# CLINICAL EVALUATION OF THIOTHIXENE IN ACUTE NEWLY ADMITTED SCHIZOPHRENIC PATIENTS

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## SYNOPSIS

**Nineteen newly admitted male Schizophrenic patients were treated with Thiothixene (Navane) for a trial period of 16 weeks. Progress in the patients' symptoms and behaviour were recorded at prescribed intervals on standard psychiatric and nurse rating scales.**

**The results showed that 90% of the patients recorded moderate to marked improvement at the end of the trial. Florid symptoms of acute Schizophrenia were well controlled. This study confirmed the previous reports of the potent anti-psychotic properties of Thiothixene.**

**Blood and urinalysis including liver function were evaluated and there were no serious toxic effects. Extrapyramidal symptoms were however very common and 17 of the 19 patients had either tremors, rigidity or akathisia.**

Thiothixene (Navane) is a new potent psychotherapeutic drug which has been extensively investigated and found to have anti-psychotic activity similar to the phenothiazines.

The drug is the cis isomer of N, N-dimethyl-9-3-(4-methyl-1-piperazinyl)-propylidene thioxanthene-2-sulfonamide.

Most trials that were done on chronic schizophrenics recorded improvement in behaviourial areas of agitation, aggressiveness as well as apathy and withdrawal. Drowsiness was infrequent, and the side effects were mainly extrapyramidal symptoms.

Gallant, Bishop *et al* conducted a double-blind evaluation of thiothixene in chronic schizophrenics, comparing the drug with thioridazine and found that there were "no significant differences in therapeutic efficacy between the two drug groups". Extrapyramidal side effects were more frequently associated with administration of thiothizene while lethargy and orthostatic hypotension were observed only in the thioridazine group.

The Thiothixene tablet used in the trial was a special form of tablet which caused the tablet to disintegrate in the mouth within 30 seconds without aftertaste. This 'Rapid Dispersal' tablet ensured certain ingestion and absorption of medication by difficult patients.

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Bishop in another double blind study compared the efficacy of thiothixene with that of trifluoperazine on forty newly-admitted schizophrenic patients and concluded that thiothixene showed therapeutic efficacy at least equal to that of trifluoperazine.

However, Hekimian *et al* studied the effect of thiothixene on twenty newly-admitted schizophrenic patients and concluded that the anti-psychotic properties although present were not marked. There was a high incidence of extrapyramidal symptoms (17 of 20). Associated with these overt extrapyramidal reactions were severe insomnia and restlessness. Furthermore, a much more serious effect was the apparent activation of psychotic symptoms and signs (6 of 20) with a suicidal attempt in one case.

The purpose of this study was to evaluate the activity of thiothixene in acute newly-admitted schizophrenic patients.

## METHOD

All male patients admitted for the first time to Psychiatric Unit II, Woodbridge Hospital with the diagnosis of Schizophrenia were included in the trial. Schizophrenic patients with a previous history of admission and those over the age of 60 were excluded.

The patients were jointly interviewed by the psychiatrists, the diagnosis confirmed and after one to three days observation, treatment was instituted beginning with a dose of 5 mg. b.i.d. This initial dose was increased by 5 to 10 mg. at weekly inter-

vals until an effective dose was attained or until the severity of any side effects precluded further increase. The maximum daily dose used was 30 mg. The drug trial period was 16 weeks. Benzhexol (Artane) 2 mg. b.i.d. was added on the appearance of extrapyramidal symptoms.

## RATING

A four-point psychiatric rating scale (Appendix I) was used to assess the progress of the patient with regard to nine target symptoms viz irrelevancy, thought disorder, depression, congruity of affect, anxiety, delusions, hallucinations, activity and hostility.

The nursing staff were also required to rate the behaviour of the patient on a 5-point rating scale (Hamilton) Appendix II.

Each patient was assigned a psychiatrist and a nurse who was responsible for the ratings throughout the trial. Ratings were made at the initial interview before the commencement of the drug, and at the end of the 1st, 2nd, 4th, 6th, 12th and 16th week of treatment. The difference between the baseline rating score and subsequent scores at each interview would indicate the progress of the patient.

The total rating score at the start of the drug trial was compared with the score at the end of the trial. The difference indicated the improvement during the sixteen weeks.

Wherever possible, the patients were kept under observation in the ward during the trial period of 16 weeks. However in some patients, a marked improvement occurred and when relatives were eager to take the patient home from the ward, they were allowed to do so.

These patients continued the drugs as an outpatient and were recalled to keep their appointments on the specified days for the psychiatric ratings and laboratory studies to be completed. The nurse rating scales were omitted in such cases.

## LABORATORY INVESTIGATIONS

The following laboratory studies were investigated before the treatment and thereafter at 4 weekly intervals.

Complete Blood Count
Haematocrit
SGOT
SGPT
Urinalysis

Liver function tests (serum bilirubin, alkaline phosphatase and serum proteins) were done if the SGOT and SGPT were abnormal.

## MATERIAL

Altogether 19 males were included in the trial. Their ages ranged from 14 to 35 (mean 24). All were suffering from acute schizophrenia with a short history of acute symptomalogy before admission.

The subtypes of schizophrenia were:

14 acute undifferentiated schizophrenia
2 Paranoid
2 Catatonic
1 Hebephrenic

The duration of illness ranged from 3 days to 1 year.

## RESULTS

The overall results in the 19 patients were as follows:

| Marked Improvement | Moderate Improvement | Slight Improvement | No Change | Worse |
|---|---|---|---|---|
| 9 | 8 | 1 | 1 | 0 |

The effect of thiothixene on the target symptoms were remarkable. Analysis of the psychiatric rating scores showed that 16 of the 19 patients had their initial rating scores halved by the end of the 2nd week. By the end of the 6th week, 9 patients had rating scores of zero.

Seven patients were socially improved to be sent home at the end of the 4th week. This number increased to 13 by the 8th week. At the end of the trial 2 patients were still in the hospital.

Three patients failed to respond to thiothixene and were given electroconvulsive therapy.

T7. A young boy of 16 years of age; Hebephrenic Schizophrenia of gradual onset. Thought disorder was predominant and emotional blunting marked. There was loss of volition. He was particularly sensitive to thiothixene where side effects were concerned with marked tremors and akathisia. ECT was considered advisable. In spite of a course of 6 ECT, his condition did not improve appreciably. His overall result was graded as slight improvement.

# APPENDIX I

Name of Patient: Admission No.:

## PSYCHIATRIC RATING SCALE

SPEECH

1. **Relevance to Questions Asked**

| | |
|---|---|
| Direct and relevant | 0 |
| Somewhat rambling and tangential | 1 |
| For the most part irrelevant | 2 |
| Wholly irrelevant | 3 |

2. **Speech Associations**

| | |
|---|---|
| Coherent | 0 |
| Slightly incoherent, evasive, talking past the point | 1 |
| Inconsequential speech with loose associations, thought block | 2 |
| Completely incoherent, mumbling, disjointed | 3 |

AFFECT

3. **Depression**

| | |
|---|---|
| None | 0 |
| Slight | 1 |
| Moderate | 2 |
| Severe | 3 |

4. **Congruity of Affect**

| | |
|---|---|
| Normal | 0 |
| Decreased or shallowed response | 1 |
| Apathy | 2 |
| Inappropriate | 3 |

5. **Anxiety**

| | |
|---|---|
| None | 0 |
| Slight | 1 |
| Moderate | 2 |
| Severe | 3 |

MENTAL CONTENT

6. **Delusions**

| | |
|---|---|
| None | 0 |
| Suspicious, with ideas of reference or influence | 1 |
| Delusions probable | 2 |
| Delusions present with firm conviction | 3 |

7. **Hallucinations**

| | |
|---|---|
| None | 0 |
| Probably hallucinated or occasionally hallucinated | 1 |
| Hallucinated part of the time with some/full insight | 2 |
| Hallucinated with no insight | 3 |

BEHAVIOUR

8. **Activity**

| | | | |
|---|---|---|---|
| Normal | 0 | | |
| Lethargic | 1 | Overactive | 1 |
| Retarded | 2 | Restless | 2 |
| Resistive | 3 | Agitated | 3 |

9. **Hostility**

| | |
|---|---|
| None | 0 |
| Slight hostile, irritable, resentful | 1 |
| Moderate hostility, bitter, caustic | 2 |
| Much hostility; fights, disturbed | 3 |

Date: Name of Rater:

# APPENDIX II

Name of Patient: Admission No.:

## NURSE'S RATING SCALE FOR BEHAVIOUR IN WARD

**Attitude to Work**

| | |
|---|---|
| Normal attitude, co-operative | 0 |
| Can do simple jobs only | 1 |
| Requires some supervision | 2 |
| Needs constant supervision and urging | 3 |
| Refuses work, passively or actively | 4 |

**Attention to Dress and Person**

| | |
|---|---|
| Attends to clothes and appearance normally | 0 |
| Dresses himself, but looks untidy | 1 |
| Dresses himself, but needs adjustments | 2 |
| Requires help to get dressed and cleaned | 3 |
| Has to be dressed and washed | 4 |

**Relation to Other Patients**

| | |
|---|---|
| Helpful and friendly, co-operative in activities | 0 |
| Occasionally talks or helps others | 1 |
| Will talk when spoken to | 2 |
| Will only say a word or so | 3 |
| Ignores other patients and may strike them | 4 |

**Relation to Medical and Nursing Staff**

| | |
|---|---|
| As with 'other patients' | 0 |
| | 1 |
| | 2 |
| | 3 |
| | 4 |

**Behaviour at Meals**

| | |
|---|---|
| Normal manners and behaviour | 0 |
| Peculiar habits and unco-operative with others | 1 |
| Stealing and snatching food | 2 |
| Wolfing and gobbling food, seldom using cutlery | 3 |
| Requires supervision or encouragement to eat | 4 |

**Toilet Behaviour**

| | |
|---|---|
| Goes normally to lavatory | 0 |
| Requires to be taken or fetched out | 1 |
| Occasionally incontinent | 2 |
| Frequently incontinent | 3 |
| Smearing sometimes | 4 |

**Activity**

| | | |
|---|---|---|
| Normal activity and mobility | | 0 |
| Lethargic | Overactive | 1 |
| Tends to sit about | Restless | 2 |
| Has to be moved | Never still | 3 |
| Resistive and rigid | Rushing about | 4 |

**Speech**

| | |
|---|---|
| Normal speech and conversation | 0 |
| Taciturn, inconsequential, no real conversation | 1 |
| Says only a few words, or speech disorganised | 2 |
| Occasional mumbles | 3 |
| Mute or incomprehensive speech | 4 |

Date: Name of Rater:

T14. A youth, 17 years old, had a one month history of paranoid ideas of reference, persecutory delusions and auditory hallucinations. Admission was precipitated by an attempt at suicide by jumping from a height. There was a family history of a sister having schizophrenia. He responded well to treatment with thiothixene initially and was free of symptoms at the end of 6th week. He relapsed when he was taken home and was irregular with the drugs. He was brought back in an acutely disturbed state of agitation and aggression. Thiothixene at 30 mg. failed to control his agitation and ECT was administered. This patient registered on the overall results as No Change at the end of the 16th week trial.

T19. Age 25. Father had a history of mental illness. The patient was admitted with a 2 week history of aggression and violent behaviour. He was acutely agitated on admission and ECT was given in view of his excited state not controlled by thiothixene. He had 4 treatments and subsequently the improvement was maintained with thiothixene. At the end of the trial he was rated as moderately improved.

Three patients therefore had combined treatment of Thiothixene and ECT of which two did not improve. These two were young schizophrenics one of whom (T7) was a characteristic hebephrenic. The poor response to thiothixene of patient T7 would not be unexpected as hebephrenics generally have a poor prognosis.

## SIDE EFFECTS

No serious side effects were observed. The most common were extrapyramidal reactions followed by dryness of mouth and drowsiness and sweating. Two patients complained of giddiness. Two patients were completely free of any side effects.

17 of 19 patients developed extrapyramidal reactions at the low dose of 10 mg. daily. Tremors (13) were the most common with rigidity (7) and akathisia (2). These appeared within a mean period of three weeks, the earliest 7 days.

Two patients developed a dull expressionless stare which was disturbing to observers. Two patients had developed a peculiar rocking motion involving the trunk which was poorly controlled with Benzhexol.

The other extrapyramidal symptoms were generally well controlled with Benzhexol.

## LABORATORY STUDIES

There were no significant changes noted in the blood and urinalysis. In 9 patients, the SGPT and SGOT showed normal baseline values. There were transient rises in the transaminases level which reverted to normal with continued treatment.

In the three cases where SGOT SGPT were raised, serum bilirubin, serum alkaline phostastase and the albumin/globulin ratio were investigated and found to be normal.

In 9 other patients where the baseline values of either SGOT or SGPT were initially abnormal, continued administration of thiothixene did not cause any gross changes in the values.

## DISCUSSION AND CONCLUSION

This is a small evaluative study of the use of thiothixene in the treatment of 19 acute newly-admitted schizophrenic patients. The study confirms most previous observations on the potent antipsychotic properties of thiothixene and that it is a valuable and effective drug for the treatment of acute schizophrenics.

The effect on the florid symptoms of acute schizophrenia was dramatic with rapid improvement in the symptoms evident within two weeks in as many as 84% (16) of the cases. 90% (17) of the patients were either markedly improved or moderately improved at the end of the trial period and were discharged from the hospital.

The daily dosage ranged from 10 mg. to 30 mg. There were no dangerous side effects. Extrapyramidal side effects were however very common and seen in 90% of the patients. They were generally well controlled with Benzhexol. Other side effects, dryness of mouth, sweating, drowsiness and giddiness were generally mild and not a problem. The activation of psychotic symptomatology observed by Hekimian *et al* was not present in this study. This could be due to the higher dosage used in their study.

The results of the laboratory studies in blood, urinalysis and liver functions tests showed no adverse changes.

A further controlled trial comparing thiothixene with a phenothiazine such as trifluoperazine on a local patient population would be indicated.

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