FLUPENTHIXOL DECANOATE AND FLUPHENAZINE DECANOATE IN CHRONIC SCHIZOPHRENIA

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SYNOPSIS

The therapeutic and side effects of flupenthixol decanoate and fluphenazine decanoate were studied in a group of 21 chronic schizophrenic patients on regular follow-up, 16 of whom elected to be treated with flupenthixol. Results indicated that flupenthixol tended to improve significantly symptoms of depression, withdrawal and motor retardation ($p<0.05$). There is also a significant reduction in the frequency of side-effects previously experienced prior to treatment with flupenthixol ($p<0.002$). It is concluded that a group of schizophrenic patients characterised by depressive symptoms and/or side effects due to a prescribed neuroleptic would benefit from a switch to treatment with flupenthixol.

INTRODUCTION

The maintenance treatment of schizophrenic patients with neuroleptic medication is now an accepted practice to prevent patients from going into a relapse. This has been proven by many double-blind studies. (1, 2). In a review of 24 such studies, Davis (3) concluded that maintenance medication is of value in the prevention of relapses in schizophrenic patients. Similarly, Dencker et al (4) have shown that on withdrawal from neuroleptic drugs, 81% of patients relapsed within 12 months and within 2 years, 93% of patients not on active drug had relapsed. Other double-blind discontinuation studies generally reached the same conclusion (5).

The advent of depot neuroleptics have made the objective of prophylaxis against relapse in schizophrenic patients more readily attainable. This is because depot neuroleptics compared to oral medication appear to have a faster recovery rate from active illness and a lower relapse rate during remission in patients with schizophernia. (6,7) Fluphenazine decanoate (Modecate) and flupenthixol decanoate (Fluanxol) are both long acting depot neuroleptic preparations. While both drugs appear to be equally active in their anti-psychotic effects, there appear to be differences in both therapeutic and side-effects profile. Thus comparative studies of fluphenazine decanoate and flupenthixol decanoate have shown that in contrast to fluphenazine, flupenthixol has mood-elevating property. (8,9,10) Flupenthixol also appear to have a reduced number of and severity of side effects.

While fluphenazine decanoate has long been established as the standard depot neuroleptic in Singapore, flupenthixol decanoate has only been introduced here in 1983. The limited experience with flupenthixol amongst practitioners here have generally been favourable. It would therefore be of benefit to study the therapeutic and side effects of both drugs on local patients. Such a study would enable us to answer the question of whether there is any merit in prescribing a particular choice of depot neuroleptic over another.

PATIENTS AND METHODS

21 patients diagnosed as suffering from chronic schizophrenia and followed up at a psychiatric outpatient clinic were selected for study. They had to be stabilised on fluphenazine decanoate for a period of at least 6 months to qualify for inclusion. Patients with known medical condition or whose psychiatric status were linked to organic illnesses were excluded. As an open study design was adopted, patients were offered a choice of drugs, so that 16 elected to be treated with flupenthixol decanoate while 5 continued with fluphenazine decanoate.

All patients had their depot injections every 4-weekly, and they were assessed each time they presented themselves for follow-up. Assessments were carried out by either one of the investigators and the following assessment measures were used:

1) *Clinical Global Impressions (CGI)* (11) This is a global assessment of the severity of the illness on a 7-point scale.
2) *The Brief Psychiatric Rating Scale (BPRS)*, (12) to assess for the presence of psychiatric symptoms.
3) *The Hamilton Rating Scale for Depression (HDS)* (13), to assess the severity of any depressive symptoms present using the first 17 items of the scale.
4) *A Side Effects Checklist* consisting of 21 various side-effects commonly encountered in psychiatric practice in response to prescribed neuroleptic drugs.

Assessments were conducted at the time of admission into the study (week 0) and subsequently at weeks 4, 8 and 12 respectively. The Hamilton Rating Scale (HDS), was however applied at the time of admission (week 0) and at the end of study (week 12) only.

For the purpose of comparison, 40 mg of flupenthixol was considered to be equivalent to 25 mg of fluphenazine following Johnson & Malik (8). All patients in the flupenthixol group received 40 mg every 4 weeks, and all patients in the fluphenazine group received 25 mg every 4 weeks. 13 out of 16 in the flupenthixol group and 4 out of 5 in the fluphenazine group received benzhexol as an antiparkinson agent. Chlorpromazine was given to some patient as night medication and diazepam was also prescribed as an anxiolytic. There was no significant difference between the two groups as far as additional supplementary medication is concerned.

Non-parametric statistics was used throughout for the statistical analysis of the data obtained.

RESULTS

The sex and age distribution of the patients studied, as well as their duration of illness are as shown in Table 1 and 2.

The sex distribution of patients in both groups were very similar. However, patients in the flupenthixol group tended to be much older, so that the mean age of patients in the flupenthixol group is significantly higher than in the fluphenazine group ($p < 0.05$). From Table 2, patients in the flupenthixol group also appeared to have a longer duration of illness, but this difference between the group is not statistically significant.

The results of the BPRS assessments are as shown in Figure 1.

The total scores of the fluphenazine group remained fairly constant over the 12 week treatment period. In the flupenthixol group a certain reduction of score was recorded, and after 12 weeks of treatment the mean score of the flupenthixol group was significantly lower than that of the fluphenazine group ($p < 0.01$, Mann-Whitney U-Test).

TABLE 1
SEX AND AGE CHARACTERISTICS OF PATIENTS

Patient Group	Sex ratio M/F	Age (Range 29 – 55 years) 20 – 29	30 – 39	40 – 49	50 – 59	Average Age (yrs)	S.D.
Flupenthixol decanoate n = 16	7/9	2	9	4	1	38.69*	7.28
Fluphenazine decanoate n = 5	2/3	2	3	0	0	29.40	3.71

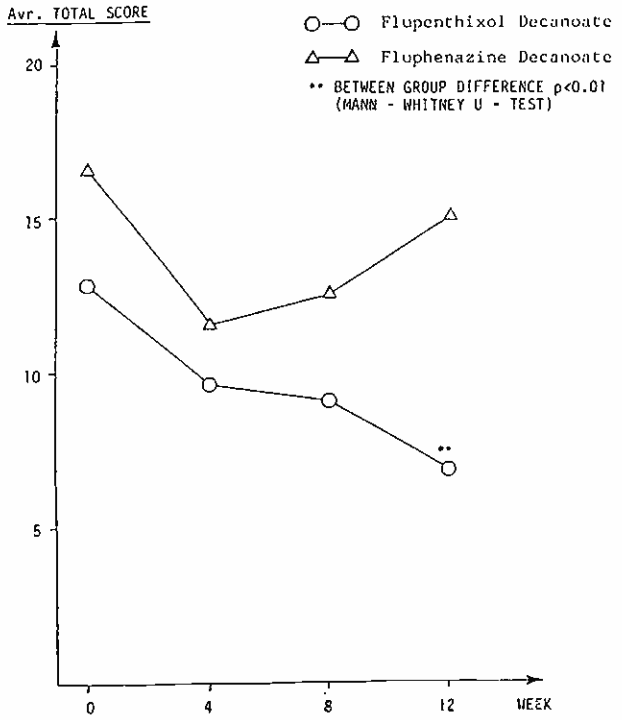
* Between Group differences $P < 0.05$, Mann Whitney U-Test.

TABLE 2
TOTAL DURATION OF ILLNESS IN PATIENTS

Group	Number of Patients			
	2 – 3 years	3 – 5 years	5 – 10 years	10 – 20 years
Flupenthixol Dec.	1	2	5	8
Fluphenazine Dec.	2	1	2	0

FIGURE 1

BPRS SCORES



The BPRS scores were further analysed into symptoms groups. Table 3 shows the result of the BPRS Symptom Group analysis.

It may be seen that the symptoms of "withdrawal-retardation" and those of "anxious-depression" responded well to treatment with flupenthixol. After 12 weeks of treatment, the scores on the "withdrawal-retardation" items of the BPRS of the flupenthixol group was significantly lower than that of the fluphenazine group ($p < 0.05$, Mann-Whitney U-Test).

The scores of patients on the Hamilton Depression Scale are as shown in Table 4.

It was observed that the initial scores of the two groups of patients on the HDS were very similar, but after 12 weeks the score of patients in the flupenthixol group was significantly lower than that of the fluphenazine group ($p < 0.05$). In the flupenthixol group the mean initial score was halved, whereas the score in the fluphenazine group remained unchanged.

On the global ratings of severity (CGI), the flupenthixol group showed a similar decrease in scores after 12 weeks of treatment (see Table 5) so that the difference in scores at week 0 and at week 12 in this group was statistically significant ($p < 0.05$, Wilcoxon Signed-rank Test). The scores between the two groups on the CGI were not significantly different however.

The results of evaluation of side-effects on the Checklist is as presented in Table 6.

It is evident from the table, that the patients who had

TABLE 3
PATIENTS' SCORES ON BPRS FACTORS

BPRS Factor	Drug	Score at Status (Week)			
		0	4	8	12
1. Thinking Disturbance (Items 4, 12, 15)	F	0.9	0.8	0.9	0.9
	M	3.4	2.8	2.3	3.0
2. Withdrawal — Retardation (Items 3, 13, 16)	F	5.0	3.7	3.1	2.4*
	M	5.8	3.8	3.5	6.0
3. Hostile — Suspiciousness (Items 10, 11, 14)	F	1.1	0.9	1.6	0.8
	M	2.8	2.6	3.8	2.6
4. Anxious — Depression (Items 2, 5, 9)	F	3.4	2.4	1.3	1.3
	M	1.2	0.2	0.8	1.0

* Between Group Differences $P < 0.05$ (Mann-Whitney U-Test)
F = Flupenthixol decanoate
M = Fluphenazine decanoate

TABLE 4
PATIENTS' SCORES ON HAMILTON DEPRESSION RATING SCALE (17 ITEMS)

Patient Group	Average Total Score	
	Status 0 Weeks	Status 12 Weeks
Flupenthixol Decanoate	9.8	4.4*
Fluphenazine Decanoate	8.0	8.6

* Between Group Difference $p < 0.05$ (Mann-Whitney U-Test)

TABLE 5
PATIENTS' SCORES ON THE CGI (INDICATING SEVERITY OF ILLNESS)

Patient Group	Score at Status (Week)			
	0	4	8	12
Flupenthixol Decanoate	2.19	1.93	1.67	1.60*
Fluphenazine Decanoate	1.40	1.75	1.67	1.60

* Wilcoxon Signed-rank Test for Flupenthixol group at week 12 compared to week 0 is $p = 0.031$.

TABLE 6
SIDE EFFECTS EXPERIENCED BY ALL PATIENTS

	No. of Side Effects at Status (Week)							
	Flupenthixol D.				Fluphenazine D.			
	0	4	8	12	0	4	8	12
Dizziness	7	3	1	1	0	0	1	0
Insomnia	4	4	1	1	0	0	0	0
Drowsiness	12	9	4	5	1	2	1	2
Depressive reactions	9	6	4	3	0	0	0	0
Anxiety	3	2	3	2	0	1	1	3
Akinesia	4	1	0	0	0	0	1	0
Parkinsonism	0	3	1	1	1	2	0	0
Acute dystonia	1	2	1	0	0	1	1	0
Akathisia	4	3	2	2	1	1	2	2
Other	45	37	17	18	4	3	4	3
Total Number	89	70	34	33*	7	10	11	10+
N	16	15	15	16	4	4	3	4
Avr. No. per Patient	5.6	4.7	2.3	2.1	1.8	2.5	2.8	2.5

* Wilcoxon signed-rank test for the difference in total scores for patients in the flupenthixol group at Week 0 and at Week 12 is $p < 0.001$.

+ Mann — Whitney U-Test for difference in average improvement between both groups is $p < 0.002$.

switched from fluphenazine decanoate to flupenthixol decanoate experienced many side-effects initially. Thus depressed mood was a problem in 9 of the patients and drowsiness in 12. Akinesia and akathisia were also recorded in some of the patients. It was also clear that the frequency of side effects decreased during the first 8 weeks of treatment with flupenthixol. In fact after 12 weeks of treatment with flupenthixol the frequency of side effects compared with that at week 0 was significantly lowered ($p < 0.001$, Wilcoxon Signed-rank Test). The average improvement in the two groups was also significantly different at the level of $p < 0.002$. The decrease in frequency of side-effects in the flupenthixol group was due largely to a reduction in symptoms such as "depressed mood", "drowsiness", "akinesia", and "dizziness" which had improved with flupenthixol.

DISCUSSION

On the basis of this present study it seems reasonable to conclude that a certain group of chronic schizophrenic patients may benefit from being switched from fluphenazine decanoate to an equivalent dose of flupenthixol. This patient group would be characterised by symptoms of depression, emotional withdrawal, motor retardation, drowsiness, or extrapyramidal symptoms.

The BPRS ratings indicated that flupenthixol decanoate had at least as strong an antipsychotic effect as fluphenazine decanoate. The total BPRS scores were considerably reduced in the flupenthixol group during the 12 weeks of treatment and this was due largely to decrease in scores on items of "anxious-depression" and "withdrawal-retardation".

It is therefore not surprising that the scores on the Hamilton Depression Scale were considerably reduced as a result of treatment with flupenthixol. This would confirmed findings by many investigators that flupenthixol decanoate has a marked antidepressant effect (8,9,10). In patients with depressive symptoms therefore, it would be advantageous to administer flupenthixol instead of another neuroleptic with the addition of an antidepressant.

In the group treated with flupenthixol side effects were found to be less frequent than previously when they were receiving medication with fluphenazine. Similar observations have also been made by Trueman & Valentine. (14) Side effects that are likely to improve with flupenthixol include drowsiness, dizziness, depressed reaction and the extrapyramidal effect of akinesia.

Although we have studied a small number of patients the results we obtained do demonstrate that flupenthixol decanoate is generally much better tolerated than fluphenazine in some patients. These would be the patients with depressive symptoms and who experienced side effects from fluphenazine. This conclusion is not only based on ratings obtained as a result of this study but also on the subjective preferences which the patients indicated after the clinical study was over.

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