

## PROCHLORPERAZINE IN ANXIETY

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### SUMMARY

Seventy patients suffering from primary anxiety state were selected for this clinical trial. They were randomly assigned to Prochlorperazine (Group I) and other drugs eg., Chlordiapoxide etc. (Group II). Hamilton's anxiety scale was employed to rate the anxiety. With the 4 weeks of therapy there was significant fall in score in both the groups of patients but the fall in score is more in Group I cases as compared to Group II ( $t = 11.5$ ,  $df = 68$ ,  $P < 0.001$ ). The reduction in score (less than 10) and clinical improvement (medium to optimal improvement) was significantly more and faster in Group I (85%) cases as compared to Group II (70%) cases ( $\chi^2 = 5.225$ ,  $df = 1$ ,  $P < 0.02$ ). The side effects were least in Group I cases.

Prochlorperazine (Stemetil) has given a significant anxiolytic effect without adversely affecting the mental function. In the dosage used prochlorperazine was free from the side effects and can be effectively employed in the management of anxiety.

Too many drugs are being prescribed for the relief of anxiety and its associated symptoms. In 1973 more than 46 million prescriptions for sedatives and anti-anxiety drugs were dispensed by retail pharmacists in the National Health Services in England and Wales, and the increase since 1970 has been of the order of one million annually (Tyrrer 1976). Major tranquillizers eg., Chlorpromazine, Promazine, Trifluoperazine, Fluphenazine, Oxypertine etc., in lower dosage are commonly given in anxiety (Hamilton et al 1963, Milne and Fowler 1960). Their disadvantages are of producing extrapyramidal disorders and dependence. With the further studies on the phenothiazines (Chlorpromazine) for antiemetic effect, Prochlorperazine emerged out as an antiemetic and was less active than Chlorpromazine as central sedative. Clinical studies demonstrated its (Prochlorperazine) considerably greater psychocorrective proper-

ties (St. Laurent et al 1962, Pennington 1959, Nashipury and Moulick 1977, Ahuja 1974).

Drug therapy has an important place in the relief of anxiety but this is being eroded by indiscriminate and sometimes irresponsible prescriptions. Since most phenothiazines in low dosage have been said to be effective in the treatment of anxiety states, it was decided to study the value of Prochlorperazine (Stemetil) in the treatment of anxiety.

### Material and Methods

The study was undertaken in 70 patients who were suffering from varying degree of anxiety and in whom the diagnosis of anxiety state was agreed upon by two consultants (Nashipury and Moulick 1977, Ahuja 1974, Ramchandran and Menon 1977). Only those patients in whom anxiety was diffuse and not limited to any particular object

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or situation were taken up for the study. None of them were receiving any tranquilizer at the time of study. A detailed case history was taken, physical and psychological examination was done. Hamilton Anxiety Scale (Hamilton 1959) was employed to rate the anxiety state at the beginning and end of the trial.

Before the commencement of the trial all patients underwent basal investigations consisting of complete hemogram, erythrocyte sedimentation rate, urine and stool examination, liver function tests, X-ray/screening of chest and electrocardiograms. Physiological measures eg., P.G.R., and fore-arm blood flow were employed wherever possible to assess anxiety. Investigations were carried out initially, in the middle and end of the trial.

After a thorough physical and psychiatric assessment the patients were randomised into two groups (Ahuja 1974):-

Group I: 40 patients who were given Prochlorperazine (5 mg) 2 tablets three times a day or more or less as needed.

Group II: 30 patients who were given other drugs, like Chlordiazepoxide, Trifluoperazine in their recommended doses.

The patients were examined at pretreatment level and at weekly intervals throughout the 4 weeks trial, improvement or otherwise in the symptoms were noted in anxiety evaluation charts. As and when score came to less than 30 the dose of prochlorperazine in Group I patients were reduced gradually and when it came to less than 10 the drug was withdrawn within one week of time (Ahuja 1974).

Following rating scales were used in or-

der to assess the clinical response of the patients under the trial (Dube et al 1969):-

- 1 = worsened,

0 = No change,

+ 1 = Slight improvement (Score 20 to 30),

+ 2 = Medium improvement (Score 10 to 20) i.e., substantial recovery from illness,

+ 3 = Optimal improvement (Score less than 10) i.e., complete recovery.

### Results

Initially 82 patients were registered in this clinical trial but 70 of them could complete all the stages of trial. Majority of them were from 4th (31.4%) and 3rd (37.2%) decade of life (mean age =  $33.28 \pm 10.04$  years) with male to female ratio of 4 : 1 (Table 1).

Table 1  
Age and Sex distribution

Age groups	Male	Female	Total	Percentage
Upto 20 years	3	2	5	7.1%
21-30 years	17	9	26	37.2%
31-40 years	20	2	22	31.4%
41-50 years	11	1	12	17.2%
51-60 years	5	-	5	7.1%
Total	56	14	70	100%
Youngest (Years)	18	16	16	
Eldest (Years)	59	45	59	
Sex ratio	4 : 1			

Anxiety manifested both physically and psychologically in these patients (Table 2). Somatic manifestations (Table 2 A) included autonomic symptoms in the form of palpitation (54.2%), frequency of micturition (51.4%).

Psychic manifestations were apparent when patients were describing it (Table 2 B) and most of them had feeling of dread

Table 2  
Presenting Features

	No. of cases	%
<b>A. Somatic and autonomic features :</b>		
Palpitation	38	54.2 %
Difficulty in breathing	32	45.7 %
Dryness of mouth & sweating off and on	36	51.4 %
Nausea and vomiting with cold skin	25	35.7 %
Frequency of micturition	36	51.4 %
Muscular tension, tremors and giddiness	42	60.0 %
Abdominal churning, gastric distress etc.	52	74.5 %
<b>B. Psychic manifestations :</b>		
Apprehension, panic and restlessness	68	97.1 %
Irritability and inability to relax	38	54.3 %
Tension with worrying over trivia	48	68.5 %
Difficulty in concentration	46	65.7 %
Insomnia	48	68.5 %

and threat (97.1 %). Quite a good number of them were panicky and restless (82.8 %).

Hamilton anxiety scale was employed to rate the symptoms at the beginning and at the end of the trial, which is able to express quantitatively whether the improvement is observed clinically as compared to other methods (Ramchandran and Menon 1977,

Lader and Marks 1971). In Hamilton's anxiety scale, the initial average score in Group I was  $38.6 \pm 6.14$  and at the end of the trial the average score was  $15.84 \pm 8.16$  (Table 3). Initial average score in Group II patients was  $36.11 \pm 7.15$  and at the end of trial  $18.08 \pm 7.86$ . In both groups drugs caused the reduction in anxiety but on comparing the fall in score in these two groups the fall in score was significantly more in Group I as compared to Group II patients ( $t = 11.2, df = 68, P < 0.001$ ).

Score during the whole period is depicted in Table 4. The recovery rate was higher and rapid in Group I (87.5 %) as compared to Group II (70 %) cases which was statistically significant ( $X^2 = 5.22, df = 1, P < 0.02$ ). The final assessment of the

Table 4  
Score during the trial period

Score	Before treatment	After treatment 1	2	3	4 weeks
<b>Group I (n = 40)</b>					
more than 30	25	15	8	6	2(5%)
10 - 30	15	12	8	7	3(7.5%)
less than 10	-	15	24	27	35 (87.5%)
<b>Group II (n = 30)</b>					
more than 30	15	9	7	5	4(13.3%)
10 - 30	15	8	8	7	5(16.7%)
less than 10	-	13	15	18	21(70%)

Comparing the two groups in attaining score less than 10 in 4 week time:  $X^2 = 5.225, df = 1, P < 0.02$  significant.

Table 3  
Clinical Improvement - Analysis of Hamilton's Anxiety Scale.

	Group I (n = 40)		Group II (n = 30)	
	Initial Score	Final Score	Initial Score	Final Score
Mean Score $\pm$ S. D.	$38.6 \pm 6.14$	$15.84 \pm 8.16$	$36.1 \pm 7.15$	$18 \pm 7.86$
t	10.3		6.6	
df	39		29	
P	< 0.001		< 0.001	

Comparison of fall of score between the two groups:  $t = 11.2, df = 68, P < 0.001$  Significant

therapeutic response (Table 5) showed 87.5% had medium to optimal improvement in Group I patients while it was 70% in Group II cases.

humorally by the release of adrenaline and other catecholamines (Tyrrer 1979, 1982). This leads to an increase in cardiac output and shunting of blood from skin and gut to

Table 5  
Rating of Clinical response of therapy

Rating	Group I (n = 40)		Group II (n = 30)		
	No. of Cases	%	No. of Cases	%	
- 1 or worsened	-	-	1	3.3%	
0 or no response	2	5%	4	13.3%	
+ 1 or slight improvement	3	7.5%	4	13.3%	
+ 2 or medium improvement	12	30%	8	26.8%	
+ 3 or optimal improvement	23	57.5%	13	43.3%	70%

Comparing the medium and optimal improvement in two groups  $X^2 = 5.225$ ,  $df = 1$ ,  $P < 0.02$  Significant

Drug (Prochlorperazine) did not show any significant side effects. Slight transient drowsiness was noted in 3 patients (7.5%) of Group I cases but it was not of an order to warrant reduction in dosage or withdrawal of the drug. Extrapyramidal side effects were noted in 3 cases (10%) of Group II and many of them had drowsiness and dryness of mouth etc (5 cases or 16.6%), which warranted to reduce the dose and even withdrawal of drug in 2 patients of Group II.

### Discussion

The present study was on 70 cases in whom anxiety manifested both bodily and psychologically, which are commonly described as somatic and psychic anxiety. Both showed clearly as separate entities when analysed on anxiety rating (Hamilton et al 1963, Hamilton 1959). Somatic group includes autonomic symptoms that are not under voluntary control and the word psychic has more than one meaning. Cannon (1979) has described the physiology of the symptoms. The awareness of anxiety leads to feeling of dread and threat and other psychological symptoms. The 'fight' or 'flight' reaction is aroused by stimulation of the sympathetic nervous system, both through stimulation of sympathetic nerves and

cardiac and voluntary muscles. The somatic symptoms of palpitation, difficulty in breathing, dryness of mouth, cold skin, muscular tension and tremor follow rapidly from these physiological changes if neither fight nor flight is appropriate.

Many inventories and scales are available to measure the level of anxiety. In the present study mainly time tested and accepted Hamilton's anxiety scale was employed at the beginning and end of the trial to measure the levels of anxiety. Hamilton's anxiety scale is able to express quantitatively the clinically observed improvement (Ramchandran and Menon 1977) and it can be correlated significantly with clinical improvement which is not possible with other anxiety scales (Lader and Marks 1971). In Hamilton's anxiety scale the initial average score in Group I patients was  $36.6 \pm 6.14$  and at the end of the trial was  $15.86 \pm 8.16$  and in Group II patients it was  $36.11 \pm 7.15$  and  $18.08 \pm 7.86$  respectively. This showed the significant reduction in score in both the groups with the treatment but the reduction was significantly more in Group I cases as compared to Group II cases (Table 3,  $t = 11.2$ ,  $df = 68$ ,  $P < 0.001$ ).

Beneficial response of prochlorperazine in small doses was reported in patients with a variety of somatic complaints leading to tension, uneasiness of mind and ill defined nervous feelings (Tyrer 1976, Milne and Fowler 1960, St Laurent et al 1962, Naishpury and Moulick 1977, Ahuja 1974). It is effective in geriatric patients suffering from anxiety and agitation associated with organic diseases. In the present series of cases 62.5 % in Group I and 50 % in Group II had an initial score more than 30 and 37.5 % in Group I and 50 % in Group II had score between 10-30, while no one had score less than 10. The recovery rate and rate of improvement was faster in Group I patients as compared to Group II cases. Ahuja (1974) and Naishpury and Moulick (1977) reported similar results with prochlorperazine in low dosage in anxiety. Paterfy and Pinter (1972) concluded that it had comparable and significant anxiolytic action when administered in low dosage. Least side effects had been noted with prochlorperazine while in Group II there was extra-pyramidal effects in few patients. In view of encouraging results obtained prochlorperazine (Stemetil) can be effectively employed in the management of anxiety.

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#### References

- AHUJA, I. S. (1974), Prochlorperazine in anxiety neurosis, *Indian Journal of Medicine & Surgery*, 39:1
- CANNON, W. B. (1979), Bodily changes in pain, hunger, fear and rage., Appleton, New York.
- DUBE, K. C., PAREKH, D. C. & YADAV, B. S. (1969), Phase-I, Clinical trial on GO 3315, a major tranquilizer, *Indian Journal of Psychiatry*, 11:75.
- HAMILTON, M. (1959), The assessment of anxiety states by rating, *British Journal of Psychology*, 32:50
- HAMILTON, M., HORDOEN, A., WALDROP, F. N. & LOFFT, J. (1963), Controlled trial on the value of prochlorperazine, trifluoperazine and intensive group treatment, *British Journal of Psychiatry*, 109:510.
- LADER, M. & MARKS, I. (1971), *Clinical Anxiety*, London William-Heinman, Page 86.
- MILNE, H. B. & FOWLER, A. B. (1960), A clinical trial of chlorpromazine, prochlorperazine, methotrimeprazine, *Journal of Mental Sciences*, 106:1105.
- NASHIPURY, J. N. & MOULICK, P. (1977), Prochlorperazine (Stemetil) in anxiety and tension states, *Ind. Pract.*, 30:61.
- PENNINGTON, V. M. (1959), Prochlorperazine in the treatment of schizophrenia. *American Journal of Psychiatry*, 115:820
- PATERFY, G. & PINTER, E. J. (1972), Comparative therapeutic evaluation of anxiolytic drugs, *Current Therapeutic Research*, 24:9
- RAMCHANDRAN, V. & MENON, M. S. (1977), A clinical trial of Pimozide (R 6238) in anxiety states, *Indian Journal of Psychiatry*, 19:79
- ST. LAURENT, J., COHN, C. H. & BAN, T. A. (1962), Treat\*of Psychiatric patient with a pehnothiazine derivative (Prochlorperazine) with special reference to after care, *American Journal of Psychiatry*, 118:938.
- TYRER, P. (1976), Drugs for anxiety, *Journal for Applied Medicine*, 2:955
- TYRER, P. (1979), Anxiety, Recent Advances in Clinical Psychiatry Edited by Graville-Grossman, K. Volume 3, page 161, Churchill Livingstone, Edinburgh.
- TYRER, P. (1982), A major common symptom in Psychiatry - Anxiety, *Journal for Applied Medicine*, 9:691.

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