A COMPARATIVE CONTROLLED TRIAL OF METHOTRIMEPRAZINE ("VERACTIL") IN CHRONIC SCHIZOPHRENIA

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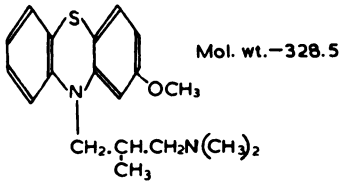
INTRODUCTION

DESPITE the good results reported in recent years in many cases of chronic schizophrenia following the use of tranquillizing drugs, there remains in mental hospitals a group of chronic and often deteriorated patients who have shown a strong resistance to all forms of treatment. In many such cases disturbances of behaviour are modified and sometimes controlled by such drugs as chlorpromazine and reserpine. Nevertheless, the overall situation is far from satisfactory and the search for more effective drugs continues.

Methotrimeprazine has the characteristic central action of chlorpromazine, some anti-adrenaline activity and anti-histaminic properties comparable to those of promethazine.



Mol. wt.—328.5

It is prepared for clinical use by May & Baker Ltd. under the name "Veractil" in the form of its acid maleate which contains 73 per cent. of the active base.

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Previous Clinical Studies

Deschamps and Madre (1957, 1958) suggested that methotrimeprazine was of value in cases of melancholia and schizophrenia. Lambert *et al.* (1957) carried out a trial of the drug on 94 in-patients with various psychiatric disorders and found that its effects were similar to those of chlorpromazine, though it had a more marked sedative action. Sigwald *et al.* (1956) reached similar conclusions, adding that the effective dose of methotrimeprazine was rather lower than that of chlorpromazine. Baker and Thorpe (1958) selected 28 female schizophrenics showing deterioration who had relapsed after being given chlorpromazine. They too obtained results comparable to those of chlorpromazine. Substantially similar results have been obtained by Teulié *et al.* (1958), Baruk *et al.* (1958), Deshaies *et al.* (1958), Larue and Gosselin (1958), Collier and Martin (1958) and Gurtler *et al.* (1958). With the exception of the trial conducted by Baker and Thorpe, none of these studies was controlled.

Method

The present study was designed to compare the therapeutic effects of methotrimeprazine with those of a placebo and with chlorpromazine in chronic schizophrenia.

A total of 146 patients suffering from schizophrenia, 72 male and 74 female, were included in the trial. Selection was made on the basis of chronicity and lack of satisfactory response to previous treatment where this had been instituted. All the patients had been in hospital for at least one year and frequently for much longer than this. Of the patients interviewed, a number were excluded from the trial on the grounds of diagnostic uncertainty, severe deafness precluding adequate contact, or serious concomitant physical disease. The average age of the male patients—35 years with a range of 24 to 67 years—was less than that of the females—49 years with a range of 26 to 78 years.

Matching. Male and female patients were separately divided into three fairly comparable therapeutic groups A, B and C, based on age, length of stay in hospital and degree of deterioration. The latter was assessed using somewhat different criteria in the male and female groups. Amongst the male patients it was estimated largely on working capacity. Patients were placed into three categories: work grade 1—those who worked well without prompting; work grade 2—those whose work was satisfactory but required prompting; work grade 3—those who worked poorly or not at all. The female patients were also graded into three categories. In grade 1 there was fairly good personality preservation and retention of contact with the environment; in grade 2, personality changes were obvious with flattening of affect, withdrawal and loss of interest; and in grade 3, there was severe personality dilapidation with gross affective changes.

Table I overleaf shows the distribution of patients amongst the three therapeutic groups, together with their mean ages, mean durations in hospital and work or deterioration grades.

Previous Treatment

Some of the older patients who had been in hospital for many years had never had any special treatment. There were 22 such patients, 4 male and 18 female. The remainder had had standard forms of treatment in the past (see Table II). Although previous treatment was not considered as a criterion in matching the three groups, it so happened that from this point of view the distribution of the patients was fairly even.

TABLE I

Distribution of Patients in the 3 Therapeutic Groups According to Age, Length of Stay in Hospital and Work or Deterioration Grades

Male Patients

Group	No. of Patients	Mean Age (in years)	Mean Length of Stay in Hospital (in years)	Work Grade 1	2	3
Placebo (A)	25	36	6	11	8	6
Chlorpromazine (B) ..	23	37	6	8	10	5
Methotrimeprazine (C) ..	24	33	7	8	11	5
Totals	72	35	6	27	29	16

Female Patients

Group	No. of Patients	Mean Age (in years)	Mean Length of Stay in Hospital (in years)	Deterioration Grade 1	2	3
Placebo (A)	25	48	11	7	7	11
Chlorpromazine (B) ..	25	50	15	7	7	11
Methotrimeprazine (C) ..	24	49	15	5	7	12
Totals	74	49	14	19	21	34

TABLE II

Previous Treatment Received

Treatment Group	E.C.T.	Tranquillizers	Deep Insulin	Leucotomy	None
		Male			
Placebo	18	20	9	2	4
Chlorpromazine	21	22	8	2	0
Methotrimeprazine ..	15	23	8	1	0
Total	54	65	25	5	4
		Female			
Placebo	14	17	7	3	6
Chlorpromazine	14	15	5	2	6
Methotrimeprazine ..	15	15	5	4	6
Total	43	47	17	9	18

(NOTE: Many patients have received more than one form of treatment.)

Effects of Withdrawal of Treatment Prior to the Trial

Eighty-seven patients (43 male and 44 female) were actually under treatment when selected for the trial, the great majority being on chlorpromazine or reserpine. In all these, therapy was suspended for a period of six weeks before the actual trial commenced. During this period, 8 (4 male and 4 female) improved, 41 (26 male and 15 female) became worse and 38 (13 male and 25 female) showed no change. One female paranoid schizophrenic, aged 59, who was originally selected for the trial became extremely disturbed and restless

when her daily 3 mg. of reserpine was stopped. She responded poorly to resumption of treatment and died a fortnight later. No post-mortem was done but for several months previously she had exhibited a persistent sinus bradycardia.

Administration and Dosage

Tablets identical in appearance were made up in stock tins for each patient. The active tablets each contained 50 mg. of chlorpromazine or methotrimeprazine. Only the pharmacist was aware of the identity of the tablets until the trial was over and he allocated the treatment to the three groups. Group A received placebo, group B chlorpromazine and group C methotrimeprazine. In all cases, treatment was commenced with one tablet twice daily. Patients were seen weekly and the dosage increased to 75, 100, 150, 200, 250 and 300 mg. in divided doses daily over a period of 7 weeks. The maximum daily dose (300 mg.) was continued for a further 2 weeks until the trial ended after 9 weeks.

During the period of the trial, patients remained in their original wards so that as far as possible environmental changes were minimized.

Assessment of Mental State

(a) *Clinical Evaluation.* All patients were interviewed on selection, and thereafter at weekly intervals. No attempt was made to standardize the interview. Notes were made on the mental state and any changes were recorded. At the end of the investigation, the clinical state of each patient was assessed on the following scale:

"Worse"—objective deterioration in the patient's condition.

"No change"—absence of any apparent alteration in the psychosis.

"Slightly improved"—lessening in intensity of symptoms, with some improvement in overall behaviour but without any change in the basic psychotic pattern.

"Moderately improved"—substantial improvement in behaviour and rapport with marked lessening or disappearance of overt psychotic signs.

(b) *Nursing Staff Evaluation.* Nursing assessments were recorded on a behavioural rating chart adapted freely from the behavioural rating scale described by Baker and Thorpe (1956). Nine items were used as follows—general activity, dressing, talk, excretory habits, sociability, work, aggression, overt hallucinations and expressed delusions. Each item was graded on a 4 or 5 point scale and each point was given an arbitrary value of 1. The sisters, charge nurses and their deputies were instructed in the use of the scale and a separate item sheet was completed for each patient weekly. At the conclusion of the trial a score of $+1$ or -1 was given for each point representing improvement or deterioration. The sum of the scores for each item represented the direction of behavioural change during the course of the trial. It must be emphasized that figures have been used only for convenience. The steps indicated by the figures are unequal and no figure therefore can validly be compared with any other figure. The final results were recorded as "worse", "no change" or "improved".

RESULTS

The results are shown in Table III and a statistical analysis of these in Table IV. Examination of the combined figures reveals that the proportion of patients showing no change clinically is approximately the same in the three drug groups and is high, being 50 per cent. or over in all groups. This is in

TABLE III

Results—All Patients

Assessment	Drug	No Change	Slightly Improved	Moderately Improved	Worse	Total
Clinical	Placebo	28 (56)	6 (12)	2 (4)	14 (28)	50
	Chlorpromazine ..	28 (58)	8 (16)	7 (15)	5 (11)	48
	Methotrimeprazine ..	24 (50)	11 (23)	9 (19)	4 (8)	48
Nursing Staff	Placebo	7 (14)	24 (48)		19 (38)	50
	Chlorpromazine ..	9 (19)	26 (54)		13 (27)	48
	Methotrimeprazine ..	3 (6)	34 (71)		11 (23)	48

Results—Male Patients

Assessment	Drug	No Change	Slightly Improved	Moderately Improved	Worse	Total
Clinical	Placebo	11 (44)	6 (24)	1 (4)	7 (28)	25
	Chlorpromazine ..	11 (48)	3 (13)	5 (22)	4 (17)	23
	Methotrimeprazine ..	8 (33)	8 (33)	7 (30)	1 (4)	24
Nursing Staff	Placebo	3 (12)	14 (56)		8 (32)	25
	Chlorpromazine ..	5 (22)	12 (52)		6 (26)	23
	Methotrimeprazine ..	3 (13)	20 (83)		1 (4)	24

Results—Female Patients

Assessment	Drug	No Change	Slightly Improved	Moderately Improved	Worse	Total
Clinical	Placebo	17 (68)	0	1 (4)	7 (28)	25
	Chlorpromazine ..	17 (68)	5 (20)	2 (8)	1 (4)	25
	Methotrimeprazine ..	16 (67)	3 (13)	2 (8)	3 (12)	24
Nursing Staff	Placebo	4 (16)	10 (40)		11 (44)	25
	Chlorpromazine ..	4 (16)	14 (56)		7 (28)	25
	Methotrimeprazine ..	0	14 (58)		10 (42)	24

(Percentages in brackets)

TABLE IV

Statistical Analysis of Results

	Assessment	Comparison*	χ^2	P (Df.=2)	Significance
All Patients	Clinical	P × C	6·355	P<·05	Significant
		P × M	10·970	P<·01	Highly significant
		C × M	1·333	·5<P<·7	Not significant
	Nursing Staff	P × C	1·415	·3<P<·5	Not significant
		P × M	5·419	·05<P<·1	Not significant
		C × M	4·233	·1<P<·2	Not significant
Male Patients	Clinical	P × C	0·803	·5<P<·7	Not significant
		P × M	7·866	P<·02	Significant
		C × M	4·385	·1<P<·2	Not significant
	Nursing Staff	P × C	0·858	·5<P<·7	Not significant
		P × M	6·486	P<·05	Significant
		C × M	6·053	P<·05	Significant
Female Patients	Clinical	P × C	9·000	P<·02	Significant
		P × M	4·278	·1<P<·2	Not significant
		C × M	1·344	·5<P<·7	Not significant
	Nursing Staff	P × C	1·556	·3<P<·3	Not significant
		P × M	4·696	·05<P<·1	Not significant
		C × M	4·511	·1<P<·2	Not significant

* P=placebo: C=Chlorpromazine: M=Methotrimeprazine.

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contrast to the nursing figures where the percentages showing no change are considerably lower (6–19 per cent.) with all three drugs.

The percentage of patients showing clinical improvement (combining the figures for "slight" and "moderate" improvement) is 16 per cent. with the placebo, 31 per cent. with chlorpromazine and 42 per cent. with methotrimeprazine, indicating a substantial difference between the placebo and the two "active" drugs. The advantage of chlorpromazine over the placebo is statistically significant ($p<0\cdot05$) and that of methotrimeprazine over placebo is highly significant ($p<0\cdot01$). Nursing staff assessment showed improvement with placebo in 48 per cent., with chlorpromazine in 54 per cent. and with methotrimeprazine in 71 per cent., thus showing the same trend, but statistically these results are not significant.

Of the male patients, 28 per cent. on the placebo, 35 per cent. on chlorpromazine and 63 per cent. of those on methotrimeprazine showed clinical improvement. Corresponding nursing assessment percentages indicate equal improvement scores with the placebo and chlorpromazine but a much greater response to methotrimeprazine, the figures being 56 per cent., 52 per cent. and 83 per cent. respectively. Both the clinical and nursing percentages for deterioration show that a considerably smaller proportion of patients deteriorated while on methotrimeprazine.

Among the female patients, clinical assessment showed an improvement rate in the placebo group of 4 per cent., with chlorpromazine of 28 per cent. and with methotrimeprazine of 21 per cent. The nursing assessment showed corresponding percentages of 40 per cent., 56 per cent. and 58 per cent.

Although the figures show trends suggesting that methotrimeprazine is somewhat superior to chlorpromazine, the differences are not significant statistically.

Side-Effects. No special arrangements were made to detect covert changes due to methotrimeprazine. Blood pressure recordings were not taken regularly and no blood counts were carried out. No reduction in dosage was made for elderly patients and all patients remained ambulant during the course of the trial. Side-effects were noted as they appeared and none was seen in the placebo group. Lethargy and drowsiness appeared in 6 male and 8 female patients on methotrimeprazine and in 3 male and 7 female patients on chlorpromazine. Dizziness was reported by one female patient on methotrimeprazine. Parkinsonian features occurred in 2 male and 3 female patients on methotrimeprazine. Only one male patient showed evidence of parkinsonism on chlorpromazine. The extra-pyramidal dysfunction was mild in each case and resolved on reduction of the dosage in the final week of the trial. There was one exception, a severely deteriorated catatonic female aged 43 years who developed severe parkinsonian rigidity with difficulty in swallowing during the last fortnight of the trial. The dosage of the methotrimeprazine was reduced without improvement and after a few days it was discontinued. Before any appreciable change could occur, she died suddenly. Post-mortem examination showed a bilateral bronchopneumonia with fibrofatty degeneration of the myocardium and fatty changes in the liver.

One paranoid middle-aged female patient on methotrimeprazine, in addition to drowsiness developed severe urinary incontinence which had not previously been a feature of her illness. No example of jaundice was seen during the trial. Baker and Thorpe (1958) noted leucopenia in one of their patients and a generalized erythematous rash occurred in another. One case of fatal agranulocytosis has been reported.

Relationship of the Number of Patients Clinically Improved, to Age, Length of Stay in Hospital and Working Capacity (Male) or Grade of Deterioration (Female). (See Table V)

TABLE V

Relationship of Number of Patients Clinically Improved to Age, Length of Stay in Hospital, Work Grade (Male) and Grade of Deterioration (Female)

(*a*) Relationship of Number of Patients Improved Clinically to Age

Age	Placebo		Chlorpromazine		Methotrimeprazine	
	Number of Patients in Group	Number Improved	Number of Patients in Group	Number Improved	Number of Patients in Group	Number Improved
20–29 ..	9	0	5	2	5	3
30–39 ..	18	7	19	6	19	9
40–49 ..	8	1	12	3	11	6
50–59 ..	7	0	5	0	6	2
60–69 ..	6	0	5	4	5	0
70–79 ..	2	0	2	0	2	0
Total ..	50	8	48	15	48	20

(*b*) Relationship of Number of Patients Improved Clinically to Hospitalization

Years in Hospital	Placebo		Chlorpromazine		Methotrimeprazine	
	Number of Patients in Group	Number Improved	Number of Patients in Group	Number Improved	Number of Patients in Group	Number Improved
0– 9 ..	40	7	28	10	31	15
10–19 ..	4	1	11	4	10	4
20–29 ..	3	0	8	0	4	1
30–39 ..	3	0	1	1	3	0
Total ..	50	8	48	15	48	20

(*c*) Relationship of Number of Male Patients Improved Clinically to Work Grade

Work Grade	Placebo		Chlorpromazine		Methotrimeprazine	
	Number of Patients in Group	Number Improved	Number of Patients in Group	Number Improved	Number of Patients in Group	Number Improved
1	11	4	8	2	8	7
2	8	3	10	4	11	5
3	6	0	5	2	5	3
Total ..	25	7	23	8	24	15

(*d*) Relationship of Number of Female Patients Improved Clinically to Grade of Deterioration

Deterioration Grade	Placebo		Chlorpromazine		Methotrimeprazine	
	Number of Patients in Group	Number Improved	Number of Patients in Group	Number Improved	Number of Patients in Group	Number Improved
1	7	1	7	3	5	2
2	7	0	7	3	7	1
3	11	0	11	1	12	2
Total ..	25	1	25	7	24	5

(a) *Age.* It might be expected that the age of the patients would show a relationship to improvement and this is confirmed. There were 106 patients between the ages of 20 and 49 years and of these 37 (35 per cent.) showed improvement clinically compared with 6 patients out of 40 (15 per cent.) between the ages of 50 and 79 years. The effect of age was apparent in all three treatment groups.

(b) *Hospitalization.* Of 124 patients who had spent from 1 to 19 years in hospital, 41 (33 per cent.) showed improvement clinically. Of 22 patients who had been between 20 and 39 years in hospital, only 2 (9 per cent.) improved clinically.

(c) *Work Grade* (male patients). The figures for male patients show a direct relationship between clinical improvement and working capacity. Of 27 patients in grade 1, 13 (48 per cent.) improved. This compares with 12 out of 29 improved in grade 2 (41 per cent.) and 5 out of 16 improved in grade 3 (31 per cent.).

(d) *Grade of Deterioration* (female patients). The number of patients improved clinically bears an inverse relationship to the degree of deterioration. Of 19 patients in grade 1, 6 (32 per cent.) improved. In grade 2 there were 21 patients and 4 (19 per cent.) improved. In grade 3, out of 34 patients only 3 (9 per cent.) showed any improvement.

Relationship of Clinical Improvement to Alterations in Weight During the Trial

Of those patients who improved, 70 per cent. gained and 20 per cent. lost weight, the remaining 10 per cent. showing no weight change. Of the patients who showed no clinical change in their mental state, 54 per cent. gained weight, 31 per cent. lost weight and 15 per cent. remained the same. Thirty-nine per cent. of those who deteriorated gained weight compared with 48 per cent. who lost weight and 13 per cent. whose weight remained unaltered. Thirty-four patients showed an increase in weight with methotrimeprazine, 24 with chlorpromazine and 16 with the placebo.

Effects of the Drugs on Behaviour as Recorded on the Item Sheet by the Nursing Staff (see Table VI)

TABLE VI

Effect of the Drugs on Behaviour as Recorded by the Nursing Staff

Behaviour Item	Treatment Group	No Change	Improved	Worse	Total
Activity ..	Placebo	35	7	8	50
	Chlorpromazine ..	33	8	7	48
	Methotrimeprazine	31	11	6	48
Dressing ..	Placebo	37	6	7	50
	Chlorpromazine ..	39	3	6	48
	Methotrimeprazine	34	7	7	48
Talk	Placebo	34	8	8	50
	Chlorpromazine ..	36	11	1	48
	Methotrimeprazine	26	16	6	48
Habits ..	Placebo	42	6	2	50
	Chlorpromazine ..	40	5	3	48
	Methotrimeprazine	38	6	4	48

TABLE VI—*continued*

Behaviour Item	Treatment Group	No Change	Improved	Worse	Total
Sociability ..	Placebo	36	5	8	50
	Chlorpromazine ..	35	8	5	48
	Methotrimeprazine	37	9	2	48
Work ..	Placebo	31	10	9	50
	Chlorpromazine ..	35	7	6	48
	Methotrimeprazine	27	12	8	48
Aggression ..	Placebo	37	8	5	50
	Chlorpromazine ..	23	23	2	48
	Methotrimeprazine	22	24	2	48
Hallucinations	Placebo	33	8	9	50
	Chlorpromazine ..	25	12	11	48
	Methotrimeprazine	30	13	5	48
Delusions ..	Placebo	31	12	7	50
	Chlorpromazine ..	30	13	5	48
	Methotrimeprazine	26	14	8	48

"Activity" shows a slight advantage of methotrimeprazine over the placebo and chlorpromazine.

"Talk"—the numbers improved are substantially greater with methotrimeprazine and this is true also for improvement in "sociability". Both chlorpromazine and methotrimeprazine influenced "aggression" favourably in a much greater number of patients than the placebo. The effect on "hallucinations" also suggests some superiority for both the active drugs over the placebo. In the case of "dressing", "excretory habits", "work" and "delusions", there was no advantage shown for the chlorpromazine and methotrimeprazine over the placebo.

DISCUSSION

Early assessment of the effects of new drugs in psychiatric practice is of fundamental importance and this can only be done with any degree of accuracy by controlled therapeutic trials. Foulds (1958) in his survey of the Anglo-American literature noted that success in treatment was claimed in only 19 per cent. of controlled studies as compared with 85 per cent. of uncontrolled trials. Marley (1959) referring to the work of Wolf (1950), Beecher (1955) and Tibbets and Hawkings (1956) comments that a 15–58 per cent. favourable response may follow administration of a placebo.

Many writers have indicated the problems and difficulties which such trials raise, not the least of which is their time-consuming nature, as Hargreaves *et al.* (1957) have pointed out. Moore and Martin (1957) observed that controlled blind investigations, satisfactory to statisticians, are difficult to arrange with drugs which have obvious side-effects; and in illnesses such as schizophrenia, the natural history of which is in any case fluctuating and subject to remission, the results may be influenced by the increased attention paid to the patients by the staff.

In this study, all the patients were chronically disabled, many to a very severe degree. It was originally intended that they should be classified into hebephrenic, catatonic and paranoid sub-groups. Many of the patients were so disorganized that it was impossible to type them with any degree of accuracy

and it was felt that any results based on such a classification would serve little or no useful purpose.

It is necessary to consider possible reasons for the disparity in the results of the clinical as compared with the nursing assessments. The numbers of patients recorded as showing "no change" in all three therapeutic groups are much smaller when assessed by the nursing staff than by the medical staff. On the other hand, in all other groups—"worse" as well as "improved"—the percentages are higher when assessed by the nurses. This may be an expression of the fact that nurses are in closer and more constant contact with the patients and in a position to observe and note minor changes of behaviour which would not be revealed in the interview situation. Alternatively they might indicate that the nurses are more impressionable than the medical staff and are less content to accept a negative result. This view is supported particularly by the high incidence of improvement recorded by nurses in the placebo group.

Doubt may be felt about the reliability of "global" clinical assessments of the mental state, whether carried out by nursing or medical staff. Marley (1959) in his recent paper contrasts the subjective and objective assessment of the effects of drugs and considers that the ideal would be to combine as many subjective and objective criteria as expedient. He adds that "quantification" of drug response by arbitrary rating rather than clinical assessment may be helpful, but quotes Lorr (1954), who comments that "attempts to refine clinical judgment with rating scales and check lists have not proved the superiority of such measures".

The results of this trial show that both chlorpromazine and methotrimeprazine are more effective in chronic schizophrenia than a placebo. The figures are rather more impressive in the case of male than female patients. This may well reflect differences in age, length of hospitalization and degree of deterioration. As a group, the male patients were younger, their stay in hospital shorter and their degree of deterioration less. It is clear that neither chlorpromazine nor methotrimeprazine is a panacea for the long-stay deteriorated schizophrenic and in no case could the improvement be described as more than moderate in degree. It is likely that many of the patients included in this trial have passed beyond the reach of pharmacological remedies and must be regarded as permanently crippled mentally.

In this trial only one level of dosage was employed and this was the same for chlorpromazine and methotrimeprazine. It is likely that in practice the optimum dose would vary from case to case and the therapeutic response might be altered. Although methotrimeprazine appears to be well tolerated when taken by mouth, and elderly patients did not seem to be particularly prone to side-effects, parkinsonism was more frequent than with chlorpromazine and its incidence may be related to the dosage employed. Sigwald *et al.* (1956) and Lambert *et al.* (1957) found that a smaller dose of methotrimeprazine is required than with chlorpromazine and the ratio they both suggest is 2 to 3 (i.e. 30 mg. methotrimeprazine is equivalent to 45 mg. chlorpromazine).

A point of some importance emerged shortly after the original selection of the patients. Following withdrawal of drugs and of maintenance E.C.T., 47 per cent. of the patients who had been receiving treatment showed deterioration in behaviour. This tended to produce anxiety in the nursing staff concerned and was particularly disturbing where many such patients were in the same ward. In these circumstances the support and encouragement of the medical staff is necessary and very helpful. Education of all grades of nursing staff in the methods and aims of therapeutic trials is an essential prerequisite to their success.

Summary

A double-blind controlled investigation of a new phenothiazine derivative —methotrimeprazine (Veractil)—in a group of 146 male and female chronic schizophrenic patients is described. The trial was designed to compare the effects of the drug with those of chlorpromazine and with a placebo. As a group, the female patients were older, had been longer in hospital and were more deteriorated. The male patients generally were more actively psychotic but less deteriorated and their average age and length of stay in hospital was less than the female.

Methotrimeprazine in the dosage employed was found to be a potent drug and to be at least as effective as chlorpromazine. Parkinsonism and drowsiness were more frequently encountered with methotrimeprazine and one female patient who subsequently died was severely affected. Disparity in the results of clinical and nursing assessments are described and discussed.

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