

## A LONG-TERM CLINICAL EVALUATION OF A NEW TRANQUILLIZER—TOLNATE

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'The medico-social problem of making adequate arrangements for the ageing members of the population is an ever-increasing one and is receiving the most sympathetic consideration'.<sup>1</sup> Nobody can disagree with this statement and it is becoming more and more important with the ever-increasing life expectancy.

The psychoses associated with old age, e.g. senile dementia, psychoses owing to arteriosclerosis or to other organic lesions of the brain, pose quite a problem, which can be of a social and/or therapeutic nature. Usually patients suffering from such conditions are admitted to hospital for social reasons, because they have become a danger to themselves, or their behaviour makes their stay with relatives intolerable.

The therapeutic considerations can also be difficult because of the usually poor prognosis. This generally accepted view of the poor prognosis of senile dementia calls for a reminder that other forms of psychosis, of the types seen in adults of all ages, can occur and recur in the aged as well. These conditions have their own characteristic prognosis which may, however, be influenced by such additional factors as cerebral arteriosclerosis, or manic-depressive tendencies.

It is particularly important to recognize the acute organic reaction in the elderly, the group usually described as toxic (infective) exhaustion psychosis, in varying combinations of these terms. The prognosis of this latter group can be good even in octogenarians.

In the main, however, we are still faced with the degenerative group of poor prognosis presenting therapeutic difficulties. The treatment in them is largely symptomatic with nursing care—the amelioration of symptoms is justified since it reduces the suffering of the patient and brings about calm, cooperative behaviour. Tranquillizers, especially chlorpromazine, are useful for controlling their restlessness and agitation.

As Davison *et al.*<sup>2</sup> so aptly put it 'it is accordingly important that the elderly should be maintained in such a mental condition that they are acceptable as ordinary members of the community'. And also that 'it has therefore become desirable for the general practitioner to have at hand drugs which will alleviate those acute exacerbations of abnormal behaviour'.

It was felt, therefore, that it would be worth while to evaluate a new phenothiazine, 'tolnate', in aged patients and also, if the opportunity presented itself, in a few acute young patients.

The active principle of tolnate, prothipendyl hydrochloride, is a phenothiazine analogue with the chemical formula 10-dimethylamino-propyl-1-azaphenothiazine hydrochloride hydrate. Its main appeal for us was in its low toxicity and lack of serious side-effects, even with high dosage. Jessel (1960)<sup>3</sup> treating 400 patients with doses of up to 1,200 mg. daily, reported no extrapyramidal side-effects.

\*It is with regret that we have to remind our readers that Dr. Fismar died recently.

## METHODS AND MATERIALS

Sixteen patients were treated with tolnate. All patients (except the 2 who died of intercurrent physical conditions during treatment), were treated and followed up for 6 months or longer. They were all males, the ages ranging from 22 to 81 years. There were 11 patients aged 60 and over, 1 aged 52, and 4 aged 22-39 years. The disorders treated were as follows:

- 5 cases of cerebral arteriosclerosis with psychosis
- 5 cases of senile psychosis
- 2 cases of psychosis owing to organic disease of the CNS
- 4 cases of schizophrenia

Tolnate tablets containing 40 mg. of prothipendyl hydrochloride were used and the dosage ranged from 120 mg. to 480 mg. per day, 120 mg. per day being the maintenance dose used.

Results were assessed as follows at the end of 6 weeks' treatment:

*Excellent.* Complete or almost complete remission of symptoms.

*Good.* Decided improvement, partial remission of symptoms.

*Fair.* Slight improvement but sufficient to alter status or care of the patient.

*Poor.* Condition unchanged or worse.

## RESULTS

The results obtained are shown in Table I.

The results obtained in the various disease categories are summarized in Table II.

It will thus be seen that the results were excellent to good in 10 patients, and fair to poor in 6. The patients who responded best were the cerebral arteriosclerotics with psychosis—4 out of 5 being assessed as excellent and good, and the 4 schizophrenics—all 4 being rated excellent and good.

The results obtained in the schizophrenics are remarkable—all had had various forms of previous treatment, ranging from ECT, insulin shock, chlorpromazine, trifluoperazine, plus leucotomy in 2.

It is noteworthy that practically all patients were previously treated with other phenothiazines with results that could not compare with the success subsequently obtained when using tolnate.

All patients have maintained their initial improvement up to the present and there have been no relapses.

## CASE REPORTS

*Patient A.R.S., aged 70 years.* Cerebral arteriosclerosis with psychosis of 3 months' duration. On admission, this patient was confused, impulsive and suicidal. He could not orientate himself correctly for time or place, and he was unable to give a coherent account of himself. His memory was poor and he had no insight. Both his physical and mental condition showed improvement after 4-weeks' treatment, and at the end of the eighth week he was virtually symptom-free. He was discharged (on maintenance therapy) after 4 months as having recovered. At this time the only abnormal finding was a short period of amnesia covering the first 3 weeks of his detention in hospital. He remains well after his discharge from hospital.

*Patient F.H.S., aged 39 years.* Schizophrenic—15 years. Previous treatment, before 1950: ECT, insulin coma and eventually prefrontal leucotomy. In past 5 years he has been treated with chlorpromazine and later trifluoperazine.

Before treatment with tolnate was started, this patient was asocial, emotionally blunted and indifferent to his surroundings. His powers of reasoning and judgment were defective and he had poor insight. He gave a vague, rambling and inconsequential account of himself. He was at times neologistic and actively deluded. After 6-weeks' treatment he was pleasant and sociable, and took an active part in recreational facilities. His conversation was rational and he gained insight into his condition. He has been on leave from hospital for many months and has been seen regularly as an outpatient. Improvement has been maintained on 40 mg. of tolnate *t.i.d.* His mental state is better than I have ever known it to be in the 5 years I have treated him.

TABLE I. RESULTS OBTAINED WITH TOLNATE

Diagnosis	Age	Duration of illness	Duration of treatment	Results	Discharged from hospital	Effects
Cerebral arteriosclerosis with psychosis .. ..	70	18 months	Over 6 months	Excellent	Yes	Nil
Cerebral arteriosclerosis with psychosis .. ..	60	18 months	Over 6 months	Good	Yes	Nil
Senile psychosis .. .. .	74	16 months	Over 6 months	Excellent	Yes	Nil
Cerebral arteriosclerosis with psychosis .. ..	69	2 years	Over 6 months	Good	No	Slight drowsiness on 360 mg. day
Cerebral arteriosclerosis with psychosis .. ..	65	1 year	Over 6 months	Fair	No	Nil
Cerebral arteriosclerosis with psychosis .. ..	70	3 months	Over 6 months	Excellent	Yes	Nil
Senile psychosis .. .. .	81	6 months	Over 6 months	Fair	No	Nil
Senile psychosis .. .. .	81	2 years	Over 6 months	Fair	No	Nil
Senile psychosis .. .. .	74	1 year	6 months	Poor	No	Nil
Senile psychosis .. .. .	77	4 months	6 weeks	Fair	Died	Nil†
Psychosis from org. dis. CNS .. .. .	68	6 months	6 months	Fair	No	Nil
Psychosis from org. dis. CNS .. .. .	52	6 years	6 months	Excellent	Died	Nil‡
Schizophrenia .. .. .	22	5 years	Over 6 months	Good	Yes	Nil
Schizophrenia .. .. .	39	15 years	Over 6 months	Excellent	Yes	Nil
Schizophrenia .. .. .	32	8 years	Over 6 months	Excellent	No	Nil*
Schizophrenia .. .. .	27	5 years	Over 6 months	Good	Yes	Nil

\*This patient is well enough to be discharged but has nowhere to go and cannot find employment.

†Died of cerebral haemorrhage.

‡Died of coronary thrombosis.

TABLE II. SUMMARY OF DISEASE CATEGORIES

Diagnosis	Total	Excellent	Good	Fair	Poor	Discharged from hospital
Cerebral arteriosclerosis with psychosis .. .. .	5	2	2	1		3
Senile psychosis .. .. .	5	1		3	1	1
Psychosis from org. dis. CNS .. .. .	2	1		1		
Schizophrenia .. .. .	4	2	2			3
	16	6	4	5	1	7

#### Side-effects

A remarkable feature was the virtual absence of side-effects. Only 1 patient developed slight drowsiness on 360 mg. per day.

#### DISCUSSION

It was agreed that all cases treated had a relatively poor prognosis before treatment with tolinate was commenced, and that the overall results obtained were, therefore, all the more encouraging.

The drug was very well tolerated even in the elderly and frail patients, and is remarkable for its almost complete absence of side-effects and no evidence of toxic effects—a most desirable feature.

It is ideal for treatment of active and ambulant patients as well as for treatment of outpatients and maintenance therapy of patients on leave from hospital and, therefore, not under constant medical supervision.

It has been effective in many cases where other forms of treatment had produced comparatively poor results—notably in the schizophrenics treated.

One point which struck me most forcibly was the marked change in the atmosphere of the ward in which the 12 elderly patients were treated. The change was from that of a feeling

of despondency to one of almost infectious optimism on behalf of both the patients and the staff (who eagerly co-operated feeling that they really had something at last which benefited the patient).

Instead of a group of dull, apathetic, drowsy patients, or those who were restless, resentful and uncooperative, the scene changed to relaxed, contented and alert patients who were both willing and eager to assist themselves and the staff to the best of their ability. This change naturally took a great deal of pressure of work off the staff, who were consequently better able to maintain contact with their patients and to stimulate interest in their surroundings, instead of just attending to their physical needs.

Another change of attitude was noticed in the visitors to the hospital, both relatives and friends, who commented on the improved behaviour of patients and their increased interest in their surroundings. As a result, visits of relatives and friends have increased considerably and they are now far more willing to take patients out for the day or at weekends, because of the patients' increased cooperation and also the increased benefits the patients seem to derive from these outings.

I therefore feel that tolinate has proved itself as a most useful and effective drug and should prove a valuable addi-

tion to the psychiatrist's armamentarium, especially because of the absence of dizziness and drowsiness, with the attendant danger of falls in the elderly.

#### SUMMARY

1. Sixteen patients, aged 22 - 81 years, were treated with tolinate for 6 months or longer.
2. Results were excellent to good in 10, and fair to poor in 6.
3. The response to treatment in 5 cases of cerebral arteriosclerosis with psychosis were excellent to good in 4, and fair in 1; in 5 cases of senile psychosis, excellent in 1 and fair to poor in 4; in 2 cases of psychosis from organic disease of CNS, excellent in 1 and fair in 1; and in 4 cases of schizophrenia the results were excellent to good in all 4.

4. The virtual absence of side-effects and toxic effects was a remarkable feature.

5. It is felt that tolinate is a most useful and effective drug.

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