

Psychiatric Complications of Chloroquine

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The expanding awareness of medication induced behavioral changes among non-psychiatric patients and an increasing number of drug-related hospital admissions has increased the role of psychiatrist in a general hospital(1). Certain drugs, such as isoniazid, steroids, reserpine, clonidine, levodopa and primaquin cause psychiatric symptoms but the behavioral toxicity and mortality due to chloroquine have received little attention in the medical and psychiatric literature(2). For several years, it was thought that chloroquine was devoid of psychiatric side effects but now a large number of reports mention side effects including psychosis(3-5), neurosis(5), seizures(6), suicide and deaths due to overdose(2). The aim of the present study was to know the clinical pattern of chloroquine induced psychiatric complications.

Material and Methods

Thirty cases of chloroquine induced psychiatric complications, seen during

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January, 1987 to December 1992 at the Smt. Sucheta Kriplani and Guru Teg Bahadur Hospitals, Delhi are described. All the cases were first seen by the pediatrician, who took a detailed history, and examined them thoroughly. Investigations including hemogram, peripheral smear, X-ray chest, EEG, ECG and fundus examination were performed prior to their referral to the Psychiatric Outpatients Department.

The detailed present, past and family history of mental illness was taken. The cases with history of previous physical illness or intake of medication with known psychiatric complications, past history of mental illness, mental retardation or epilepsy were excluded. The cases were diagnosed according to criteria reported in literature(2,4): (i) the similarity of the patients' symptoms to the reported cases; (ii) absence of previous psychiatric history; (iii) neurological and other investigations within normal limits; and (iv) rapid recovery on stoppage of chloroquine. The clinical features were categorized according to International Classification of Diseases—9th edition(7).

A control group consisting of 30 patients (age and sex matched taken from pediatric ward) who were administered similar doses of chloroquine but did not show psychiatric complications, were selected as controls.

Results

Of 30 cases, 14 (46.7%) were between 10-12 years and 12 (40%) between 7-9 years. The patients who took chloroquine with milk were significantly more ($p < 0.001$) in the study group (53.3%) as compared to controls (13.3%).

The dose, salt of drug (phosphate or sulphate) and mode of intake of drug (whether empty stomach or after meals) was, however, not significantly different in study and control groups. Amongst the side effects of chloroquine, headache and sleeplessness were reported significantly more by the patients belonging to the study group. The relationship of psychiatric complications with onset and duration is shown in *Table I*.

Discussion

The age-wise prevalence of psychiatric complications of chloroquine is not known. In the present study, the cases showed a decline in prevalence with age.

Among the side effects, headache and sleeplessness were significantly more frequent in the study group. The other side effects as reported by Rollo(8), such as nausea, vomiting, diarrhea, anorexia, urticaria, blurring of vision, *etc.* were statistically insignificant.

Since, Burrel *et al.*(9) reported the first case of chloroquine induced psychosis, many more cases have been add-

ed(4,5,10,11). The psychosis has been reported to appear after intake of 2.4 to 6 g of chloroquine between 4 and 40 days but the cases in our series, developed psychosis after receiving a total dose of 1.0 to 2.4 g between 2 to 7 days (period of onset was minimum for organic psychosis followed by schizophrenia, depression and mania). The exact mechanism of chloroquine induced psychosis is not known but the role of different neurotransmitter systems, *i.e.*, polyamines (especially spermidine) excess(12), dopamine excess(4), acetylcholine imbalance(13) and prostaglandin-E antagonism(14) have been postulated. The duration of behavioral changes ranged from two days to eight weeks(3,4) but in our series, all cases improved within three weeks after cessation of chloroquine. Many cases of attempted suicide and suicide have been reported both in children and adults(2) and the fatal dosage reported in the literature is as little as 1 g of chloroquine phosphate in children and 6 g in adults(2). However, in our series, suicidal and homicidal ideations were communicated by 2 cases but there was no attempt.

TABLE I—*Neuro-psychiatric Complications Due to Chloroquine*

Complications	No. (n=30)	Onset (days)	Duration (days)
Organic psychosis	16 (53.2)	2-4	2-14
Schizophrenia like	6 (20.0)	3-6	12-21
MDP-Mania like	2 (6.7)	5 & 7	4-15
MDP-Depression like	2 (6.7)	4 & 7	7-20
Anxiety state	2 (6.7)	2 & 3	2- 3
Seizures (grand mal)	2 (6.7)	3 & 4	Within 1

* Figures in brackets indicate percentage.

Although the symptoms resembling acute anxiety attack have been reported following chloroquine therapy(2,4), there were only two cases in the present series who presented with these symptoms within 48 to 72 hours after taking 2 g of chloroquine sulphate.

Cases of seizures have been reported after therapeutic and toxic doses of chloroquine(2). We observed two cases of seizures (grandmal type) following intake of therapeutic doses of chloroquine. An important observation is that these cases had heralding signs of toxicity (like vomiting, diarrhea, abdominal cramps, *etc.*) prior to the seizure.

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