THE EFFECT OF THIOPROPERAZINE ADMINISTERED BY A CONTINUOUS METHOD ON LONG-TERM SCHIZOPHRENIC PATIENTS

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Introduction

Thioproperazine is a phenothiazine compound with a piperazine nucleus in the side chain. The pharmacological investigations of Courvoisier *et al.* (1958) indicate that it is much less sedative than other phenothiazines and that it has weak anti-adrenaline, anti-histamine and anti-serotonin activity. Clinical reports by Delay *et al.* (1958), Perrin *et al.* (1958), Denber *et al.* (1959), Levy and Maarek (1960) and Perret *et al.* (1961) indicate improvement in schizophrenic patients, but their papers described trials of this drug in which both recent and long-term cases or other diagnostic groups were included. Denham and Carrick (1961) reported the total remission of symptoms in 32 of 58 chronic schizophrenics treated by the discontinuous method with significant improvement in a further 25. Their acceptance of the view that improvement was correlated with the occurrence of hypertonic syndromes and that failure of treatment was likely if anti-parkinsonism drugs were used to suppress the hypertonicity, excludes the possibility of the type of continuous treatment employed with other phenothiazines. Denber *et al.*, however, advocated the suppression of these drug effects and Perret *et al.* reported 47% improvement using the continuous method in another mixed group of chronic patients.

In this report we describe the effect of a continuous method in the treatment of 46 chronic schizophrenic patients. Other methods of treatment, i.e., phenothiazines, reserpine, deep insulin, etc., had been tried with these patients with poor long-term results and all had a maintenance dose of a phenothiazine or reserpine when selected. Our aim was to discover the extent to which the patients would improve further with thioproperazine.

Selection of Patients and Method

The patients selected were 20 men and 17 women who had been in hospital suffering from schizophrenia for at least ten years and 5 men and 4 women whose hospitalization for the same illness was less than five years. The short-term hospitalization group were essentially long-term patients, some of whom had managed to live out of hospital intermittently. The age range of the men was 20–55 years and of the women 26–66 years.

The patients were examined physically and white cell counts and serum glutamic-pyruvic transaminase estimations were checked before and after the trial. Medication was stopped for between four and seven days before commencing thioproperazine. On selection each patient was reviewed by psychiatric

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interview and rated on a five-point scale designed to indicate the severity of his schizophrenic condition. This procedure was repeated after two weeks on the drug and subsequently after four weeks. Only patients who were moderately or severely ill were included. The nurse in charge of the ward recorded observations daily on physical changes and a nurse's rating of seven aspects of behaviour and mental state was submitted weekly.

The patients were given "Majeptil" (thioproperazine methanesulphonate) 5 mgms. t.i.d. for two days. The dose was then raised to 10 mgm. t.i.d. and, after further similar intervals, to 20 mgms. t.i.d. It was planned to raise the dose finally to 30 mgms. t.i.d. at which level it was to be maintained for four weeks. Benztropine ("Cogentin") 2 mgms. was given twice daily throughout with additional doses in the presence of side effects. Paraldehyde 3 c.c. was given intramuscularly for severe hypertonicity, oculogyric crises or excitomotor attacks. The patients were intentionally kept to the same routine with regard to occupation and social rehabilitation as before the trial.

Results

On the rating scales 36 patients were regarded as suffering from very severe or severe schizophrenic symptoms; the remaining 10 showed signs of moderate severity at the beginning of the trial. Predominantly paranoid types numbered 14 and non-paranoid 32. Four had been leucotomized.

In 15 cases no undesirable drug effects occurred. In spite of benztropine, however, drug effects were observed as follows: Oculogyric crisis 4, dysphagia 2, catatonia 1, hypertonicity and parkinsonism 15, blurred vision 4, akathisia 8, apathy and depression 2, visual hallucinations 1, nausea 2, sudorrhoea 8. Two patients were withdrawn from the trial owing to excitement and one because of dysphagia. No special association was recognized between duration of treatment and the drug effects described above. Though improvement in the complexion and a "bright eye" occurred in some cases, others presented an appearance of severe illness.

The following effects of the drug on the clinical categories of patients were observed: Paranoid schizophrenics—9 of 14 improved; non-paranoid—13 of 32 improved; of those hospitalized for more than ten years—19 of 37 improved; those hospitalized for less than five years—3 of 6 improved. The degree of improvement amounted to one point on the five-point scale in all cases, but did not produce any major change towards rehabilitation. Of the four patients who had undergone leucotomy, one improved.

Discussion

Though the amount of benztropine prescribed (2mgms. b.d.) was insufficient to suppress all neurological side effects, 43 of the 46 patients were able to take thioproperazine continuously. The incidence of side effects was so great even with the anti-parkinsonian agent that it is unlikely that a blind trial could have been accomplished successfully. Though the majority of the side effects were noticed during the first week, these potentially dangerous complications of treatment occurred intermittently throughout the trial.

The results of this method of administration of thioproperazine in our trial were disappointing compared with those of Denham and Carrick and were more akin to those reported by Cramond (1962) and Ollendorff (1962) who obtained poor results applying the discontinuous method in a series of

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long-term schizophrenics. Unlike Denham and Carrick we did not find any correlation between hypertonicity, recrudescence of symptoms or early improvement and final result. In our experience previous leucotomy did not prevent response. The response did not justify the detailed nursing supervision required. The treatment is not suitable for patients who are likely to be out of observation for long periods. It may interfere with work and recreational activities.

The problem of activating apathetic patients or suppressing hallucinations in chronic paranoid schizophrenics does not appear to be solved by the prescription of thioproperazine. It has perhaps been naively assumed that chemical stimulation of the basal ganglionic region, if intense enough, would alleviate these conditions. We anticipate, however, that other syndromes within the schizophrenic group will be recognized in the same way that alcoholic and amphetamine hallucinosis have been described. The recognition that some schizophrenic illnesses are resistant to all phenothiazines sustains the idea that these conditions are heterogeneous in origin. It may be prudent financially to recognise that this group exists.

Summary

Forty-six long-term schizophrenics who had previously been on other phenothiazine drugs or reserpine were observed during the administration of thioproperazine for four weeks in dosage rising to 90 mgm. per day together with benztropine 2 mgm. b.d. Improvement was noted in 22 cases, but this was only marginal. In spite of anti-parkinsonian drugs, neurological complications of treatment occurred throughout the duration of the trial.

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