

*LETTER TO THE EDITOR*

CHLOROQUINE AND PREGNANCY

Sir,

( Received on August 3, 2007 )

Despite wide-spread resistance in some parts of the world (including sub-Saharan Africa) chloroquine (CHQ) is one of the safest antimalarials if taken correctly during pregnancy. However, I believe that deliberate acute CHQ intoxication usually results in death and can be detectable in body fluids, post-mortem specimens and corpses (1, 2). CHQ poisoning is common in Africa and the Far East. Hypotension is often the first clinical manifestation of poisoning, followed by cardiogenic shock, pulmonary oedema and cardiac arrest. Agitation, acute psychosis, convulsions and coma may follow. Hypokalaemia usually occurs as a consequence of CHQ-induced potassium channel blockade (3). Ciszowski et al. describes a 16-year old girl who ingested 5-g of CHQ in a suicide attempt (4). The patient experienced general seizures after 2 hr followed by ventricular fibrillation and cardiac arrest. Following resuscitation 14-h later she had another cardiac arrest as a consequence of bradysystole. Although an external pacemaker and electrostimulation were applied, spontaneous circulation did not return and the patient died. Post-mortem toxicological examination of blood, vitreous humour, bile and the liver revealed extremely high concentrations of CHQ (252.15 mg/L in plasma). Another patient, a 15-year old girl, ingested 7.5 g of CHQ and developed significant hypotension requiring intravenous infusion of fluids and catecholamines, and respiratory distress

positively treated with endotracheal intubation and mechanical ventilation. In both cases of CHQ poisoning, hypokalaemia and prolonged QT<sub>c</sub> intervals were observed (4). High performance liquid chromatography has been used to determine the concentration of CHQ in bodily fluids and tissues following death from CHQ overdose, determined at 16.71 mg/L in blood (5). Indeed moderately low doses of CHQ can result in rapid death possibly through a drug-induced alteration of mood or a toxic confusional state resulting in unintended overdose and death (6, 7).

A study on knowledge and misconceptions among secondary school students and teachers revealed that 28.3% believed CHQ could cause abortion (8). In a study in Uganda, 93.3% of women knew about CHQ and 83% believed it was used for treatment of malaria, not its prophylaxis. Some women believed CHQ could cause abortions (9, 10). There have been questions raised on the safety of antimalarial drugs in pregnancy, teratogenicity being observed when these drugs are administered at high dosages (11). CHQ and its metabolites cross the placenta and can be detected in cord blood, neonatal systemic blood and neonatal urine (12). The authors showed that rates of spontaneous abortion and birth defects are comparable in pregnant women taking mefloquine, compared with CHQ-proguanil, or pyrimethamine-sulfadoxine prophylaxis in the first trimester of pregnancy. In a study approximately 60% of women from CHQ and

mefloquine (MQ) groups had side effects after a treatment dose (13). Major side effects included itching, dizziness and gastrointestinal disturbances. Spontaneous abortion rate was 1.2% and stillbirth 3.9%. These findings suggested antimalarial treatment and/or prophylaxis for all pregnant women are fairly safe, but if drugs are in short supply, they should be prescribed in their first or second pregnancy (13). In the case of CHQ-resistant malaria, however, treatment with mefloquine should be employed particularly in cases of dire necessity in pregnant women during the first trimester (14). Primaquine should be avoided for the treatment of relapsing malaria until after delivery. Weekly CHQ can be taken in the interim to prevent relapse (15). In a study in Guatemala, CHQ injections were preferred to tablets and believed to be approximately three times as potent as tablets of the same concentration (16). About two-thirds of interviewees believed that pregnant and lactating women with malaria should avoid the use of CHQ because it could cause spontaneous abortion or dry up breast milk. Bouree and Palies (17) and Levy et al. (18) argue that although the use of CHQ and hydroxychloroquine (HCHQ) in the treatment of malaria prophylaxis during pregnancy is probably safe, the use of much higher doses for treatment of systemic lupus erythematosus (SLE) and rheumatoid arthritis during pregnancy is risky. In their study of 24 pregnant women with a total of 27 pregnancies who had taken these

antimalarials during their first trimester of pregnancy, 14 deliveries resulted in normal babies, six were aborted, three were stillborn, and four spontaneously aborted (18). The seven pregnancies associated with foetal loss occurred particularly in patients with active SLE. Stillbirth and spontaneous abortion occurred in patients with rheumatoid arthritis and in two of three patients treated prophylactically for malaria, suggesting a cumulative risk associated with antimalarials (18). The risk of malaria flare and the loss of pregnancy from discontinuing therapy outweigh any risks to foetuses from continuing the medication (19, 20). Ochsendorf and Runne (21) advocate in pregnancy that there is the risk of foetal damage (hearing loss, abortion) following CHQ consumption given that the lethal dose is 4 g for adults. Deliberate attempts to induce abortions often occur amongst the younger women in Africa who may take large overdoses of CHQ (22). Primary Antiphospholipid Syndrome (PAPS) may be a forerunner of lupus, and it may also coexist with SLE as an independent autoimmune disorder. Pregnancy loss may therefore be related to PAPS rather than CHQ per se (23).

Therefore, CHQ should be prescribed with caution in patients with mental health disorders and in pregnant women.

#### Conflicts of interest

None are reported.

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