Indian J Physiol Pharmacol 2008; 52 (1): 97–98

LETTER TO THE EDITOR

CHLOROQUINE SHOULD BE USED WITH CARE IN MENTAL HEALTH DISORDERS

Sir,

(Received on October 27, 2007)

Current literature on the involvement of chloroquine (CHQ) in causing schizophrenia is limited and mostly points to possible toxic effects following concurrent administration of CHQ with chloropromazine (1). Open treatment with hydroxy CHQ results in no improvements in positive and negative symptoms in schizophrenic patients (2).

Mania may result in patients predisposed to mood disorder following CHQ treatment. CHQ is probably capable of inducing bipolar disorder (3), although the evidence is less scientifically secure (4). However, it should rather be used cautiously in patients predisposed to mental illness.

CHQ and hydroxy CHQ may result in severe psychosis-like side effects, the clinical presentation being fairly homogenous including delirium, hallucinations, manic episodes or depression ranging from a few hours to 40 days (5). In comparative studies on the risk imposed by antimalarials on depression, CHQ proved less effective at inducing psychosis and panic attacks than mefloquine (6). This was confirmed in Boudreau at al. where depressive feelings were noted in two or three times more individuals in mefloquine groups than in CHQ groups early in the course of the study (7). Elderly arthritic patients may have raised levels of CHQ due to reduced renal clearance (8) contributing to depression.

Psychosis induced by CHQ may be significantly attenuated if there is a deliberate avoidance of drug-drug interactions. This may include avoidance of neuropsychiatric side effects inducible in chloroquine prophylaxis during co-administration of antidepressants and neuroleptics. Additionally, avoidance of intake of different types of antimalarial drugs especially those chemically related to CHQ and mefloquine is important. CHQ and mefloquine may also be used for non-malarial applications such as HIV and cancer (9). Genetic screening for psychosis may also be a useful part of preventative medicine. Appropriate counselling strategies (10) should be in place if side effects are likely to exacerbate mental health disorder in pre-disposed patients.

CHQ may precipitate the mental health condition by binding to specific cellular receptors. Hydroxy CHQ may be responsible for tonicoclonic seizures in predisposed subjects (11). Lower doses of CHQ (1.0–5.0 mg kg^{-1}) increase the onset time to the clonic component of convulsions and reduced the incidence of the tonic phase of convulsions and mortality (12). At a higher dose range of 10.0–50.0 mg kg^{-1}, CHQ had opposite effects. Enhancement and inhibition of

GABAergic neurotransmission respectively attenuate and potentiate CHQ seizures (13). There are, however, some conflicting notions that CHQ, by inhibiting the functions and proliferation of glial cells in the hippocampus and cerebral cortex, can alleviate seizure activities and be an ideal anticonvulsant in preventing and treating epilepsy (14).

CHQ should therefore be used cautiously in patients with a family history of mental health disorder and/or recently diagnosed cases.

R. G. COOPER

Division of Physiology,
Faculty of Health,
Birmingham City University, Baker Building, Room 701,
Franchise Street, Perry Barr, Birmingham B42 2SU, UK.
Tel.: +44 121 1331 6227;
Fax: +44 121 311 5498;
E-mail address: rgcooperuk@yahoo.com

REFERENCES

1. Makanjuola RO, Dixon PA, Oforah E. Effects of antimalarial agents on plasma levels of chlorpromazine and its metabolites in schizophrenic patients. *Trop Geogr Med* 1998; 40: 31–33.
2. Desta M, Tadesse A, Gebre N, Barci BM, Torrey EF, Knable MB. Controlled trial of hydroxychloroquine in schizophrenia. *J Clin Psychopharmacol* 2002; 22: 507–510.
3. Akhtar S, Mukherjee S. Chloroquine induced mania. *Int J Psychiat Med* 1993; 23(4): 349–356.
4. Peet M, Peters S. Drug-induced mania. *Drug Saf* 1995; 12: 146–153.
5. Ferraro V, Mantoux F, Denis K, Lay-Macagno MA, Ortonne JP, Lacour JP. [Hallucinations during treatment with hydroxychloroquine] [Abstract in English]. *Ann Dermatol Venereol* 2004; 131: 471–473.
6. Meier CR, Wilcock K, Jick SS. The risk of severe depression, psychosis or panic attacks with prophylactic antimalarials. *Drug Saf* 2004; 27: 203–213.
7. Boudreau E, Schuster B, Sanchez J, et al. Tolerability of prophylactic Larium regimens. *Trop Med Parasitol* 1993;; 44: 257–265.
8. Brooks PM, Kean WF, Kassam Y, Buchanan WW. Problems of antiarthritic therapy in the elderly. *J Am Geriatr Soc* 1984; 32: 229–234.
9. Alisky JM, Chertkova EL, Iczkowski KA. Drug interactions and pharmacogenetic reactions are the basis for chloroquine and mefloquine-induced psychosis. *Med Hypotheses* 2006; 67: 1090–1094.
10. Albright TA, Binns HJ, Katz BZ. Side effects of and compliance with malaria prophylaxis in children. *J Travel Med* 2002; 9: 289–292.
11. Malcangi G, Fracticelli P, Palmieri C, Cappelli M, Danieli MG. Hydroxychloroquine-induced seizure in a patient with systemic lupus erythematosus. *Rheumatol Int* 2000; 20: 31–33.
12. N'Gouemo P, Ben Attia M, Belaidi M. Effects of chloroquine on pentylenetetrazol-induced convulsions in mice. *Pharmacol Res* 1994; 30: 99–103.
13. Amabeoku G. Involvement of GABAergic mechanism in chloroquine-induced seizures in mice. *Gen Pharmacol* 1992; 23: 225–229.
14. Zhang S, Zhu C, Liu Q, Wang W. Effects of chloroquine on GFAP, PCNA and cyclin D1 in hippocampus and cerebral cortex of rats with seizures induced by pentylenetetrazole. *J Huazhong Univ Sci Technolog Med Sci* 2005; 25: 625–628.