closely. Apparently, doctors take this as part and parcel of the problem and quickly shift the responsibility of correct and adequate dosage to the patient and the family.

Replies of patients when asked by their doctors why they changed the dose or schedule of dosage do indicate the presence of the element of fear or distrust; the patient tries to gain control of the situation by some token manipulation of the drug.

When it comes to psychotropic medication, the fear or distrust can be understandably exaggerated by an overanxious or depressed or psychotic patient. The non-psychotic patient is only too eager to be helped and with little difficulty, obeys instructions. The depressed patient of course views the pill with the same pessimistic outlook that he does everything else. "Will I get addicted?" "If I take this, I may never wake up", "This might really make me snap" are frequent remarks by such patients before they agree to try the drug.

The doctors also mentioned the opposite extreme in attitude, namely, a readiness to accept and over-value drugs. In such instances, only a prescription gives validity to the medical consultation. A doctor who does not give a prescription during the patient's visit for one reason or another (e.g., more work-up needed) is reminded by the patient to please prescribe "something".

A published study by one Filipino doctor about patient-attitudes states that Filipino patients associate a drug with a certain specific symptom, rather than with an illness. Thus patients think that the drug can be given to anyone with the same symptom. Partly, this is responsible for self-medication and for recommendation of a drug to friends or relatives, without medical consultation. The same author makes the claim with supporting statistics that the pharmaceutical industry in the Phillipines ranks with steel and oil in size and importance. By the same token, doctors mention a frequent observation: that many of the houses they visit have "pocket" drug-stores for a medicine cabinet, with a different drug for every symptom.

In conclusion, one may hypothesize that the contradictory patterns in attitudes towards drugs reflect changes in the orientation of the society towards the practice of medicine. Whenever a society undergoes changes, traditional beliefs compete with new ideas. Individual members react and adapt to change, each in his own way. The doctor, because he wants his tools to be effective and because he has to make a living, then tries to adopt a style of prescribing drugs which he feels will work with a majority of patients.

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A CLINICAL TRIAL OF COMBINED THERAPY WITH CHLORPROTHIXENE AND NORTRIPTYLINE IN PSYCHOTIC PATIENTS WITH DEPRESSIVE SYMPTOMS

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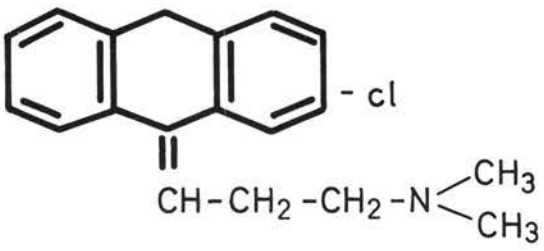
The use of a combination of known effective drugs has become widespread during the past decade. Fairly numerous reports [1, 2, 3, 4, 5, 6, 7, 8, 9] have appeared in the past ten years on the use of a combination of antidepressive agents and neuroleptic drugs in the treatment of schizophrenia. The author reported favorable results in treating psychotic patients with depressive symptoms with combined Pericyazine Trimipramine.[10]

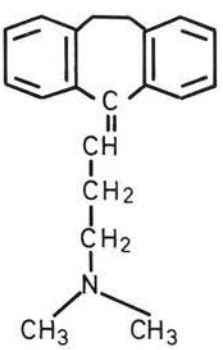
Chlorprothixene, the oldest known member of thioxanthene group of tricyclic neuroleptic has been developed by Research Laboratories of Lunbeck in 1958. It differs from phenothiazine

derivatives in that the nitrogen atom in the phenothiazine ring is replaced by a carbon atom to which the side chain is attached by the double bond.

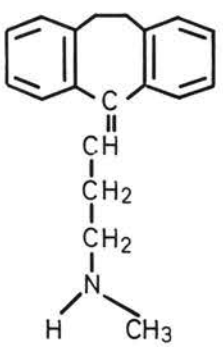


Preliminary animal and human studies seem to suggest that its pharmacodynamic and therapeutic properties are similar to those of Chlorpromazine and should be given in doses of the same order of magnitude as chlorpromazine [11] Chlorprothixene appears to exert approximately the same antipsychotic effect as Chlorpromazine.[12] It was observed that chlorprothixene exert a weak antidelusional and antihallucinatory effect, so that the drug should be combined with another neuroleptic which has more potent neuroleptic action.[13] In schizophrenia, 33 to 80.3 per cent of patients had good to excellent results,[11, 14, 15] Particularly good response was obtained in paranoid varieties[15] and in schizophrenic patients who manifested depression and or anxiety.[16] A favourable result was seen also in depressive neuroses.[15] It is more indicated as the drug of choice in agitated depression. It is beneficial to the result in treating disturbed geriatric patients [18] and alcoholic psychosis.[19]

Side-effects were: orthostatic vertigo and collapse, tachycardia, allergic dermatitis,[20] slurred speech,[11] dryness of mouth, akathisia, convulsion.[14] It seems to show no serious toxic effects, particularly the extrapyramidal symptoms were rarely encountered.[21]



AMITRIPTYLINE



NORTRIPTYLINE

I.F. Benett introduced nortriptyline in the clinic in 1962. From the clinical point of view nortriptyline is the demethyl derivative of amitriptyline (desmethylamitriptyline).

Early reports suggested that nortriptyline, aside from being an antidepressant could also be used as a minor tranquillizer.[22, 23, 24] Later reports did not support such effect. On the other hand, many others found that nortriptyline has slight anxiety and restlessness producing effect and possibly exerts a selective effect upon depression inhibition syndrome with quick onset of action [25, 26, 27]

Mendels,[28] in a comparative trial of nortriptyline and amitriptyline found that patients with nortriptyline responded significantly more rapidly than patients treated with amitriptyline, but there was no difference in response to the two drugs after six weeks of treatment.

This drug has been found to be effective in the treatment of childhood enuresis[29] and useful in the symptomatic treatment of autisti children. [30] Because of its activating effect, it should not be used or contra-indicated in agitated depression.[31, 32]

Side-effects were: dryness of mouth, increased psychomotor activity, insomnia, panic episode, increase in irritability particularly in the paranoid schizophrenic patients, dizziness, blurring of vision, sweating nausea, weakness and constipation has been reported.

The purpose of this study is to determine synergistic effect of the two agents by adding tranquillizing and antipsychotic effect of Chlorprothixene to the activating and mood elevating of nortriptyline.

METHODOLOGY

A pilot study was conducted by using Chlorprothixene and nortriptyline to determine therapeutic effect in newly admitted or readmitted psychotic patients with depressive symptoms. The study was carried out in the Female Section of the In-Patient Department of Somdet Chaopraya Hospital. The patients belonged to the following diagnostic Categories:

– Involutional Melancholia	5
– Manic Depressive Psychosis, depressive phase	3
– Senile dementia with depressive symptoms	1
– Schizophrenia paranoid type with depressive symptoms	4

– Schizo – affective, depressed 7

The patients were randomly selected, assessed and Scored on the Verdun Target Symptoms Rating Scale (Table I) and Verdun Depression Rating Scale (Table II) by the author prior to treatment and every fortnightly during the six-week period. Apart from physical and mental examinations, routine laboratory examination was performed at the beginning and again at the end of the treatment period of six weeks. Blood pressure was recorded every day during the first two weeks.

The patients ranged in age from 23 to 66 yeras (average 39.9 years). They were started on the combination of chlorprothixene 200 to 800 mg. and nortriptyline 50 to 200 mg. daily in two or four divided doses. The dosage was gradually increased until clinical improvement was noted.

Table I 12 items of the Verdun Target Symptoms Rating Scale.
(0 = none, 1 = slight, 2 = medium 3 = severe)

1. Excitement
2. Suspiciousness
3. Hostility
4. Anxiety
5. Depression
6. Impairment in object Relation
7. Hallucination
8. Disturbance of Thinking
9. Delusion
10. Memory Disturbance
11. Impairment of Consciousness
12. Impairment of Expected Social Response

Table II 12 items of the Verdun Depression Rating Scale
(0 = none, 1 = slight, 2 = medium, 3 = severe)

1. Mood
2. Facial Expression
3. General Appearance
4. Psychomotor Retardation (Observed)
5. Impairment of Work and Social Interests
6. Agitation
7. Depressive Ideation
8. Suicidal Tendencies
9. Insomnia
10. Somatic Compaints
11. Loss of Appetite
12. Loss of Weight

Table III Duration of admission

Duration of admission	1st week	2nd week	4th week	6th week	more than 6th week
	3*		10	2	5

* Against medical advice.

The following criteria were used to rate improvement:–

Excellent – if there was complete remission of symptoms or a minimal residue of symptoms, and the patient was being considered for release from hospital.

Good – if the patient was almost asympatomatic with improvement in the majority of symptoms.

Fair – if the patient became adjusted to the hospital environment, but psychotic and depressive symptoms were still present.

Poor – when there was no demonstrable improvement.

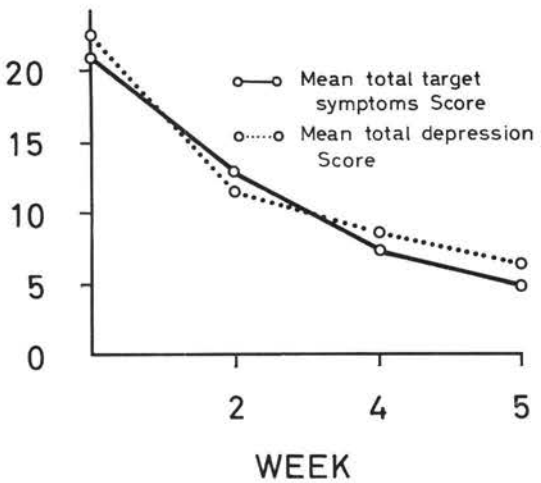
RESULTS

During the six-week period of study, 3 patients left the hospital against medical advice. Only two cases needed E.C.T. to control depression.

Results of improvement are shown in table IV. The mean total target symptoms Score and depression Scores are shown in Figure 1.

Table IV Results of improvement

Diagnosis	No. of Cases	Results of improvement				
		Excellent	Good	Fair	Poor	Against Medical advice
Involutional Melancholia	5	2	1	–	–	2
Manic Depressive Psychosis, depressive phase	3	–	3	–	–	–
Senile dementia with depressive symptoms	1	1	–	–	–	–
Schizophrenia paranoid type with depressive symptoms	4	2	–	2	–	–
Schizo-effective, depressed	7	–	2	2	2	1
Total	20	5	6	4	2	3



SIDE-EFFECTS

During the study, two cases attempted suicide. Almost all of the patients showed mild degree asymptomatic hypotension. Only one case complained of fainting and a few complained of dry mouth. There was no detectable extrapyramidal symptoms or other serious side-effects.

DISCUSSION

The author has the impression that the combination of such two agents provides some synergistic effect and yields favourable results in pure affective disorders. So this drug combination should be tried in double-blind method in both manic-depressive psychosis, depressive phase and in Involutional Melancholia.

SUMMARY

Uncontrolled pilot study was done in 20 cases of newly admitted or readmitted psychotic patients with depressive symptoms. The results of this clinical trial showed that the combination of such drugs was beneficial to pure affective disorders for controlling both psychotic and depressive symptoms. There was no observable serious side-effects. The results are sufficiently encouraging to warrant controlled clinical trial in depressive psychotic patients.

ACKNOWLEDGEMENT

The author wishes to thank Dr. Hatai Chitanondh for his permission to present this paper and B.L. Hua Company for supplying drugs for this clinical trial.

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