PSYCHIATRIC COMPLICATIONS OF CHLOROQUINE

M.S. BHATIA, S.C. MALIK

Sixty patients with chloroquine induced psychiatric complications are reported in the present series. Psychosis was the most common complication followed by anxiety state and seizures. The maximum number of patients were between the ages of 6 and 10 years and females (70.0%) outnumbered the males (30.0%). Headache and sleeplessness were found to be more common among patients developing psychiatric complications of chloroquine. The symptoms disappeared within 2 to 21 days after the discontinuation of chloroquine.

Key words: chloroquine, psychoses, neuroses, seizures.

INTRODUCTION

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 a psychiatrist in a general hospital (Shader, 1972). It is now widely known that certain drugs, such as isoniazid, steroids, reserpine, clonidine, levodopa, etc. cause psychiatric symptoms, but the behavioral toxicity and lethality of chloroquine have received little attention in the medical and psychiatric literature (Good & Shader, 1977). A large number of reports are now available which mention chloroquine induced psychiatric side effects (Reagan, 1985; Bhatia et al, 1988; Bhatia, 1991), suicide (Good & Shader, 1977) and lethality due to overdose (Wilkey, 1973; Good & Shader, 1977). The present study was designed to explore the pattern of psychiatric complications induced by chloroquine.

MATERIAL AND METHODS

The present study analyses sixty patients with chloroquine induced psychiatric complications, seen in a general hospital psychiatry OPD (of Smt. Sucheta Kriplani and Guru Teg Bahadur Hospitals, Delhi) over a period from January 1987 to December 1992. All were first seen by the pediatrician or medical specialist, who evaluated and investigated the cases thoroughly before referring the patients to a psychiatrist. Patients with a past history of mental illness, mental retardation or epilepsy were excluded from the study. The cases were classified according to ICD-9 (WHO, 1978). A control group consisting of thirty age and sex matched patients who took chloroquine within the therapeutic range for antimalarial purposes, but without psychiatric complications, were chosen from medical and pediatric wards to compare the side effect profile of chloroquine. These patients were also subjected to similar inclusion criteria.

RESULTS

Of a total of sixty patients with chloroquine induced psychiatric complications, the maximum belonged to the 6-10 age group (23.3%) followed by the 11-15 age group (20.0%). There were a minimum of patients below the age of 5 or above the age of 35. Females (70.0%) outnumbered males (30.0%) significantly (p<0.001). Patients who took chloroquine with milk were significantly (p<0.001) more in the study group as compared to the control group; there was no difference in the dose, salt of the drug (phosphate or sulphate) and mode of intake of drug (whether empty stomach or after meals) between the study and control groups.

When the side effects of chloroquine as reported by patients in the study and control groups were compared, headache and sleeplessness were reported significantly more by patients belonging to the study group. The distribution of patients according to psychiatric complications, age, sex, dosage and duration of onset is shown in Table 1.

| Table 1 |
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| Psychiatric complications |
| Complication | Age (yr) | Male | Female | Dosage (g) | Onset (days) |
| 1. Organic psychosis (n=32) | 6 to 36 | 12 | 20 | 1.0 to 2.4 (Mean 1.8) | 2 to 4 |
| 2. Schizophrenia like (n=12) | 13 to 35 | 4 | 8 | 1.25 to 2.0 (Mean 1.6) | 3 to 6 |
| 3. Mania like (n=4) | 10 to 16 | - | 4 | 1.5 & 2.2 | 5 to 7 |
| 4. Depression like (n=4) | 16 to 30 | - | 4 | 1.5 & 2.4 | 4 to 7 |
| 5. Anxiety state (n=4) | 28 to 32 | - | 4 | 2.0 | 2 to 3 |
| 6. Seizures (n=4) | 12 to 28 | 2 | 2 | 1.0 & 2.0 | 3 to 4 |
DISCUSSION

Though the exact psychosocial details and prevalence of psychiatric complications of chloroquine are not yet known, 43.3% patients in the present series were found to be children. In the present study, more patients were found to be females. This is similar to other reports (Bhatia et al, 1988) but the exact cause of this is not known.

When the mode of the intake of chloroquine was compared, the patients who took chloroquine with milk were found to be more in the study group as compared to the control group. This could be due to the fact that milk might cause rapid absorption of chloroquine resulting in toxicity in some predisposed individuals. This hypothesis needs more elaboration by doing the serum levels of the drug in further studies. Among the side effects reported by the patients, headache and sleeplessness were found to be significantly more in the study group. The other side effects as reported by Rollo (1980) like nausea, vomiting, diarrhoea, anorexia, urticaria etc. were not found to be significantly different between the study and the control groups.

Psychosis was found in 86.7% of patients. Though Burrell et al (1958) reported the first case of chloroquine induced psychosis, many more cases have been added since then (Good & Shader, 1977; Reagan, 1985; Bhatia et al, 1988; Garg et al, 1990; Bhatia, 1991). The psychosis that appeared in these cases after an intake ranging from 2.4 to 6.0 gm of chloroquine had occurred over a period between 4 and 40 days; however, the cases in our series developed psychosis after receiving a total dose of 1.0 to 2.4 gm, and within 2 to 7 days. The period of onset was minimum for organic psychosis followed by schizophrenia-like, depression-like and mania-like psychosis.

The common behavioral changes noted in patients were agitation, confusion, disorientation, irrelevant and incoherent talk, hallucinations (visual and auditory), delusions (control, reference, grandiose and somatic) and suicidal and homicidal ideas. Other studies also report similar findings (Nasr, 1981; Reagan, 1985); the reported duration of behavioral changes ranged from two days to eight weeks (Reagan, 1985), but in our series all fifty two cases improved within three weeks after cessation of chloroquine.

Many cases of attempted suicide have been reported both in children and adults (Good & Shader, 1977), but in our series, suicidal and homicidal ideation were communicated by six cases (three cases each); there was, however, no suicidal or homicidal attempt.

Although symptoms resembling acute anxiety attacks such as dryness of mouth, sweating, palpitations, tremors, sinking sensation, sleeplessness, difficulty in concentration etc., have also been reported following chloroquine therapy (Good & Shader, 1977), we have seen only four patients (28 to 32 years old) who presented with these symptoms within 48 to 72 hours after taking 2 gm of chloroquine sulphate.

Cases of chloroquine induced seizures have been reported after taking therapeutic and toxic doses (Kiel, 1964) of chloroquine; we observed four patients with seizures (grandmal type) following intake of therapeutic doses of chloroquine. An important observation is that these patients had heralding signs of toxicity (like vomiting, diarrhoea, abdominal cramps etc.) prior to the seizure. The exact mechanism of seizures remains unknown but the evidence seems to point towards an idiosyncratic reaction in sensitive individuals.

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