# COMPARATIVE SHORT-TERM EVALUATION OF PENFLURIDOL AND TRIFLUOPERAZINE IN CHRONIC SCHIZOPHRENIA

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**Summary :** A double blind comparative study was conducted to evaluate the efficacy and safety of penfluridol and trifluoperazine in patients of chronic schizophrenia. Penfluridol was administered once weekly while trifluoperazine was administered twice daily by preparing identical capsules.

The data revealed that both the compounds were similarly effective in maintaining control of symptoms of chronic schizophrenia. However, penfluridol has a definite advantage over trifluoperazine since it is administered once a week instead of twice a day.

**Key words :** penfluridol, drug trial, antipsychotic efficacy, schizophrenia, trifluoperazine

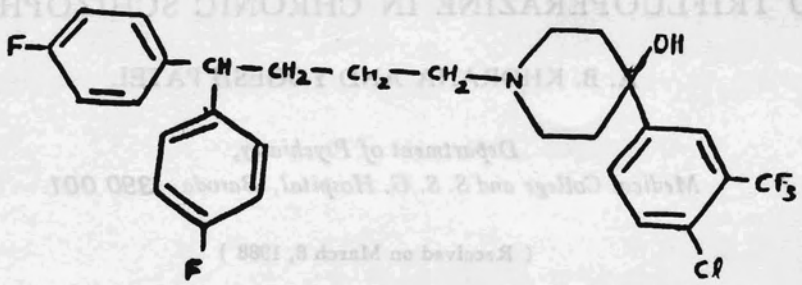
## INTRODUCTION

Maintenance therapy of chronic schizophrenia in the community is now available and possible with the introduction of newer antipsychotic drugs. However, the potential effectiveness of maintenance therapy was only partly achieved due to poor patient compliance.

The development of long-acting antipsychotics viz. fluphenazine enanthate and fluphenazine decanoate to be administered parenterally by the nursing/health care personnel on a weekly or bimonthly basis offers the advantage of ensured intake of the medication (3). Subsequently, the introduction of penfluridol, a new oral, long-acting neuroleptic administered once a week has reduced this problem of patient compliance and enabled better maintenance therapy for chronic schizophrenic patients.

Clinical studies in Europe and North America have demonstrated that penfluridol administered orally once a week has been effective and safe in controlling the symptoms of schizophrenia (1, 2, 8). Penfluridol, a diphenylbutylpiperidine (Fig. 1), has high lipid

solubility and hence, a long duration of action. It is readily absorbed after oral administration and is selectively concentrated and slowly released from the brain. It is metabolized by the liver.




Penfluridol

The present study was conducted in the Department of Psychiatry, S. S. G. Hospital, Baroda, to evaluate the efficacy and safety of this new orally long acting neuroleptic compound, in comparison with that of trifluoperazine.

## MATERIAL AND METHODS

Out of the 50 patients included in the trial 32 chronic schizophrenic patients completed the 12 week trial. The consent of the parents/guardian of all the patients were obtained prior to the initiation of the trial. Eighteen patients discontinued/dropped out for several reasons, the main being difficulty in transportation On random allocation, 15 patients were in the penfluridol group and 17 in the trifluoperazine group.

The age and sex distribution are shown in Table I. There is no significant difference ($P>0.05$) in relation to mean age and sex distribution between the two treatment groups.

TABLE I : Age (in years) and sex distribution.

| *Description* | *Penfluridol* | *Trifluoperazine* |
|---|---|---|
| *Mean Age* | 27.4000 | 31.1875 |
| S. D. | 8.8058 | 10.3423 |
| S. E. | 2.2736 | 2.5856 |
| *Sex* | | |
| Male | 11 pts. (73.33%) | 10 pts. (58.83%) |
| Female | 4 pts. (26.67%) | 7 pts. (14.17%) |

The patients were randomly assigned to one of the two groups. The first group continued on penfluridol administered on Monday morning and had placebo in capsules identical to penfluridol administered on Monday afternoon and during the rest of the week twice daily (morning and afternoon). The second group was treated with trifluoperazine administered in the form of capsules identical to those in the first group, given twice daily.

The dose of penfluridol was 20 *mg*/week and that of trifluoperazine was 70 *mg*/week i.e. 10 *mg*/day. No other medications were administered during the study except trihexphenidyl hydrochloride or procyclidine for the control of extrapyramidal symptoms.

Patients were given weekly packets (14 capsules per packet) as prepared above with randomisation and assessed every week.

The psychometric measurements used for evaluation (Table II) employed a modified rating scale which was derived from BPRS (5), Hamilton (4), Wing (7) and Venables and O'Connor Scales (6).

## RESULTS

Table II demonstrates the initial and final mean scores of individual variables which were significantly improved in both the treatment groups. Within group comparisons showed

TABLE II : Initial and final mean scores.

| | *Penfluridol* | | | *Trifluoperazine* | | |
|---|---|---|---|---|---|---|
| | *Initial* | *Final* | *Change* | *Initial* | *Final* | *Change* |
| Unco-operativeness | 1.7500 | 0.6667 | 1.000** | 2.300 | 0.600 | 1.700** |
| Emotional withdrawal | 2.4000 | 1.8000 | 1.6666** | 2.4285 | 0.5714 | 1.7857** |
| Mannerisms and Posturing | 2.6000 | 1.4000 | 1.2000** | 2.4667 | 0.2667 | 2.2000** |
| Motor retardation | 1.8889 | 0.6667 | 1.2222* | 1.8571 | 0 | 1.8571** |
| Conceptional disorganisation | 2.5833 | 0.7500 | 1.1667** | 1.1667 | 0.6000 | 1.0667** |
| Hallucinatory behaviours | 2.000 | 0.8182 | 1.1818** | 2.0000 | 0.3846 | 1.6154** |
| Suspiciousness | 1.6667 | 0.7775 | 0.8888** | 1.5555 | 0.3333 | 1.2222** |
| Anxiety | 2.2500 | 0.7500 | 1.5000* | 1.4000 | 0.2000 | 1.2000** |
| Blunted affect | 2.1428 | 0.8571 | 1.4285** | 2.6000 | 0.6000 | 1.9000** |
| Speech | 1.8000 | 0.4000 | 1.4000** | 1.5555 | 0.4444 | 1.1111** |
| Cleanliness | 1.4000 | 0.6667 | 0.7333* | 1.6154 | 0.3076 | 1.3077** |
| Social withdrawal | 1.4285 | 0.2857 | 1.1428** | 1.3571 | 0.1428 | 1.2143** |
| Laisure activities | 1.7143 | 0.6429 | 1.01144* | 1.667 | 0.4667 | 1.2000** |
| Work attitude | 2.7143 | 0.8571 | 1.8571** | 2.2667 | 0.6825 | 1.5625** |

Test : t - test
Within group = paired t - test
Between group = t - test

*Significant $P<0.05$
**Highly significant $P<0.01$

a significant reduction in the mean scores of these parameters with penfluridol and trifluoperazine therapy. Between group comparisons of the final scores revealed no significant difference thus indicating that both the drugs were equally effective in controlling these symptoms of schizophrenia.

All the BPRS factors shown in Table III showed significant improvement for both the groups. The difference between the two groups was not significant, which reveals that penfluridol is an equally effective neuroleptic when compared to trifluoperazine.

TABLE III : Mean BPRS factor scores.

| *BPRS factors* | *Penfluridol* | | | *Trifluoperazine* | | |
|---|---|---|---|---|---|---|
| | *Initial* | *Final* | *Change* | *Initial* | *Final* | *Change* |
| Anxiety depression | 2.8182 | 1.3636 | 1.4545* | 2.7692 | 0.3846 | 2.3846** |
| Anergia | 5.7333 | 2.2000 | 3.5333** | 4.2941 | 0.8824 | 3.6250** |
| Thought disturbance | 5.5333 | 2.2667 | 3.5000** | 5.3750 | 1.3125 | 4.0620** |
| Hostile suspiciousness | 2.8000 | 1.0667 | 1.9230* | 2.8667 | 0.9333 | 2.0714** |

Test : t - test
Within group = paired t-test
Between group = t - test

*Significant $P<0.05$
**Highly significant $P<0.01$

As shown in Table IV, the incidence of side effects was almost equal in both the groups, commonest were insomnia, fatigue and a few extrapyramidal symptoms which appeared from the first week of treatment.

TABLE IV : Side effects.

| | *Penfluridol* | *Trifluoperazine* |
|---|---|---|
| I. Insomnia | 9 | 8 |
| II. Fatigue | 5 | 6 |
| III. Extra pyramidal reactions | | |
| 1. Akathisia | 5 | 5 |
| 2. Tremors | 13 | 11 |
| 3. Rigidity | 4 | 5 |
| 4. Acute dystonia | 1 | 1 |
| 5. Lack of facial expression | 7 | 6 |

## DISCUSSION

The results of this study confirm earlier investigations indicating that a once a weekly oral dosage of penfluridol provides adequate and relatively safe control of chronic schizophrenia and it can maintain the level of improvement previously achieved by short acting neuroleptic agents. The data reveals that both the compounds i.e. penfluridol and trifluoperazine were similarly effective in maintenance treatment of schizophrenia. However, it should be understood that penfluridol has an advantage over trifluoperazine since it has a long duration of action and is to be administered once a week orally, thus increasing patient acceptance and improving compliance.

Although this study tested and confirmed the therapeutic efficacy of penfluridol, because of the double blind conditions penfluridol patients were required to take capsules twice a day (1 capsule of penfluridol+13 capsules of placebo as against 14 capsules of trifluoperzine for 1 week). But in actual clinical usage the maximum advantages of once a week oral administration of penfluridol could be realized in the following manner. For patients with adequate education and insight, or with reliable and informed family members, a regimen of patient-administered weekly doses and follow-up should provide effective maintenance treatment. For the less reliable patient, weekly administration of medications by health care professionals should produce maximum benefits. Not only is the burden of dispensing medication relieved but more importantly, the patient is not constantly reminded of his disease and feels less disabled. However the development of extra pyramidal effects if present may necessitate appropriate daily medications to control them. In the present study 5 patients of penfluridol group and 6 patients of trifluoperazine were given trihexphenidyl 2 *mg* b.d. initially, but since the extrapyramidal symptoms disappeared after few days of neuroleptic treatment. A. P. drug was discontinued.

Since penfluridol is the only long-acting (once a week) drug for oral administration so far available it has the clear practical advantage of being easier to administer, especially for the maintenance treatment of those patients who refuse injections or where the use of injectable depot neuroleptics is not possible for practical reasons.

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