CHLOROQUINE-RELATED DEPRESSION

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SUMMARY

Drugs are known to induce depressive states. Chloroquine, an antimalarial, in therapeutic doses administered for malaria therapy, may produce symptoms rather indistinguishable from endogenous depression. The possible mechanisms of production of depression related to chloroquine use are hypothesised.

One of the most common diseases of our time is depression with a prevalence of nearly 3 per cent. It may be speculated that drugs having effect on the neurotransmitters may have increased the prevalence of depression. Drugs commonly implicated in inducing depression are long-acting antipsychotics, barbiturates, ethanol, oral contraceptives and antihypertensive agents (Whitlock & Evans, 1978). The present communication describes two cases of depression related to the administration of chloroquine as an antimalarial agent.

Case reports:

1. A 40 years old female reported to the psychiatric clinic with complaints of sleeplessness, loss of interest in doing any work and feeling sad, all these started on the fourth day after ingestion of a total dose of 1.5 gm of chloroquine for malaria. She was premorbidly sound with no previous history of mental illness or any family loading of mental illness. Mental status examination revealed features of moderate to severe depression with suicidal ideas and weeping spells. Insight was impaired. No evidence of any organic deficit was detected. She was started on antidepressant (amitryptiline) 100 mg per day, but she improved after 4 days.

2. 32 years old female after administration of 1.8 gm of chloroquine for malaria five days prior to attendance in psychiatric clinic was found to have a depressive mood, psychomotor retardation, suicidal and paranoid ideas. Though she was put on tricyclic antidepressant, dramatic improvement was noted on the fifth day. She also did not have any previous or family history of mental illness.

DISCUSSION

Chloroquine administration for various clinical conditions has resulted in the development of psychosis (Burrel and Martinez, 1958; Mustakalio et al., 1962; Dornhorst and Robinson, 1963; Rab, 1963; Sapp, 1964; Brookes, 1966; Kabir, 1969 and Bomb et al., 1964). Most of the reports describing toxic confusional states. But, chloroquine is known to produce either a 'psychic type' or a 'psycho-organic' type of syndrome. Neff described a 15 years old boy developing depression with suicidal thoughts, insomnia and acute panic reaction with ego disorganisation, after 10 days of chloroquine therapy for facial granuloma annulare. On cessation of the drug the symptoms disappeared, while a new trial with 250 mg to 375 mg of the drug, produced the same symptoms (Neff, 1964). Drew (1962) had drawn attention to the development of depression in 43 per cent of his 21 patients treated with chloroquine sulphate for rheumatoid diseases. Depression ranged from mild to severe degree and several patients required antidepressant drugs and one patient had to be given EGT. Other symptoms noted were claus-
trophobia, inferiority feelings, loss of sleep, and suspiciousness. All these symptoms disappeared on withdrawal of the drug. Even the case described by Brookes had evidence of depression (Brookes, 1969). Another interesting case report of a stuporous state after the intake of ten tablets of chloroquine for malaria suggested a diagnosis of depressive stupor with dramatic improvement on the tenth day (Advani et al., 1978).

The mechanism of causation of depression after chloroquine use is still not clear. Advani et al. (1978) postulate a depressant action on adrenal cortex producing a depressive state akin to that in Addison's disease (Advani et al., 1978). A possible acetyl cholinesterase inhibitory mechanism of the drug in the production of psychosis is also suggested (Mustakallio, 1962). The authors have hypothesised a hyperdopaminergic mechanism in the production of mania-like picture after chloroquine use. (Advani et al., 1978). Neuropharmacologically, it is known to have at least two types of depression—noradrenergic depression and serotonin depression (Adolphe et al., 1977). According to catecholamine hypothesis, there has to be a deficiency in noradrenaline and dopamine in depression (Bunney and Gulley, 1978). Enkephalins also appear to alter central mono-amine function (Pollard et al., 1977; Eidelberg, 1976). Thus one wonders whether there is any hypodopaminergic-endorphin excess state? or Is there any cholinergic-noradrenergic imbalance? or multiple interactions of the biological amine systems, neuro-endocrine system, endorphin system are operating? 

REFERENCES

Adolphe, A. B., Dorsey, E. R., Nfpolieille, M. J. (1977). The Neuropharmacology of depression. Dis. Nerv. Syst., 38, 10, 841.

Advani, G. B., Gajwani, A. K., Bakhshwal, S., et al. (1978). Chloroquine-induced depression. The Clinician, 42, 1, 28.

Bom, B. S., Bedi, H. K., Bhatnagar, L. K. (1975). Chloroquine Psychosis. Trans. R. Soc. Trop. Med. Hyg., 69, 523.

Brookes, D. B. (1966). Chloroquine psychosis. Brit. Med. J., 1, 963.

Bunney, W. E., Jr., Gulley, B. L. (1976). The current status of research in the catecholamine theories of affective disorders. In: Usdin E, Mandell AJ (Eds). Biochemistry of mental disorders. mod. Pharmacology. toxicology, Vol. 13, Marcel Dekker Inc : New York, pp. 83.

Burrell, Z. L., Jr., Martinez, A. G. (1958). Chloroquine and hydroxychloroquine in the treatment of cardiac arrhythmias. New Eng. J. Med., 298, 798.

Dornhorst, A. C., Robinson, B. J. (1963). Chloroquine Psychosis? Lancet, 1, 106.

Drew, J. F. (1962). Concerning the side effect of antimalarial drugs used in the extended treatment of rheumatic diseases. Med. J. Australia, 2, 618.

Eidelberg, E. (1976). Possible actions of opiates upon synapses. Proo. Neurobiol., 6, 81.

Kabir, S. M. A. (1969). Chloroquine psychosis. Trans. R. Soc. Trop. Med. Hyg., 63, 549.

Mustakallio, K. K., Putkonen, T., Pihkanen, T. A. (1962). Chloroquine Psychosis?. Lancet, 2, 1977.

Nepp, L. (1964). Drug reactions in adolescence. G. P. (Kansas), 29, 112.

Pollard, H., Llorens-Cortes, L., Schwartz, Z. L. (1977). Enkephalin receptors on dopaminergic neurons in rat striatum. Nature (Lond.), 268, 743.

Rab, S. M. (1963). Two cases of chloroquine psychosis. Brit. Med. J., 1, 1275.

Saff, O. L. (1964). Toxic psychosis due to quinacrine and chloroquine. JAMA, 187, 379.

Whitlock, F. A., Evans, L. E. J. (1978). Drugs and Depression. Drugs, 15, 53.