Indian Journal of Psychiatry, October 1987, **29**(4), pp. 333-336

PENFLURIDOL MAINTENANCE THERAPY IN SCHIZOPHRENIA: A CONTROLLED STUDY

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SUMMARY

Twenty eight chronic schizophrenics were assigned in a double blind fashion to treatment with penfluridol or placebo for a period of 12 weeks. The clinical picture including the side effects were monitored regularly, whenever the clinical picture deteriorated haloperidol in individually adjusted doses was added to the treatment regimen. By the end of the study 12 out of the 14 placebo patients required haloperidol as compared to only 1 of the 14 penfluridol patients. Evaluation of the results showed no significant differences between the two groups or between the baseline and the final ratings in each group. This trial has confirmed the previous reports that penfluridol is a suitable drug for maintenance therapy in schizophrenic patients.

Introduction

The value of neuroleptic medication in preventing schizophrenic patients from relapsing has been well documented (Davis 1975). Patients on maintenance therapy who take neuroleptics irregularly are particularly at high risk for psychotic decompensation (Groves and Mandell 1975). Successful maintenance drug treatment of chronic schizophrenia is often limited by patient non-compliance. In addition to the intrinsic limitations on compliance stemming from the illness itself, difficulties result from the necessity of daily and often multiple daily drug ingestions.

This problem has led to the search for longer acting drugs. The initial approach was to use depot injectable preparations of fluphenazine. However, injections are often fraught with drawbacks and this led to the search for long-acting orally administered neuroleptics, resulting in the discovery and use of diphenylbutylpiperidine group of drugs. On these, the longest acting is penfluridol (Lapierre 1978).

Penfluridol is a potent, long-acting orally effective neuroleptic drug (Janssen 1970) which safely controls schizophrenic symptoms when administered on a weekly basis (Van Praag et al 1971; Donlon and Ellen Meyer 1978). Side effects may occur during the first 2 days, but they are very mild and can be controlled with antiparkinsonian agents (Tanghe and Verecken 1972).

In the present study the efficacy and safety of penfluridol as a maintenance therapy was evaluated double blind in chronic schnizophrenic patients who previously had been successfully maintained with other neuroleptics for at least 6 months.

Material and Methods

The subjects for this study were 30 patients diagnosed as chronic schizophrenics (DSM III) attending the Occupational Therapy and Rehabilitation department of the National Institute of Mental Health and Neurosciences (NIMHANS), Bangalore. All of them required maintenance neuroleptic therapy for control of

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continued symptoms and had been so stabilised for at least 6 months before entry into the study. All the subjects were in good general health. The purposes and procedures and the risks involved were explained to each subject and a responsible relative and written informed consent was obtained before being admitted to the study.

The patients were assigned to either penfluridol or placebo group on a double blind basis. As Table 1 indicates the two groups were comparable with respect to age, sex, duration of illness and the amount of neuroleptic medications (in mg % Chlorpromazine equivalants per day) received.

Table 1
Characteristics of the two groups

	Penfluridol	Placebo
Number of patients	14	14
Sex : Male	7	9
Female	7	5
Mean age in years	36.35	35.73
Mean duration of illness in years	10.64	11.56
Baseline medication CPZ mg. equiv./day	290	305

The patients were abruptly transferred from the previous medication and started on the trial medication. All the patients received identical capsules once a week. The dosage of penfluridol was 20 mg in the first week, 40 mg in the second week and 60 mg / week from the 3rd to the 12th week. Whenever during this study the clinical picture of a patient deteriorated Haloperidol tablets were added to the therapy at an individually adjusted dose. This was necessary on ethical grounds because the study design would otherwise mean abrupt withdrawal of maintenance neuroleptics medication in half the number of paitents participating in the study. No other medication was administered during the entire 12 weeks study period except Trihexyphenidyl hydrochloride to control extrapyramidal symptoms.

The instruments used to evaluate the efficacy and the side effects were the Scale for Assessment of Negative Symptoms (Andreasen 1981), the Scale for Assessment of Positive Symptoms (Andreasen 1985) and Simpson and Angus (1970) Rating Scale for Extrapyramidal side effects. The patients were rated on the above scales at baseline (just prior to admission to the study) and weekly thereafter till the completion of the study. Baseline and weekly records of body weight, pulse rate, blood pressure (standing and lying down) and clinical laboratory tests e.g: blood chemistry, haematology and urine analysis were maintained.

T-test (unpaired) was used for between-group comparisons. For within-group comparisons paired t-test was used.

Results

Two patients, one from each group dropped out before the completion of the study. One from the penfluridol group dropped out due to relapse of schizophrenia and rapid decompensation despite supplemental haloperidol. The one from the placebo group withdrew the consent and therefore had to be dropped out of the study. Thus 28 patients, i.e., 14 in each group were left for the final analysis.

Excluding the drop outs only 1 patient in the penfluridol group required supplemental haloperidol while 12 among the placebo group did. This indicates a significant difference in favour of penfluridol ($p < 0.042$) proving that maintenance therapy with penfluridol is superior to placebo.

Since penfluridol 60 mg per week is equivalent to haloperidol 15 mg per day the patients receiving haloperidol were

divided into 3 groups viz., those receiving less than 15 mg per day, 15 mg per day and more than 15 mg per day. This data and the dosage schedule of penfluridol are shown in Table 2. In the haloperidol less than 15 mg per day group, one patient belongs to the penfluridol group. In fact this patient needed only 5 mg of supplemental haloperidol for control of symptoms.

Table 2
Dosage of Penfluridol and Haloperidol by week of study

Week	Pemfluridol*	No. of patients on Haloperidol		
		Less than 15mg/day	15mg/ day	More than 15mg/day
1	20 mg/week	–	–	–
2	40 mg/week	–	–	–
3-12	60 mg/week	1* + 4@	5@	3@

*Penfluridol group @Placebo group

Table 3 demonstrates the number of patients in each group started on haloperidol and the week of the trial it was done. This shows that most of the patients on placebo had shown signs of relapse in the initial phase itself.

Table 3
Starting of Haloperidol week wise

Week of trial	Placebo group N=14	Penfluridol group N=14
3	6	0
4	4	0
5	1	0
6	1	1
Total No. of patients on Haloperidol	12	1

No significant differences were found between the two groups in any of the baseline evaluations. A comparative analysis of the data showed that the two agents were equally effective in controlling the schizophrenic symptoms.

In general both penfluridol and haloperidol were well tolerated. No serious adverse effects were encountered and those present were typical of the commonly used neuroleptics. Persistant extrapyramidal side effects required daily antiparkinsonian medication in 5 patients of the placebo group. Even though 6 patients of the penfluridol group required antiparkinsonian drugs none of them required it for more than 3 days a week. This finding is consistent with the previous reports that the extrapyramidal side effects of penfluridol are short lasting in spite of the long therapeutic action.

The general physical condition and the laboratory values were unaffected throughout the study period.

Discussion

The present study confirms and corroborates the previous investigations indicating that once a week oral administration of penfluridol provides adequate and safe control of chronic schizophrenia. The higher number of patients needing haloperidol in the placebo group clearly demonstrates that penfluridol is superior to placebo. It has also been shown that penfluridol maintains the level of improvement previously achieved by long acting injectable and short acting oral neuroleptics. Compared to haloperidol, penfluridol is equally efficacious but necessitates antiparkinsonian medication for a fewer days.

Thus penfluridol is a safe and effective long acting oral neuroleptic for maintenance therapy in schizophrenia. The advantage is that the patients can avoid the discomfort of daily oral medication and fortnightly injections. This also helps the

family members to better supervise the medication regimen. All these factors would contribute to better compliance and a more successful maintenance drug treatment of chronic schizophrenia.

Acknowledgements

The authors thank Dr. P.S. Gopinath, Associate Professor and Dr. P.S.V.N. Sharma, Senior Resident, Department of Psychiatry, NIMHANS, for their help in conducting this study. We thank M/s. Jannsen Pharmaceutical for supplying the penfluridol tablets.

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