Outpatient treatment of psychotic patients with a long-acting phenothiazine: Fluphenazine decanoate

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Introduction

SINCE APRIL, 1970 the Department of Psychological Medicine, University Hospital, Kuala Lumpur, Malaysia has been using fluphenazine decanoate, a new, long-acting phenothiazine on selected psychiatric outpatients. This is a report of the first 15-month experience with this intermuscular drug.

A consistent problem in the management of psychiatric outpatients has been their refusal to take oral phenothiazine. This has often led to a relapse of symptoms, which required rehospitalisation. A recent study (Irwin, et al, 1971) which confirms older studies, found 35% of chronic schizophrenic outpatients were not taking minimal amounts of medication. A long-acting injectable phenothiazine overcomes this problem by assuring that the patient receives his medicine. This provides better control of his illness.

A second advantage of the long-acting phenothiazine is lowered accumulative toxicity for chronic patients. Relatively small quantities of the medicine is required as it is effective over several weeks due to its substained release properties. Thus the total accumulative body dose is markedly reduced. No significant delayed or cumulative toxicity, which has been found with other phenothiaziness, have appeared with fluphenazine decanoate (Grozier, 1971).

Oral fluphenathiazine hydrochloride is a major tranquilliser of the piperazinyl group. It has been prepared in two long-acting forms; enanthate, a heptanoic acid ester, and decanoate, a decanoic acid ester. Fluphenazine enanthate has been found to be an effective long-acting anti-psychotic agent (Hsu, et al, 1967; Haider, 1968; Karkalus, 1968; Kinross-Wright et al 1963; Kline, et al 1970).

The decanoate preparation was developed to give a longer duration of action as well as fewer side effects. Studies have found fluphenazine decanoate to be similar to the enanthate form in treating chronic hospitalised schizophrenics (Kurland and Richardson, 1966) and in chronic schizophrenic outpatients (Keskiner, et al, 1969; Bucci, 1970). Further work has supported the value of decanoate in chronic psychosis (Itil and Keskiner, 1970; Grosser, 1970; Neal, 1970; Keskiner et al, 1968). Grozier, in 1971, reporting on the 862 patients treated with fluphenazine decanoate in the combined studies, stated 68% had a satisfactory clinical response, 32% had extra pyramidal reactions but only 0.5% had to discontinue because of the adverse effects.

Patient Population and Method

Between April 1, 1970 and January 31, 1971, a total of 31 patients were given fluphenazine decanoate. The final evaluation of the patients was made in July 1971. Thus patients who continued taking the medication had a minimum of six months drug trial and some had as long as 15 months.

The patients were selected on the basis of chronicity of their illness, a failure to respond to oral medication or a strong suspicion that they were not taking oral medication. All but one (senile psychosis) was diagnosed as schizophrenic, usually chronic undifferentiated type. Ten patients had symptoms for more than four years, including four patients who were ill for more than seven years. The average duration since first onset of symptoms was 4.6 years. All had been on oral phenothiazine previously and most had multiple hospital admissions. Of 31 patients, 15 were males and 16 females. The patients were a mixed racial group comprising 19 Chinese, 3 Malays, 3 Indians, 4 Aborigines (Orang Asli) and 2 Eurasians.

Most patients were started on decanoate as outpatients but some were started during an inpatient admission after the acute symptoms were controlled by oral medication. The starting dosage usually was 25 mgm. intermuscularly given in the upper gluteal region. The dosage and duration were adjusted according to the clinical response. Anti-Parkinsonian medication, Benzhexol 2 mgm. b.i.d. was given to cover potential extra pyramidal effects.

Results

Dosage and duration of action: The dosage for each individual patient was quite variable in the early phases of treatment but a stable pattern for each patient emerged. The dosage ranged from 12.5 mgm. to 37.5 mgm. and the duration of action varied from three to six weeks. For the patients who were continued for six months or more, the great majority (18 of 21) required one injection every four weeks. One required medication every five weeks and two could be maintained for six weeks. The dose was 25 mgm. in 11 cases (52%) and 12.5 mgm. in eight cases (38%). Two cases required 37.5 mgm.

Clinical Response: The patients who were continued on medication were given a global rating of their clinical response at the final evaluation. This was a composite score of:

(1) self-rating of their improvement,
(2) when possible a relative or personal contact's rating of patient's behaviour, and
(3) the psychiatrist rating of the presence of psychopathology.

The following was the criteria for the 5-point scale:-

1) Excellent: Patient has no symptoms nor impairment and is able to function as well as prior to first symptoms.
(2) Much improved: Patients has residual symptoms but is able to function with minimal distress to family and community.
(3) Improved: Patient has a moderate degree of symptoms but is more stable and less disabled than previously.
(4) No change.
(5) Deteriorated: Patient has increased symptoms and more social impairment.

Table 1 shows the results of all the patients who received fluphenazine decanoate. A total of 21 patients, all those who stayed on medicine for six months or more, had at least some improvement. The majority were rated at much improved or excellent. If this total group are considered "satisfactory responses", then the overall improvement rate is 68%.

Seven or 23% dropped out from the treatment. Three stopped within two months and one at three months. Three continued past four months and were reported doing well. One patient showed continued deterioration on the drug and long-term hospitalisation was recommended.

Side Effects: As seen in Table I, two patients had much severe side-effects that further medicine could not be given. Both had received only 12.5 mgm. fluphenazine decanoate on two occasions. One became very restless and agitated for two days following each injection and refused treatment on the third injection. The other patient had severe neck stiffness, drawling, rigidity and an oculogyric crisis after the second injection. Both patients were placed on other phenothiazines but did poorly and had to be hospitalised within six months.

The overall incidence of side-effects are seen in Table II. Most side effects were mild and controlled by an anti-Parkinsonian drug, Benzhexol. Although most patients were started on Benzhexol, it was found to be unnecessary with many patients. However, when patients were urged to try without the anti-Parkinsonian drug, many reported much therapeutic value attributable to the drug and refused to give it up. This implies a strong psychological dependency and placebo-effect from daily use of an anti-Parkinsonian drug.

Table 1

Results of Patients Receiving Fluphenazine Decanoate

		Total	Percentage
Continued medication 6 months or more		21	68%
Excellent	3		
Much improved	13		
Improved	5		
No change	0		
Deteriorated	0		
Dropped out		7	23
Stopped because of side effects		2	6
Deteriorated and required hospitalisation		1	3
		31	100%

TABLE II

Fluphenazine Decanoate Side-Effects

		Total	Percentage
None		13	42%
Patients with extra-pyramidal effects		8	26
* Restless/akathesis	3		
Rigidity	4		
Tumors of hand	3		
Occulagyric crisis	1		
Stiff tongue/mouth protrude	2		
Excessive weight gain		2	6%
Drowsy		1	3
Unable to think clearly — "feel in a daze"		2	6
More withdrawn		1	3
Irritable		1	3
Poor appetite		1	3
Initial hyperactivity reported		1	3
Slightly depressed		1	3

* Many patients reported more than one extra-pyramidal symptom.

No irritation or inflammation developed at the injection site. Interestingly, one patient while on fluphenazine decanoate conceived and delivered a normal infant.

Patient's Acceptance: Seventeen patients were asked regarding their preference for monthly injections or daily oral anti-psychotic medication. Thirteen or 76% preferred the injections, indicating a high degree of acceptance.

Discussion

The results show that fluphenazine decanoate has a long duration of action of about four weeks, and is an effective drug for the maintenance of these difficult, schizophrenic patients. It has significant advantages of convenience, good tolerance and patient acceptability. Like other phenothiazines, fluphenazine decanoate rarely completely relieves all of the schizophrenic symptoms; however, over half of the patients were reported to be much improved or functioning normally. Sixty-eight per cent of our patients on long-term dosage were found to make some improvement. This is identical to Grozier's (1971) report of percentage of satisfactory responses.

Side-effects can be troublesome to some patients on an idiosyncratic basis, especially following the first few injections. Two people (6%) had to be dropped from this study because of their adverse reactions. Extra pyramidal effects were reported by 26% (eight) and some side-effects mentioned by all but 42% of the patients. The tendency to report adverse effects became much less as the drug was taken longer. Extra pyramidal side-effects generally responded to anti-Parkinsonian drugs and even this was found to be less necessary as treatment progressed. Nevertheless, many patients became psychologically dependent upon these drugs, ascribed to them specific therapeutic value, and were reluctant to give them up.

The study indicates a group of special concern — those who respond well to medication but fail to return for further injections. This drop-out group represents nearly one-fourth of the total population. This group responded well and reported few side-effects. It is possible that this group felt so much improved that they felt no need to be continued upon the medication. Considerable research indicates that the relapse rate is very high among schizophrenics who stop medication prematurely (Englehardt, 1967). This high drop-out group emphasises the need for further patient education about their illness and its treatment.

The Aborigine patients, of whom four were included in this study, indicate the unique value of fluphenazine decanoate. These patients often live in remote jungle areas far from medical facilities. Here chronic psychiatric patients are a real challenge to medical management. Fluphenazine decanoate has been used to stabilise these patients at Gombak Aborigine Hospital and then they can be returned to their homes. An Aborigine medical staff gives them their monthly injection in the jungle. They are returned for medical evaluation every three months. This has proved to be an effective therapeutic approach and currently ten patients have been maintained in this manner.

A further consideration is the substantial savings in cost. Currently a 12.5 mgm. ampule of fluphenazine decanoate costs the patient M$4.00. The great majority of patients could be maintained for M$4.00 or M$8.00 per month. Even at M$8.00 a month, the cost would be one-half of a comparable monthly maintenance drug supply of chlorpromazine and one-third the cost of perphenazine.

Summary

This report is about the University Hospital, Malaysia, first 15-month experience with fluphenazine decanoate, a long-acting intermuscular form of phenathiazine; 31 chronic psychiatric patients were started on the drug with a minimum follow-up period of six months. The drug generally could be given in a dose of 12.5 or 25 mgm. every four weeks. Sixty-eight per cent showed some improvement and 18 (58%) had much improvement or excellent response. Seven (23%) dropped out and one deteriorated and required hospitalisation. Although two were discontinued because of adverse effects, the side-effects tended to be mild, became less troublesome with longer use and controllable with anti-Parkinsonian medication. Fluphenazine decanoate has significant advantages in treating chronic psychiatric outpatients because of its long duration, of providing certainty that the patient receives his medication and because of good patient acceptance and lower cost.

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