A CLINICAL TRIAL OF MELLERIL (TP-21) IN THE TREATMENT OF MENTAL DISORDERS

F. J. G. HAUPT, B.A., M.B., CH.B. (CAPE TOWN), *Assistant Physician Superintendent, Town Hill Hospital, Pietermaritzburg*

A new phenothiazine compound, 3-methylmercapto-10-{2′ [N-methyl-piperidyl-(2″)]-ethyl-(1′)}-phenothiazine, was administered to 14 chronic, deteriorated male European schizophrenic patients and 1 paraphrenic patient. The ages of the patients varied from 30 to 40 years, and the duration of their illness from 5 to 22 years. Of these patients 14 had previously received electric convulsive therapy (ECT) and some had received insulin coma therapy or had been treated with reserpine or chlorpromazine. Three patients had undergone prefrontal bilateral leucotomies approximately 10 years previously.

Details concerning age, duration of illness, diagnosis, dosage of Melleril, symptoms before treatment with Melleril, effects of treatment, side-effects, other forms of treatment given previously, comparison with other forms of treatment, and duration of treatment are listed in Table I.

CLINICAL RESULTS

The assessment of the results of the trial was made on clinical impressions of a qualitative nature and no additional control cases were included. However, in view of the long duration of their illnesses and the different kinds of treatment given to them, these cases could, to some extent, serve as their own controls.

Of the 15 cases treated with Melleril, 6 (40%) showed a moderate to marked improvement. Of the 14 who had received ECT previously, 5 responded better to treatment with Melleril than to ECT. Of the 4 cases who had received insulin coma therapy, 2 responded better to treatment with Melleril than to insulin therapy. In 5 cases chlorpromazine, reserpine and Melleril were used. In 3 of these Melleril was equally effective to the other 2 drugs, and in 2 Melleril led to a marked improvement. Of the 3 leucotomized patients to whom Melleril was administered, 1 showed a marked improvement.

In no case did Melleril lead to an exacerbation of the patient's mental condition. No patient reached the level of complete remission; but the chronicity of the illness and the prolonged period of institutionalization of the patients in the trial should be kept in mind in this connection.

DISCUSSION

Melleril has both tranquillizing and antipsychotic properties. Its activating properties appear to be low compared with trifluoperazine, and of the same order as chlorpromazine. The sedative action of the drug is less marked than that of chlorpromazine. There is no specific relationship between dosage, length of treatment, clinical effects, and degree of relapse after cessation of treatment.

The therapeutic effect of the drug appears to be symptomatic only; 2 cases relapsed completely on cessation of administration of the drug.

The 2 hebephrenic patients both failed to respond to treatment; both were, however, chronic cases (duration of illness 14 and 15 years respectively) and both patients had had leucotomy operations.

No extrapyramidal symptoms occurred during the trial and the clinical improvement was not dependent on the occurrence of such symptoms.

Owing to the relative absence of side-effects, the patients remained amenable to group psychotherapy and group discussion. On the whole the trial had a beneficial effect on the patients.

Side-effects. One chronic catatonic patient, aged 48 years, suffered from an increased incidence of asthmatic attacks after 37 days of administration of the drug (25 mg. *t.d.s.*). It is possible, however, that this may have been a coincidental finding. The mental status of this patient remained unchanged by Melleril.

TABLE I. SUMMARY OF CLINICAL FINDINGS

Case	Age (years)	Duration of illness (years)	Diagnosis	Dosage	Symptoms before treatment with TP-21	Results of treatment with TP-21	Side-effects	Other kinds of treatment previously given	Comparison with other kinds of treatment	Duration of treatment
1	39	15	Schizophrenia, hebephrenic	50 mg. *t.i.d.*	Withdrawn, religiose, vague persecutory delusions	No change	Nil	Electric convulsive therapy (no lasting effects), prefrontal leucotomy (no lasting effect)	As ineffective as previous treatment	21 days
2	45	22	Catatonic	400 mg. *t.i.d.*	Withdrawn, severe autism, emotional blunting, stereotypy of gait, mannerisms	No change	Nil	Electric convulsive therapy (no lasting effect)	As ineffective as ECT	33 days
3	48	15	Catatonic	25 mg. *t.i.d.*	Severe withdrawal and autism, out of contact with reality, ideational poverty	Mental status unchanged (asthmatic attacks)	Increased incidence of asthmatic attacks	Electric convulsive therapy (no lasting effects)	Mental status unchanged (asthmatic attacks)	37 days
4	43	20	Catatonic	250 mg. *t.i.d.*	Asocial, withdrawn, incoherent, incontinent	Fairly sociable, continent, answers readily, fair initiative	Nil	Electric convulsive therapy (no lasting effects)	More effective than ECT	6 months
5	30	10	Catatonic	150 mg. *t.i.d.*	Asocial, constantly escaping, irrelevant, slovenly, indolent	Cooperative, neat, replies readily, no longer escapes, became a leader and organizes soccer games	Somnolence, countered by methylphenidyl acetate	Electric convulsive therapy (no effect)	Far more effective than ECT	7 months
6	32	7	Catatonic	100 mg. *t.i.d.*	Mutistic, incontinent, immobile with cyanosis, sores on legs	Replies rationally and to the point, no cyanosis of legs, no sores, plays cricket, works in garden, continent	Nil	Electric convulsive therapy (no effect)	Far more effective than ECT	3 months
7	30	10	Catatonic	50 mg. *t.i.d.*	Aggressive, mutistic, slovenly, destructive	Fair replies, neater, no longer destructive, on ground parole	Somnolence, countered by methyl phenidyl acetate	Electric convulsive therapy and insulin coma therapy, chlorpromazine, reserpine	Superior to electrical and insulin therapies; chlorpromazine and reserpine had no beneficial effect	3 months*
8	38	15	Paranoid	500 mg. *t.i.d.*	Deluded, disorientated for self and surroundings, irrelevant, grandiose	Poor response but patient gives less expression to delusional system	Nil	Electric convulsive therapy and insulin coma therapy	Equal to electric convulsive therapy, better than insulin coma therapy	5 months†
9	42	17	Schizophrenia, catatonic	400 mg. *t.i.d.*	Mutistic, aggressive, destructive, out of contact with reality, filthy, hyperactive, incontinent	Not destructive, tidy, not hyperactive, continent, rational, but gives a limited account of himself A degree of insight present	Nil	Bilateral standard leucotomy, electric convulsive therapy, insulin coma therapy, reserpine chlorpromazine (poor effect)	Superior to other kinds of therapy	6 months
10	40	12	Catatonic	300 mg. *t.i.d.*	Aggressive, withdrawn, gave very poor account of self	Answers more freely but remains dull and retarded, not aggressive	Nil	Bilateral standard leucotomy, electric convulsive therapy (no effect)	Superior (?) to other kinds of therapy	5 months
11	40	14	Hebephrenic	350 mg. *t.i.d.*	Manneristic, silly, fatuous, retarded and irrelevant, hoards rubbish	Slightly less manneristic, but still hoards rubbish, retarded, irrelevant, fatuous	Nil	Bilateral standard leucotomy, electric convulsive therapy, chlorpromazine, reserpine	Equally ineffective	7 months
12	34	9	Catatonic	300 mg. *t.i.d.*	Stutters, manneristic, nonsensical, incontinent	Less frequently incontinent, otherwise unchanged	Nil	Electric convulsive therapy, insulin coma therapy, chlorpromazine, reserpine	Equally ineffective	3½ months
13	54	12	Paranoid	25 mg. *t.i.d.*	Delusions of persecution in respect of wife and former employer	Delusions controlled but patient developed no real insight	Nil	Chlorpromazine, reserpine, electric convulsive therapy	Equally effective	3 months

TABLE I. SUMMARY OF CLINICAL FINDINGS

Case	Age (years)	Duration of illness (years)	Diagnosis	Dosage	Symptoms Before treatment with TP-21	Results of treatment with TP-21	Side-effects	Other kinds of treatment previously given	Comparison with other kinds of treatment	Duration of treatment
14	45	17	Catatonic	200 mg. *t.i.d.*	Short tempered, severely withdrawn, manneristic, gives poor account. Delusions of persecution	More cooperative, no longer aggressive, no more delusions	Nil	Prefrontal leucotomy	More effective than prefrontal leucotomy	3 months
15	51	5	Paraphrenic	300 mg. *t.i.d.*	Hyperactive, deluded, hallucinations, disorientated, disturbed sequence of thoughts	More composed, interested in gardening, volunteers for work, not impulsive yet still asocial, not hallucinated, not deluded	Nil	Electric convulsive therapy (no lasting effect)	Superior to ECT	5 months

* Patient relapsed completely when tablets were unavailable.
† Delusions became more florid when tablets were unavailable.

No psychological or neurological side-effects were noted and there were no side-effects relating to the cardiovascular or gastro-intestinal systems or to the skin and mucous membranes. There was no alteration in the weight of the patients.

Somnolence was fairly marked in 2 cases, but this was readily countered by moderate doses (20-40 mg. per day) of methylphenidylacetate. No blood dyscrasias were observed.

Dosage. The dosage of Melleril varied from 25 mg. 3 times daily to 500 mg. 3 times daily.

Conclusion. It appears that Melleril is non-toxic, fairly free from side-effects, and has a wide dosage range. It does not interfere with normal ambulatory and psychomotor activity and does not impede psychotherapy.

SUMMARY

1. This study concerns the treatment of 15 chronic schizophrenic male European patients with Melleril.

2. In no instance was the therapeutic effect of Melleril inferior to that of other kinds of therapy given previously. The effect of Melleril was equal to or slightly superior to that achieved with other methods of treatment in 8 cases (53%), and moderately or markedly superior in 7 cases (47%).

Throughout the trial the patients remained amenable to individual and group psychotherapy.

3. The nature of the improvement in these chronic cases seems to be symptomatic rather than curative, and no patient reached the level of complete remission.

4. The only side-effect noted was somnolence; however it was less marked than with chlorpromazine. This side-effect was easily controlled by the administration of methylphenidylacetate. Attacks of asthma occurred more frequently during the trial in 1 asthmatic patient—it is possible that this exacerbation of the asthma may have been caused by Melleril. The activating properties of Melleril were found to be low, approximately equal to those of chlorpromazine.

5. Improvement of the patients' mental status was in no way associated with the occurrence of involvement of the extrapyramidal tract.

I am indebted to Messrs. Sandoz Pharmaceutical Products for supplies of Melleril which were used in this work.

This paper is published with the kind permission of Dr. B. P. Pienaar, Commissioner for Mental Hygiene.

BIBLIOGRAPHY

Armbruster, W. and Pulver, W. (1959): Therap. Umsch., **16**, 161.
Bourquin, J.-P., Schwarb, G., Gamboni, G., Fischer, R., Ruesch, L., Guldimann, S., Theus, V., Schenker, E. and Renz, J. (1958): Helv. chim. Acta, **41**, 1072.
Brunold, H. (1959): Therap. Umsch., **16**, 90.
Cohen, S. (1958): Amer. J. Psychiat., **115**, 358.
Delay, J., Pichot, P., Lempérière, T. and Elissalde, B. (1959): Ann. méd.-psychol., **117**, 724.
Fleeson, W., Glueck, B.jr., Heistad, G., King, J. E., Lykken, D., Meehl, P. and Mena, A. (1958): Univ. Minn. Med. Bull., **29**, 274.
Haley, T. J., Komesu, N. and Williams, P. (1959): Fed. Proc., **18**, 399.
Haug, J. O. (1959): T. norske Lægeforen., **79**, 317.
Judah, L., Murphree, O. and Seager, L. (1959): Amer. J. Psychiat., **115**, 1118.
Keup, W., ed. Kline, N. S. (1959): *Psychopharmacology Frontiers*, p. 365. Boston and Toronto: Little, Brown & Co.
Mayer, K. (1959): Medizinische, No. 15, 733.
Péguiron, M. E. (1958): Praxis, **47**, 1193.
Remy, M. (1958): Schweiz. med. Wschr., **88**, 1221.
Idem (1959): Méd. et Hyg. (Genève), **17**, 81.
Sauter, R. (1959): Praxis, **48**, 140.
Taeschler, M. and Cerletti, A. (1958): Schweiz. med. Wschr., **88**, 1216.