman who had been breastfeeding for 9 months began taking hydroxychloroquine sulfate 400 mg (equivalent to 310 mg hydroxychloroquine base) nightly. After 6 weeks of this regimen, steady-state milk levels were 1.46, 1.09, 1.09 and 0.85 mg/L at 2, 9.5, 14 after one dose and 17.7 hours after a dose on the next day. The authors estimated that the infant would receive 0.11 mg/kg daily or about 2% of the mother's weight-adjusted dosage.[10]

Two women who had taken hydroxychloroquine 200 mg (probably sulfate equivalent to 150 mg of base) once or twice daily (the report is unclear) before and during pregnancy had milk levels measured after delivery. Hydroxychloroquine levels in the two mothers were 344 and 1424 mcg/L at unspecified times after a dose. The authors estimated an infant intake of 0.06 and 0.2 mg/kg daily in the two infants.[11] These authors also reported two other women who had milk hydroxychloroquine levels of 1131 and 1392 mcg/L at unreported times after unspecified doses (presumably 200 to 400 mg daily). The authors estimated that these two infants would receive no more than 0.2 mg/kg daily via breastmilk.[12]

Numerous samples of milk were obtained from 6 women who were receiving 400 mg (n = 5) or 200 mg (n = 1) of hydroxychloroquine daily. The average milk level was of 376 mcg/L (range 20–1463 mcg/L) of hydroxychloroquine and of 36 mcg/L (range 11–111 mcg/L) of desethylchloroquine. The authors estimated that a fully breastfed infant would receive 1 mg of hydroxychloroquine and 0.066 mg of desethylchloroquine daily.[13]

Thirteen women who were on long-term hydroxychloroquine donated milk samples at 7 time points between 0 and 18 hours after a dose. One woman taking 100 mg daily had an average milk hydroxychloroquine concentration of 416 mcg/L. Three women taking 100 mg twice daily had average milk concentrations ranging from 358 to 746 mcg/L. Four women taking 200 mg once daily had average milk concentrations ranging from 672 to 980 mcg/L. Five women taking 200 mg twice daily had average milk concentrations ranging from 1336 to 3269 mcg/L.[14]

Thirty-three women who had been taking hydroxychloroquine sulfate for at least one year and were exclusively breastfeeding had hydroxychloroquine milk levels determined at 5 times over a 12-hour period just before and after a dose. Samples were taken at a median of 4 (range 1 to 16) weeks postpartum. Dosages ranged from 200 mg once every two days to 200 mg twice daily, with most taking 200 mg once (24%) or twice (64%) daily. These dosages are equivalent to 155 mg and 310 mg of hydroxychloroquine base. The time to peak milk concentration ranged from 2 to 4 hours after the dose. Average milk levels were dose related, with levels ranging from 0.4 to 1.2 (mean 0.7) mg/L with 200 mg once daily and 0.5 to 3.7 (mean 1.4) mg/L with 200 mg twice daily. The estimated infant daily dosage averaged 0.2 mg/kg for the 400 mg daily dosage and 0.1 mg/kg for the lower dosages. These corresponded to weight-adjusted infant dosages of 1.9 to 3.2% of the maternal dosage. One woman taking 200 mg twice daily was found to have a relative infant dosage of 9.8% and was instructed to discontinue breastfeeding.[3]

Infant Levels. Relevant published information was not found as of the revision date.

Effects in Breastfed Infants

No adverse effects were reported in one 9-month-old breastfed infant whose mother was taking 310 mg hydroxychloroquine base daily for 6 weeks.[10]

Five mothers took hydroxychloroquine 200 mg daily during pregnancy and breastfeeding, one for 30 months. Flash electroretinograms performed on the infants were normal.[1,15]

Another group of investigators have reported numerous infants whose mother took hydroxychloroquine during pregnancy and were breastfed during maternal hydroxychloroquine use. An abstract reported 16 infants breastfed for 1 to 19 months and followed up at an average of 24 months (range 1 to 86 months) with no evidence of visual or hearing deficits.[16] In a letter they reported 8 breastfed infants followed up at 1, 6 and 12 months of age who had normal growth and development and who had thorough, normal eye examinations at 1 and 12 months of age.[17] In a case series, 13 mothers taking hydroxychloroquine sulfate 200 mg daily breastfed their infants for an average of 2.8 months (range 1 to 6 months). None had evidence of retinal, motor or growth abnormalities during 12 months of follow-up. The authors conclude that the benefits of breastfeeding outweigh the risk of hydroxychloroquine.[2] It appears that the 8 infants reported in the letter were included among the 13 infants in the case series, but it is unclear whether the 16 infants reported in the abstract were part of the case series.

Thirty-three women who had been taking hydroxychloroquine for at least one year and exclusively breastfeeding had hydroxychloroquine milk levels determined over a 12-hour period. Two-thirds of the women were also taking a corticosteroid. Dosages ranged from 200 mg once every two days to 200 mg twice daily. Follow-up at 1 year of the infants did not find ocular toxicity or growth abnormalities.[3]

Effects on Lactation and Breastmilk

Relevant published information was not found as of the revision date.

Alternate Drugs to Consider

(Rheumatoid Arthritis) Auranofin, Etanercept, Gold Sodium Thiomalate, Infliximab, Methotrexate, Penicillamine, Sulfasalazine

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Substance Identification

Substance Name

Hydroxychloroquine

CAS Registry Number

118-42-3

Drug Class

Breast Feeding

Lactation

Anti-infective Agents

Antiparasitic Agents

Antimalarials

Antirheumatic Agents

Antiprotozoal Agents