THE USE OF PACATAL IN LOW-GRADE MENTAL DEFECTIVES

By

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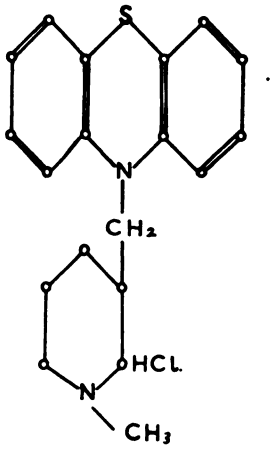
DURING recent years various tranquillizing drugs have been used therapeutically, namely, chlorpromazine hydrochloride (Largactil), reserpine (Serpasil), benactyzine hydrochloride (Suavitil) and hydroxyzine (Atarax) in mental disorders. Chlorpromazine and reserpine, though effective to a certain extent in mental disorders of the disturbed type, have the disadvantage of certain side-effects which have necessitated reduction and even cessation of the drugs, even when proving clinically efficacious.

Recently a drug has been produced, "Pacatal" (Mepazine), for which it is claimed that it has few troublesome side-effects while exerting an adequate effect on emotionally and mentally disturbed patients.

The purpose of this experiment was to test the value of "Pacatal" on a group of 30 mental defective patients showing gross disorders of conduct which were evident clinically in disturbed and difficult behaviour.

CHEMISTRY

Pacatal is a synthetic compound, N-methyl-piperidyl-(3)-methyl phenothiazine (generic name, Mepazine). It is available as the hydrochloride for oral use and the acetate for injection, both of which are photosensitive.



PHARMACOLOGY

Tolerance studies demonstrate the safety of Pacatal in human administration (Nieschulz *et al.*, 1954) and there were no adverse effects on the haemopoietic system, growth or weight, or histologically in tissues removed at autopsy from experimental animals, except when a dose equivalent to 20 times the suggested therapeutic dose for humans was administered to the animals (100 mg. per K daily for 6 months).

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The absorption and excretion of Pacatal has been studied by Hinriksen *et al.* (1956); the drug is rapidly absorbed when administered orally, and more so when injected intramuscularly or intravenously. The major part of the substance is destroyed in the body, and only a small amount is recovered in the urine. The maximum urinary concentration is within 24 hours, excretion is complete in 4 days, suggesting no serious cumulative tendencies.

The work of Neischulz *et al.* in 1954 on the pharmacology of Pacatal has been confirmed by others (Kopf, Warner-Chilcott Research Laboratories) and has shown that Pacatal inhibits and stabilizes the central and peripheral regulating mechanism of the autonomic nervous system and directly depresses the central nervous system. The more important effects are:

(*a*) Sedation and tranquillization, and potentiation of other sedative and hypnotic drugs.
(*b*) Potentiation of analgesics.
(*c*) Equal influence on the sympathetic and parasympathetic nervous systems. Its hypotensive effect is weak.
(*d*) Moderate antipyretic properties.
(*e*) Weak anticonvulsant effect.
(*f*) Specific effect on cardiac arrhythmias.

Side Effects

The side-effects of Pacatal which are described are dryness of the mouth and difficulty in visual accommodation especially with high dosages. No skin rashes, jaundice, Parkinsonism or orthostatic collapse have been recorded.

Method

A group of 30 mental defectives was chosen, all of whom showed the following symptoms, which made them a major nursing problem. These symptoms were used as criteria for assessment of any change in their condition while the drug trial was being conducted.

Hyperkineses	Incontinence
Destructiveness	Dirty feeding habits
Noisiness	Aggression and violence
Temper tantrums	

Fourteen of the 30 patients suffered from epilepsy of major and minor types. The I.Q. of 27 patients was below 30 (Terman Merrill), 3 being between 30 and 40. Their ages ranged from 8–41 years, the average age being 19·366 years.

For children of 12 or below the following dosage of Pacatal was given:

12·6 mg. t.i.d. for 3 days
25 mg. t.i.d. for 3 days, and then
50 mg. b.d. for 1 week, and thereafter
50 mg. t.i.d. for 15 days.

For patients over 12 years, the following dosage was given:

25 mg. t.i.d. for 3 days
50 mg. t.i.d. for 3 days
100 mg. b.d. for 1 week, and thereafter
100 mg. t.i.d. for 15 days.

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The experiment was conducted on the "blind" method, two types of tablets "A" and "B" being given, one Pacatal and the other a placebo, the identity of which was unknown to the assessor of the drug trial.

During the first two weeks of the trial, all previous sedation was stopped, except in the case of those patients who required anticonvulsants, which were continued unchanged throughout the experiment. During the next 4 weeks one group of 30 patients received tablets "A" and the other group of 30 were given tablets "B" in the above dosage. This was followed by a period of 2 weeks "rest" when the patients again received no sedation. During the following 4 weeks, those who had previously received tablets "A" were given tablets "B" and similarly those who had previously had tablets "B" were given tablets "A". This was again followed by 2 weeks' "rest". In a few cases, their behaviour during the rest period became extremely disturbed, and an occasional dose of paraldehyde became necessary.

Assessment of the patients' condition was made at weekly intervals when the patient was interviewed and comments by the nursing staff were recorded. Daily notes were made by the nursing staff about the patients' behaviour, and they were seen frequently in the wards in the intervals between the weekly assessments. Morning and evening temperature charts were kept throughout the periods when patients were taking tablets "A" and "B". Close observation for signs of intolerance was kept (dryness of the mouth, disturbance of visual accommodation).

Results

During the first week there was very little change in any of the patients, the higher dosage of the drug not having been reached. However, in the following weeks some of the patients showed a transient drowsiness which diminished even though the drug was not reduced.

Those who did improve were less distractable, and were able to take more interest in occupational therapy or in the television, having showed no such previous tendencies. Some exhibited an improvement in their previous incontinence, and a few were less destructive, and less noisy and interfering. These improvements continued while on Pacatal, and gradually disappeared after the cessation of the drug, so that the patient returned to his usual behaviour pattern within the next 2 weeks.

Side effects were observed in a number of cases, the most prominent was dryness of the mouth. This occurred in 8 cases during the second, third and fourth weeks of administration. No disturbance of visual accommodation was noticed, but then none of these patients was able to read, and few were able to feed themselves. Pyrexia of a mild degree occurred in 6 cases, the majority during the third week, and this, unlike the dryness of the mouth, subsided even though Pacatal was continued. Anorexia was present in 6 cases, 2 occurring during the second and third weeks, but one of these cases commenced symptoms of anorexia and vomiting during the first and second weeks *after* stopping Pacatal. The symptoms gradually subsided and no clinical signs were present. Three cases seemed "afraid to walk" during the third week, but no unsteadiness was elicited, they merely seemed to prefer to cling on to support when made to walk. This subsided when Pacatal was discontinued. Drowsiness was present in 3 cases, beginning in the third week and decreasing even though Pacatal was continued.

It was noticed that those patients who suffered from epilepsy showed a higher tendency to improvement than the non-epileptic cases.

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One patient was a juvenile psychotic (schizophrenic) and he showed moderate improvement, with diminution of the reaction of excitement to hallucinations.

A summary of the results from the record sheets of the patients listing the various aspects of their disturbance is set out in the table below:

	Total No.	%	Epileptics No.	Total No. = 14 %
Treated with Pacatal:				
Slight worsening	3	10	3	21·47
No change	18	60	3	21·47
Slight improvement	8	26·66	7	50
Moderate improvement	0	0	0	0
Marked improvement	1	3·33	1	7·11
Treated with Placebo:				
Moderate worsening	1	3·33	1	7·11
Slight worsening	3	10	1	7·11
No change	25	83·33	11	78·59
Slight improvement	1	3·33	1	7·11
Moderate improvement	0	0	0	0
Marked improvement	0	0	0	0

Discussion

From the results obtained from this trial, it can be seen that the majority of cases on Pacatal showed no change (60 per cent.) and 22·66 per cent. were slightly improved. In the group of 30 cases, 14 were epileptics, and of these cases 50 per cent. showed slight improvement in behaviour, the frequency of the fits being in no way influenced. The explanation of this improvement in the epileptics might be the potentiation by Pacatal of the sedative effect of the anti-convulsants.

Only one case in the group was a juvenile psychotic, and showed only slight improvement while taking Pacatal.

It is of interest that 4 patients developed anorexia and vomiting during the first and second weeks after the drug was withdrawn, and since no clinical symptoms of other illness were present, this suggests that Pacatal may not be as rapidly excreted as claimed and that a certain degree of cumulation does occur.

Summary

Pacatal was administered to a group of 30 low-grade mental defectives, and the results proved the drug to be of limited value, except in the case of epileptics where the sedative effect of anti-convulsants was potentiated.

Acknowledgments

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