chapter 9

A Double-Blind Controlled Study of Fluphenazine Decanoate and Enanthate in the Maintenance Treatment of Schizophrenic Outpatients

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Long-acting neuroleptic drugs have produced a major advance in the treatment of schizophrenic patients because they minimize absorption variability and overcome the major problem of noncompliance. The only long-acting phenothiazines available at present are esters of fluphenazine (fluphenazine enanthate and fluphenazine decanoate). There have been few controlled trials to compare their relative efficacy in the treatment of schizophrenia. In a single-dose controlled study of 1-month duration with 30 newly admitted psychotic patients, Van Praag and Dols (1) reported fluphenazine decanoate to be longer-acting than fluphenazine enanthate and to have less parkinsonian effects. However, Donlon *et al.* (2) did not confirm these results in a 2-month controlled trial including 30 newly admitted schizophrenic patients.

This paper presents the results of a 7-month double-blind controlled study to test whether fluphenazine decanoate could be substituted successfully for fluphenazine enanthate in a population of 50 schizophrenic patients undergoing maintenance treatment with fluphenazine enanthate. Most of these patients were remitted schizophrenic patients, a type of population that has been shown to need neuroleptics for maintenance

treatment (3, 4). Both drugs were given under double-blind conditions; fluphenazine enanthate every 2 weeks and fluphenazine decanoate every 4 weeks. To examine the duration of the effects of fluphenazine decanoate, evaluations were carried out 2 and 4 weeks after the injection.

METHOD

Study Designs

Fifty schizophrenic outpatients satisfying the study criteria given below, were selected from the Allan Memorial Institute Special Follow-up Clinic for long-term maintenance treatment of schizophrenic patients. All patients needed maintenance neuroleptic treatment and had received fluphenazine enanthate i.m. for at least 1 month before the study. Before the trial commenced, all patients underwent a further 1-month period of stabilization with fluphenazine enanthate. Twenty-five subjects were then allocated at random to each of the two drug treatments, fluphenazine decanoate or fluphenazine enanthate, which were administered for a period of 28 weeks. The procedure was double-blind.

Selection Criteria

Selection criteria required that: 1) patients be in the age range of 20–65 years; 2) a primary hospital diagnosis of schizophrenia be confirmed by the research psychiatrist [the diagnostic criteria used were those of the American Psychiatric Association (DSM-II) (5)]; 3) two or more of the following symptoms or behaviors be present at the time of interview or at index admission: thought or speech disturbances, catatonic motor behavior, paranoid ideation, hallucinations, delusional thinking other than paranoid, blunted, or inappropriate affect, disturbances of social behavior and interpersonal relations; 4) patients with physical illness, childhood schizophrenia, chronic or acute brain syndrome, mental deficiency (IQ below 70), alcoholism, epilepsy, or drug addiction be excluded from the study.

Patient Characteristics

Two patients did not complete the 28-week trial. One fluphenazine decanoate-treated patient was withdrawn from the study because of administrative reasons (leaving the country) after 12 weeks of treatment. The other patient was on fluphenazine enanthate and committed suicide after 22 weeks of treatment. These two patients were excluded from statistical analyses.

The 24 patients (12 male, 12 female) allocated to fluphenazine decanoate treatment ranged in age from 24 to 63 years (median 38.5) and in total length of outpatient treatment from 1.3 to 22.7 years (median 9.4); the 24 patients (15 male, 9 female) allocated to fluphenazine enanthate treatment ranged in age from 29 to 63 years (median 43.5) and in

total length of outpatient treatment from 0.7 to 25.9 years (median 8.1). Nineteen fluphenazine decanoate-treated patients and 22 fluphenazine enanthate-treated patients had previously been hospitalized for periods ranging in total duration from 0.5 to 38 months (median 4 months). Fourteen fluphenazine decanoate-treated patients and 12 fluphenazine enanthate-treated patients were classified as paranoid according to the APA DSM-II. The prestudy fluphenazine enanthate dosages ranged from 2.5–125 mg (median 25 mg) each 2 weeks for patients allocated to the fluphenazine decanoate group, and from 2.5–125 mg (median 25 mg) each 2 weeks for patients allocated to the fluphenazine enanthate group. The length of fluphenazine enanthate treatment before the trial ranged from 1 to 42 months (median 14 months) for decanoate patients and from 2 to 108 months (median 17 months) for the enanthate group.

Drug Administration

Fluphenazine enanthate was given i.m. every 2 weeks and fluphenazine decanoate was given i.m. every 4 weeks. Both preparations were administered as identical suspensions in oil of 25 mg per ml. So that the procedure would be double-blind, fluphenazine decanoate-treated patients received fluphenazine decanoate placebo (oil solution) i.m. 2 weeks after they received each dose of active medication. The initial dosages were based on the assumption that 1 ml of fluphenazine enanthate per 2 weeks was equivalent to 1 ml of fluphenazine decanoate per month (which could not be otherwise since the administration of the drugs was double-blind).

During the study the dosages of fluphenazine decanoate and fluphenazine enanthate were adjusted according to therapeutic response. The monthly dose received by fluphenazine decanoate-treated patients ranged from 2.5–125 mg (median 25 mg, mean 36.0 mg) for the 1st month, 2.5–150 mg (median 25 mg, mean 39.1 mg) at 3 months, and 2.5–250 mg (median 25 mg, mean 65.6 mg) at 7 months. For fluphenazine enanthate-treated patients the bimonthly dosages ranged from 2.5–125 mg per 2 weeks (median 25 mg, mean 40.2 mg) during the 1st month, 2.5–125 mg (median 28.1 mg, mean 43.1 mg) at 3 months, and 2.5–325 mg (median 50 mg, mean 69.1 mg) at 7 months.

If the patients are classified into low (less than 37.5 mg per 2 weeks) and high (37.5 mg or more per 2 weeks) dosage groups on the basis of their pretreatment fluphenazine enanthate dosages, the seven high-dose patients assigned to fluphenazine decanoate treatment required an increase in mean dosage from 75.0 mg of fluphenazine enanthate per 2 weeks to 155.3 mg of fluphenazine decanoate per month, and the 17 low-dose patients assigned to fluphenazine decanoate treatment were increased from a mean of 17.8 mg of fluphenazine enanthate per 2 weeks to 28.5 mg of fluphenazine decanoate per month. The corresponding in-

creases for fluphenazine enanthate-treated patients were from 75.0 mg per 2 weeks to 115.8 mg per 2 weeks for the 8 high-dose patients and from 20.5 mg per 2 weeks to 45.8 mg per 2 weeks for the 16 low-dose patients.

Two fluphenazine decanoate-treated patients required p.r.n. oral fluphenazine medication only for 12 and 14 days of the 28-week trial (means of 11 and 42 mg per day, respectively) compared to two fluphenazine enanthate-treated patients for 35 and 36 days (means of 3 and 8 mg per day, respectively).

Assessment Procedure

Assessment of symptoms was based on clinical interviews conducted by the psychiatrist. The mental status of patients was scored on the Brief Psychiatric Rating Scale (BPRS) (6) before treatment, at weeks 12 and 14, and again at weeks 26 and 28. Side effects were recorded on an extrapyramidal symptom rating scale (ESRS) (Chouinard and Ross-Chouinard) and on the Treatment-Emergent Symptoms form at the same time intervals.

The ESRS was completed by a neurologist and consisted of a subjective questionnaire of parkinsonian symptoms (Table 1), an objective examination of parkinsonism (Table 2) and dyskinetic movements (Table 3), and a clinical global impression (CGI) of tardive dyskinesia (Table 4). The presence of tardive dyskinesias was assessed following a standard procedure which includes tests of a routine neurological examination: 1) the patient's spontaneous behavior is observed while seated, standing, or walking; 2) since the abnormal movements are increased by voluntary movements of other muscle groups, the oral-facial region is observed while the patient carries out the pronation-supination test of both hands as fast as possible, performs rapid alternate movements of both wrists and the finger-nose-finger test; 3) the patient is asked to walk without shoes so that any choreoathetoid movements of the limbs can be

TABLE 1

Extrapyramidal symptom rating scale (Chouinard and Ross-Chouinard)

I. Parkinsonism Subjective Examination	Absent	Mild	Moderate	Severe
1. Impression of slowness or weakness, difficulty in carrying out routine tasks	0	1	2	3
2. Difficulty walking or with balance	0	1	2	3
3. Difficulty swallowing or talking	0	1	2	3
4. Stiffness	0	1	2	3
5. Cramps or pains in limbs, back, or neck	0	1	2	3
6. Restless, nervous, unable to keep still	0	1	2	3
7. Tremors, shaking	0	1	2	3
8. Oculogyric crisis or dystonic reactions	0	1	2	3
9. Increased salivation	0	1	2	3

TABLE 2

Extrapyramidal symptom rating scale (Chouinard and Ross-Chouinard)

II. Parkinsonism Objective Examination

1. Expressive automatic movements: (facial mask/speech)	0: Normal 1: Very mild decrease in facial expressiveness 2: Mild decrease in facial expressiveness	3: Rare spontaneous smile, decreased blinking, voice slightly monotonous 4: No spontaneous smile, staring gaze, low monotonous speech, mumbling	5: Marked facial mask, unable to frown, slurred speech 6: Extremely severe facial mask with unintelligible speech
2. Bradykinesia	0: Normal 1: Global impression of slowness in movements 2: Definite slowness in movements	3: Very mild difficulty in initiating movements 4: Mild to moderate difficulty in initiating movements 5: Difficulty in starting or stopping any movement, or	freezing on initiating voluntary act 6: Rare voluntary movement, almost completely immobile
3. Rigidity: R arm____ L arm____ R leg____ L leg____	0: Normal muscle tone 1: Very mild, barely perceptible 2: Mild (some resistance to passive movements)	3: Moderate (definite resistance to passive movements) 4: Moderately severe (moderate resistance but still easy to move the limb) 5: Severe (marked resistance	with definite difficulty to move the limb) 6: Extremely severe (nearly frozen)
4. Gait and posture	0: Normal 1: Mild decrease of pendular arm movement 2: Moderate decrease of pendular arm movement,	normal steps 3: No pendular arm movement, head flexed, steps more or less normal 4: Stiff posture (neck, back), small step (shuffling gait)	5: More marked, festination or freezing on turning 6: Triple flexion, barely able to walk

5. Tremor: R arm____ L arm____ R leg____ L leg____ Head____ Chin____ Tongue____

		Occasional	Frequent	Constant or Almost so
None	0			
Borderline	1			
Small amplitude	2	2	3	4
Moderate amplitude	3	3	4	5
Large amplitude	4	4	5	6

6. Akathisia	0: None 1: Borderline 2: Looks restless, nervous, impatient, uncomfortable	3: Often needs to move or to change position 4: Moves one extremity almost constantly if sitting, or stamps feet while standing	5: Unable to sit down for more than a short period of time 6: Moves or walks constantly
7. Increased salivation	0: Absent 1: Very mild 2: Mild	3: Moderate; impairs speech 4: Moderately severe	5: Severe 6: Extremely severe: drooling
8. Acute dystonia Location____	0: Absent 1: Very mild 2: Mild	3: Moderate 4: Moderately severe	5: Severe 6: Extremely severe
9. Nonacute dystonia: Location____	0: Absent 1: Very Mild 2: Mild	3: Moderate 4: Moderately severe	5: Severe 6: Extremely severe

TABLE 3

Extrapyramidal symptom rating scale (Chouinard and Ross-Chouinard)

III. Dyskinetic Movements Objective Examination			*Occasional**	*Frequent†*	*Constant or Almost so‡*
1. Lingual movements: slow lateral or torsion movement of tongue.	None	0			
	Borderline	1			
	Clearly present, within oral cavity	2	2	3	4
	With occasional partial protrusion	3	3	4	5
	With complete protusion	4	4	5	6
2. Jaw movements: lateral movement, chewing, biting, clenching.	None	0			
	Borderline	1			
	Clearly present, small amplitude	2	2	3	4
	Moderate amplitude, but without mouth opening	3	3	4	5
	Large amplitude, with mouth opening	4	4	5	6
3. Bucco-labial movements: puckering, pouting, smacking, etc.	None	0			
	Borderline	1			
	Clearly present, small amplitude	2	2	3	4
	Moderate amplitude, forward movement of lips	3	3	4	5
	Large amplitude; marked, noisy smacking of lips	4	4	5	6
4. Truncal movements: rocking, twisting, pelvic gyrations.	None	0			
	Borderline	1			
	Clearly present, small amplitude	2	2	3	4
	Moderate amplitude	3	3	4	5
	Greater amplitude	4	4	5	6
5. Upper extremities: choreoathetoid movements only (arms, wrists, hands, fingers)	None	0			
	Borderline	1			
	Clearly present, small amplitude, movements of one limb	2	2	3	4
	Moderate amplitude, movement of one limb or movement of small amplitude involving two limbs	3	3	4	5
	Greater amplitude, movement involving two limbs	4	4	5	6

* Occasional when activated or rarely spontaneous.
† Frequently spontaneous and present when activated.
‡ Very frequent, constant or almost constant.

TABLE 3—*continued*

III. Dyskinetic Movements Objective Examination			*Occasional**	*Frequent†*	*Constant or Almost so‡*
6. Lower extremities: choreoathetoid movements only (legs, knees, ankles, toes)	None	0			
	Borderline	1			
	Clearly present, small amplitude movement of one limb	2	2	3	4
	Moderate amplitude, movement of one limb or movements of small amplitude involving two limbs	3	3	4	5
	Greater amplitude, movements involving two extremities	4	4	5	6
7. Other involuntary movements: (swallowing, irregular respiration, frowning, blinking, grimacing, sighing)	None	0			
	Borderline	1			
	Clearly present, small amplitude	2	2	3	4
	Moderate amplitude	3	3	4	5
	Greater amplitude	4	4	5	6

TABLE 4

Extrapyramidal symptom rating scale (Chouinard and Ross-Chouinard)

IV. Clinical Global Impression of Tardive Dyskinesia

Considering your clinical experience, how severe is the tardive dyskinesia at this time?

1 Absent
2 Borderline
3 Very mild
4 Mild
5 Moderate
6 Moderately severe
7 Marked
8 Severe
9 Extremely severe

noted; and 4) the patient is also asked to copy a spiral with both hands and to sign his name (as the test is being performed under emotional tension, dyskinetic movements may be activated and covert dyskinesias are sometimes uncovered). In doubtful cases, the patient is asked to open the mouth while performing the pronation-supination and alternate movement tests, so that the tongue can be observed. When rating the extrapyramidal symptoms, the neurologist examined the patient for spontaneous tremors and those that were manifest when the patient extended both arms forward with palms down and eyes closed, or during performance of the spiral test and handwriting. From the individual items

summed scores were formed for the subjective assessment of parkinsonian symptoms, for the objective evaluation of parkinsonism (nonacute dystonia was excluded), and for dyskinetic movements.

Patients were withdrawn from their antiparkinsonian medication 2 days before their baseline evaluations, immediately after which antiparkinsonian medication was resumed as necessary.

RESULTS

The results on each rating scale at weeks 10, 12, 26, and 28 were analyzed separately by analysis of covariance using initial scores as covariate. There were no trends for a departure from the assumption of homogeneity of covariate regression coefficients for the two treatment groups, so a pooled covariate regression coefficient was used in each analysis of covariance (7).

Table 5 shows the initial and adjusted mean scores for the BPRS total and factors at each evaluation for patients in the two treatment groups. There were no statistically significant differences between the two groups of patients for the BPRS total or factor scores after 10 and 12 weeks of treatment. However, after 28 weeks of treatment there was a tendency ($p < .10$) for the adjusted mean BPRS total score of patients treated with fluphenazine decanoate to be higher than that of patients treated with fluphenazine enanthate, whereas at 26 weeks there was no statistically significant difference between the two groups (Figure 1). A paired t-test comparing the unadjusted mean BPRS total scores at week

TABLE 5

Initial and adjusted final mean scores at weeks 0, 10, 12, 26, and 28 of study for brief psychiatric rating scale total and factors

	Week of Study				
	0	10	12	26	28
BPRS total					
Decanoate	26.0	24.9	24.3	25.0	28.2*
Enanthate	27.3	24.9	25.0	25.8	25.6
BPRS thinking disturbance					
Decanoate	1.3	1.3	1.3	1.2	1.4
Enanthate	1.4	1.3	1.3	1.2	1.3
BPRS hostile suspiciousness					
Decanoate	1.2	1.2	1.1	1.2	1.2
Enanthate	1.2	1.1	1.1	1.1	1.1
BPRS withdrawal retardation					
Decanoate	1.8	1.8	1.7	1.7	2.0
Enanthate	2.2	1.9	1.9	1.8	2.0
BPRS anxious depression					
Decanoate	1.5	1.3	1.4	1.6	1.8
Enanthate	1.3	1.3	1.4	1.6	1.5

* Statistically significant ($p < .10$) difference between adjusted mean scores of patients treated with fluphenazine decanoate and those treated with fluphenazine enanthate.

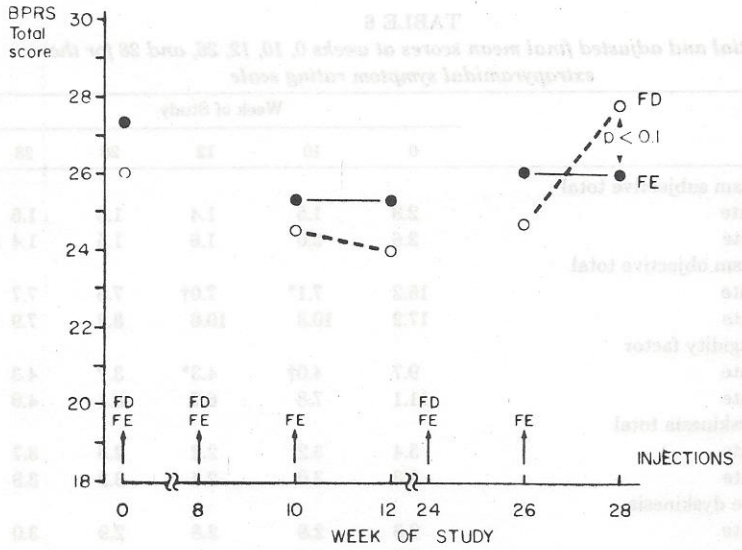

FIGURE 1. Therapeutic outcome over time as measured by unadjusted mean BPRS total scores (FE, fluphenazine enanthate; FD, fluphenazine decanoate); significant difference between treatment means at week 28 applies to adjusted means as obtained from analysis of covariance.

28 with those at week 26 showed that there had been a statistically significant ($p < .001$) increase in psychopathology of patients treated with fluphenazine decanoate during this 2-week period, whereas the mean score for patients treated with fluphenazine enanthate was unchanged.

Table 6 shows the initial and adjusted mean scores for the extrapyramidal symptoms at each evaluation for patients in the two treatment groups. There was a trend for a swifter reduction in parkinsonian symptoms among patients treated with fluphenazine decanoate than among patients treated with fluphenazine enanthate, as evidenced by statistically significant differences between the adjusted mean total scores for the objective scale (nonacute dystonia excluded) at week 10 ($p < .10$) and week 12 ($p < .05$). However, at the end of the study this difference had disappeared (Figure 2). A similar trend can be seen for the akinesia-rigidity factor score which was formed from the summed scores for expressive automatic movements, bradykinesia, rigidity, gait, and posture. With regard to tardive dyskinesia, no statistically significant differences could be detected between the adjusted mean scores for the two treatment groups during the study. However, a paired t-test comparing the unadjusted mean total scores for tardive dyskinesia at week 28 with those at week 26 showed that there had been a statistically significant ($p < .05$) increase in dyskinetic movements of patients treated with fluphenazine decanoate during this 2-week period, whereas the change in the

TABLE 6

Initial and adjusted final mean scores at weeks 0, 10, 12, 26, and 28 for the extrapyramidal symptom rating scale

	Week of Study				
	0	10	12	26	28
Parkinsonism subjective total					
Decanoate	2.8	1.5	1.4	1.8	1.5
Enanthate	2.6	2.0	1.6	1.5	1.4
Parkinsonism objective total					
Decanoate	15.2	7.1*	7.0†	7.6	7.7
Enanthate	17.2	10.3	10.6	8.2	7.9
Akinesia-rigidity factor					
Decanoate	9.7	4.0†	4.3*	3.7	4.3
Enanthate	11.1	7.8	6.7	5.1	4.9
Tardive dyskinesia total					
Decanoate	3.4	3.2	2.2	2.8	3.7
Enanthate	2.3	3.0	2.4	3.2	3.9
CGI tardive dyskinesia					
Decanoate	2.8	2.8	2.8	2.9	3.0
Enanthate	2.7	2.5	2.3	2.9	2.9

Statistically significant (*$p < .10$; †$p < .05$, respectively) difference between adjusted mean scores of patients treated with fluphenazine decanoate and those treated with fluphenazine enanthate.

mean total score for patients treated with fluphenazine enanthate did not reach statistical significance (Figure 3). At the beginning of the study 10 patients (42%) in the decanoate group and 12 patients (50%) in the enanthate group presented with symptoms of tardive dyskinesia; after 28 weeks of treatment 13 decanoate-treated patients (54%) and 17 enanthate-treated patients (58%) presented with tardive dyskinesia.

Antiparkinsonian Medication

Before the trial commenced 20 patients in the fluphenazine decanoate group and 18 patients in the fluphenazine enanthate group were receiving procyclidine HCl (Kemadrin) for their parkinsonian symptoms; the mean daily dosages during the month preceding the trial ranged from 4.5–32.9 mg (median 10.0 mg) and from 7.0–35.0 mg (median 16.8 mg) for each group, respectively. No other antiparkinsonian medication was administered. During the trial 21 patients treated with fluphenazine decanoate and 20 patients treated with fluphenazine enanthate required procyclidine HCl; the mean daily dosages throughout the trial ranged from 0.6–39.2 mg (median 13.4 mg) for patients treated with fluphenazine decanoate and from 0.3–40.7 mg (median 15.1 mg) for patients treated with fluphenazine enanthate. Neither before nor during the trial were there any statistically significant ($p < .05$) differences between the two groups of patients with regard to the number of patients requiring antiparkinsonian medication or the mean dosage received (converted to logarithms as the distribution was skew).

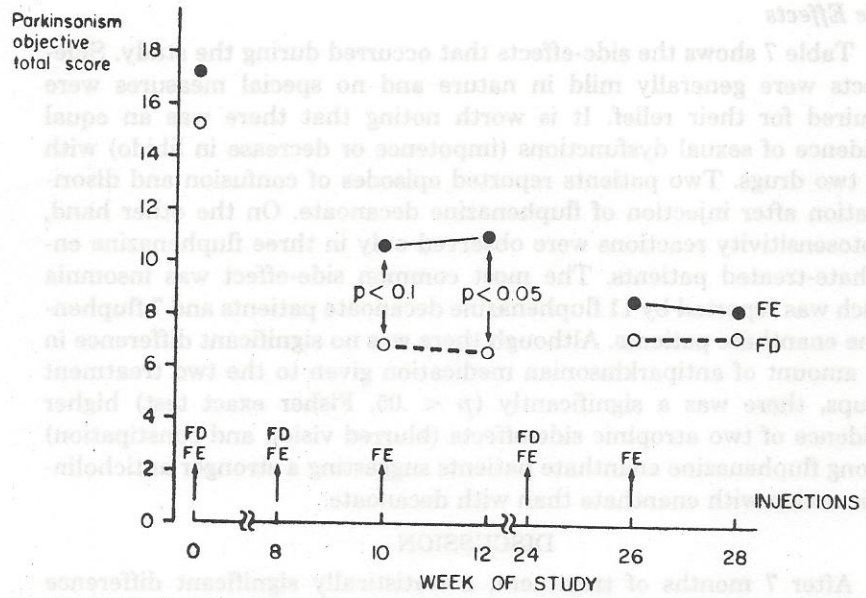

FIGURE 2. Parkinsonism over time as measured by unadjusted mean objective total scores (FE, fluphenazine enanthate; FD, fluphenazine decanoate); significant differences between treatment means at weeks 10 and 12 apply to adjusted means as obtained from analyses of covariance.

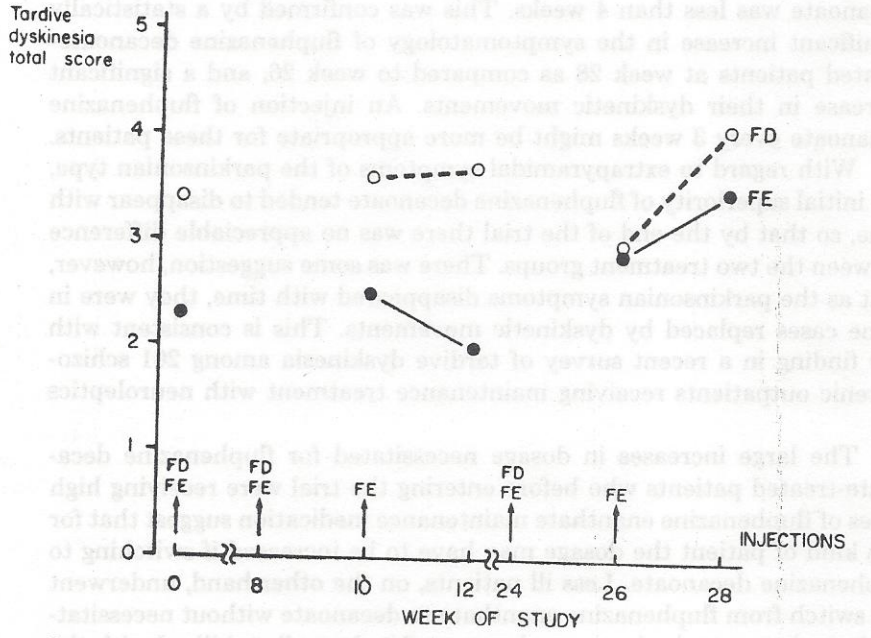

FIGURE 3. Tardive dyskinesia over time as measured by unadjusted mean total scores (FE, fluphenazine enanthate; FD, fluphenazine decanoate).

Side Effects

Table 7 shows the side-effects that occurred during the study. Side-effects were generally mild in nature and no special measures were required for their relief. It is worth noting that there was an equal incidence of sexual dysfunctions (impotence or decrease in libido) with the two drugs. Two patients reported episodes of confusion and disorientation after injection of fluphenazine decanoate. On the other hand, photosensitivity reactions were observed only in three fluphenazine enanthate-treated patients. The most common side-effect was insomnia which was reported by 11 fluphenazine decanoate patients and 7 fluphenazine enanthate patients. Although there was no significant difference in the amount of antiparkinsonian medication given to the two treatment groups, there was a significantly ($p < .05$, Fisher exact test) higher incidence of two atropinic side-effects (blurred vision and constipation) among fluphenazine enanthate patients suggesting a stronger anticholinergic action with enanthate than with decanoate.

DISCUSSION

After 7 months of treatment, a statistically significant difference between the mean psychopathologic ratings of patients treated with fluphenazine decanoate and those treated with fluphenazine enanthate occurring 4 weeks after the decanoate injection (but not after 2 weeks) suggests that for some patients the duration of the effects of fluphenazine decanoate was less than 4 weeks. This was confirmed by a statistically significant increase in the symptomatology of fluphenazine decanoate-treated patients at week 28 as compared to week 26, and a significant increase in their dyskinetic movements. An injection of fluphenazine decanoate every 3 weeks might be more appropriate for these patients.

With regard to extrapyramidal symptoms of the parkinsonian type, the initial superiority of fluphenazine decanoate tended to disappear with time, so that by the end of the trial there was no appreciable difference between the two treatment groups. There was some suggestion, however, that as the parkinsonian symptoms disappeared with time, they were in some cases replaced by dyskinetic movements. This is consistent with our finding in a recent survey of tardive dyskinesia among 261 schizophrenic outpatients receiving maintenance treatment with neuroleptics (8).

The large increases in dosage necessitated for fluphenazine decanoate-treated patients who before entering the trial were receiving high doses of fluphenazine enanthate maintenance medication suggest that for this kind of patient the dosage may have to be increased if switching to fluphenazine decanoate. Less ill patients, on the other hand, underwent the switch from fluphenazine enanthate to decanoate without necessitating large increases in dosage and appeared to be well stabilized with the monthly fluphenazine decanoate injections.

TABLE 7
Side effects

	Fluphenazine Decanoate Degree of Severity*			Fluphenazine Enanthate Degree of Severity*		
	1	2	3	1	2	3
Behavioral effects						
Depression	1	1		2		
Drowsiness	4			5	2	
Excitement	1	2	1		1	
Insomnia	7	2	2	2	3	2
Confusion/disorientation		2				
Autonomic effects						
Blurred vision	1			7		
Constipation	2			6	2	
Dry mouth	3	2		3		
Nausea/vomiting	1					
Tachycardia	1					
Sweating					1	
Endocrine effects						
Anorexia	1	1				
Increased appetite	1					
Impotence/decrease in libido			2	1	1	
Others						
Hypersomnia	6	1		4	2	
Dizziness	2			1		
Weakness/fatigue	1			1		
Photosensitivity				2	1	

* 1 = mild; 2 = moderate; 3 = severe.

REFERENCES

1. Van Praag HM, Dols LCW: Fluphenazine enanthate and fluphenazine decanoate: a comparison of their duration of action and motor side effects. *Am J Psychiatry* 130:801–804, 1973.
2. Donlon PT, Axelrad AD, Tupin JP, *et al.*: Comparison of depot fluphenazines: duration of action and incidence of side effects. *Compr Psychiatry* 17:369–376, 1976.
3. Hirsch SR, Gaind R, Rohde PD, *et al.*: Outpatient maintenance of chronic schizophrenic patients with long-acting fluphenazine: double-blind placebo trial. *Br Med J* 1:633–637, 1973.
4. Rifkin A, Quitkin F, Rabiner CJ, *et al.*: Fluphenazine decanoate, fluphenazine hydrochloride given orally, and placebo in remitted schizophrenics. *Arch Gen Psychiatry* 34:43–47, 1977.
5. The Committee on Nomenclature and Statistics of the American Psychiatric Association: *Diagnostic and Statistical Manual of Mental Disorders*, 2nd ed. (DSM-11). Washington, D.C., American Psychiatric Association, 1968.
6. Overall JE, Gorham DR: The brief psychiatric rating scale. *Psychol Rep* 10:799–812, 1962.
7. Winer BJ: *Statistical Principles in Experimental Design*, 2nd ed. New York, McGraw-Hill Book Co., 1971, pp 764–775.
8. Chouinard G, Annable L, Ross-Chouinard A: *Factors related to tardive dyskinesia* (Abstract). Scientific Proceedings of the 130th Annual Meeting of the American Psychiatric Association, May 2–6, 1977, Toronto, Canada. *Am Psychiatr Assoc* 88:52, 1977.