PSYCHIATRIC USES OF MERATRAN

By

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MERATRAN (alpha-2-piperidyl benzhydrol hydrochloride) is a cerebral stimulant with an action not unlike the amphetamine series but differing in other respects in that it does not interfere with sleep, nor appetite, nor is its use followed by depression. It is not apparently a sympathomimetic drug, since it does not cause any marked cardiovascular pressor effects. Recent reports from America (1) have suggested that the drug is of use in treating patients suffering from depression and psychomotor retardation either due to mental illness, fatigue or a side-effect of other drugs, e.g. chlorpromazine or reserpine.

The author has carried out a controlled clinical trial with Meratran on forty chronic psychotic male patients in this hospital. The "double-blind" technique was used throughout, i.e. the patients were divided into two arbitrary groups one of which received the drug and the other a placebo for a period of four weeks and at the end of this time medication of the two groups was reversed for a further four weeks. Neither patients, nurses, nor investigators were aware of the group receiving the actual drug until the completion of the trial.

The constituents of the patient sample were selected because they showed depressive features, regression or retardation. They were practically all long-stay cases, the average length of hospitalization being 7½ years. Most of the patients had been variously treated with insulin, E.C.T., chlorpromazine, and/or reserpine with little or no improvement. They were nursed in their usual wards, not grouped or segregated in any way and care was taken to interfere with the usual ward routine as little as possible.

Prior to the commencement of the trial all other treatment including sedatives was suspended. It was felt afterwards that those patients who had previously been on reserpine (11 in number) should have been rested for a longer period than a fortnight, as the absence of reserpine made itself felt amongst the placebo group for at least the first two weeks of the Meratran trial. It was also found necessary to re-introduce sedatives for those patients who became more agitated on the treatment.

The dosage of Meratran decided upon was 6 milligrams per diem, orally, in three divided doses after meals. The last dose was given at 6 p.m. and it was significant that no patient complained of difficulty in sleeping. Unfortunately the nature of the trial did not permit individual adjustment of dosage, as it is thought that the optimum dosage varies with the individual and can only be found by trial and error. From the results obtained in this investigation it would be probably advisable to start with 3 mg. daily and increase if necessary.

The nursing staff were instructed to observe the patient's mood, activity, conversation, interest and appetite, in addition to any change in psychotic symptoms. Short daily notes were kept by the nurse in charge of each ward and weekly summaries of these were made in addition to the observations by the medical officer. In particular notice was taken of the improvement or deterioration of the patients' adaptability to their surroundings, as evidenced by their ability to take part in ward-work, recreation, occupational therapy,

etc. Morning and evening pulse records were taken, and blood pressure levels, daily at first, were subsequently carried out less frequently. Weekly weight charts were kept and urinalyses performed. Complete blood investigations following four weeks treatment showed no abnormalities. No side-effects attributable to the drug were observed. Fabing (2) quotes narcoleptic cases having taken 100 mg. daily for more than a year without toxic effect. Dilatation of the pupils, sweating and flushing were not observed. No rise in blood pressure or pulse-rate was noted apart from the cases who had previously been on reserpine, and since the slight rise in both which occurred with these patients was present equally in the placebo group, it was probably due to the discontinuing of the former drug. Forster *et al.* (3) in a controlled trial with Meratran noted a mean rise in the pulse rate of the treated group of 9·1 beats per minute as compared with only 0·95 per minute in the placebo group.

The effects of Meratran appear very quickly. Subjectively patients reacting favourably describe an elevation of mood within an hour or so of the first dose. To the observer beneficial effects appear after a lapse of 48 hours, during which time in practically all patients a decrease in appetite occurs. Thereafter appetite improves, the patient is more alert in manner, the facial expression is animated, there is an increased awareness of the surroundings; the patient tends to initiate conversation with others, his capacity for ward-work and recreation is increased and signs of depression disappear. Undesirable effects appear equally rapidly, and if the treatment is continued, increase daily to a maximum in about a week. The most important of these is agitation. A depressed or schizophrenic patient with a tendency to agitation experiences a marked increase in this abnormal activity, sometimes presenting a picture of extreme tension, wringing his hands, and rubbing or tearing his hair. Lesser degrees of this agitation may be controlled satisfactorily with barbiturates, but in two cases it was necessary to discontinue treatment, when symptoms soon abated. Another contra-indication is the overtly deluded patient who experiences activation of delusional ideas, sometimes to an alarming degree. In one case treatment had to be suspended on account of this increased activation. It was not possible within the limits of this investigation to examine the effect of chlorpromazine or reserpine in combating these happenings, and it is intended to study the effect of such combined therapy in a later series. When a patient exhibits anxiety, agitation or delusions Meratran is contra-indicated and should be given with caution. Less noteworthy was increased abnormal activity such as pacing. Those patients showing unfavourable reactions also had decreased appetites and lost weight whilst on the drug.

Results

The following Table shows the constituent diagnoses of the patient sample and the improvement rate.

Table

Type	No.	Improved	No Change	Worse
Schizophrenia	27	5	12	10
Senile Psychosis	5	3	1	1
Involutional Depression ..	3	2	1	—
Neurotic Depression	1	1	—	—
Manic Depression	2	2	—	—
Epileptic Psychosis	1	—	1	—
Arrested G.P.I.	1	1	—	—
Total	40	14	15	11

https://doi.org/10.1192/bjp.102.429.801 Published online by Cambridge University Press

The results in the schizophrenic group were disappointing. The patients were drawn from the chronic schizophrenics of the hospital population who had shown little or no improvement on previous treatment. The greater part showed marked personality deterioration, some were mute and withdrawn, and others hallucinated and deluded. In the case of the five who showed improvement this was limited to an appearance of alertness, a marked quickening of response to questions, an increased speed of purposeful action and a straightening of the bearing. Of those who became worse five were so classified because they were more agitated, deluded and hallucinated, and five who were withdrawn became more so, and required prompting to eat. All ten lost weight, the average loss being 8 lb. Schut and Himwich (1) reported seven out of ten "hebephrenic" schizophrenics improved on 5 mg. daily, but that paranoid and "hebephrenic" types with delusions did not improve. Fabing (2) reported that the response in patients with "ambulatory schizophrenia has been discouraging".

The thirteen remaining patients all showed depressive features. Of these, nine were improved, three unchanged and one worse. The patient who became worse was a senile with delusions, which were accentuated, and treatment had to be withdrawn. The nine improved patients all showed alleviation of depression, increased interest and activity and increased appetite after the first two days. Weight gain varied from 2–11 lb. Several of these patients were able to be usefully employed for the first time since admission. The two manic depressive cases who were in the depressed phase at commencement of treatment showed marked improvement while withdrawal of the drug caused a return of symptoms. This occurred with all the improved patients except that employment begun whilst on Meratran had been continued albeit with diminished enthusiasm. One patient suffering from involutional depression who was well improved while on Meratran was allowed home on leave at the termination of the experiment. His relatives report that his improvement is maintained and have since requested two extensions of leave. He had previously on several occasions failed to last a full week at home. Forster *et al.* (3) found a significant increase of activity without euphoria in 11 of 23 elderly psychiatric patients. Pomeranze (1954) reported favourable results with elderly depressed patients in geriatric practice.

The control system revealed one "placebo reactor". He was a schizophrenic who suffered from auditory hallucinations of a persecutory nature which he described as reduced in intensity whilst on chlorpromazine prior to this experiment. On control tablets he volunteered that the voices had ceased entirely. No further change took place on Meratran.

Summary

The author describes a controlled clinical trial with a new anti-depressant on forty chronic psychotic patients. Beneficial effects were observed in those cases which exhibited depressive features without anxiety or a tendency to agitation. Patients suffering from delusional systems or hallucinations are not likely to improve. Whilst electro-convulsive therapy is the treatment of choice in acute endogenous depressive states Meratran may be found (*a*) to give relief of symptoms in chronically depressed patients where the depression is reactive in type, or secondary to senile change; or (*b*) to combat the lethargy induced by chlorpromazine or the depression following prolonged reserpine therapy. The results of this preliminary investigation would seem to justify further work along these lines.

Acknowledgments

I would like to thank Dr. A. C. Sinclair, Medical Superintendent of Herrison Hospital for permission to publish this report; Riker Laboratories Ltd., for a supply of Meratran; the Nursing Staff of the hospital; and Mr. H. Moore who carried out the laboratory investigation.

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