HALOPERIDOL: A CONTROLLED TRIAL IN CHRONIC SCHIZOPHRENIA

By

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HALOPERIDOL is a comparatively new tranquillizing drug synthesized by Janssen *et al.* (1959). It is chemically unrelated to other drugs acting on the nervous system. It is a substituted butyrophenone whose formula is 4-fluro-4(1-[4-hydroxy-4-(4-chloro)-phenyl-piperidino]) butyrophenone.

Several reports have been published on its use in clinical psychiatry, mainly on the Continent, and a symposium was devoted to it in Brussels in September, 1959. Di Poggio (1960) noted a rapid sedative effect on psychomotor agitation; he found a low incidence of extra-pyramidal side-effects (1·5 per cent.). Delay *et al.* (1960) found the drug "remarkably efficient and quick acting" in doses of 3 to 7 mg. daily in a mixed group of psychotic patients. Gerle (1960) reported favourable results in chronic schizophrenics failing earlier to respond to other neuroleptics. Jacobs (1960) found that it stimulated appetite and weight increase. Azima *et al.* (1960) found the drug "much less effective than claimed by European authors and with numerous side-effects". Enoch and Robin (1960) reported the drug of "limited value in the symptomatic treatment of long-standing schizophrenic patients".

METHOD

Fifty-two schizophrenic patients (32 males and 20 females) were selected from the continued treatment wards for the trial. They were divided into two groups on the basis of a list of random numbers supplied by the drug company. Each group contained 26 patients. Our pharmacist allotted the patients from an alphabetical list supplied by us. The trial was double-blind (as far as it could be, using a drug with numerous side-effects). The diagnostic sub-groups were as follows:

	Haloperidol	Control
Paranoid	9	10
Catatonic	5	4
Hebephrenic	9	8
Simple	3	4
Total	26	26

All the patients have previously been treated with one or more of the following: insulin, E.C.T., barbiturates, paraldehyde and one or more tranquillizers.

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The age and duration of illness was:

	Haloperidol	Control
Age range	32 to 64 years	22 to 66 years
Average	46·8 years	44 years
Duration of Illness:		
Range	4 to 24 years	5 to 26 years
Average	16·8 years	12·2 years
Duration of Hospitalization:		
Range	4 to 24 years	1 to 26 years
Average	13·4 years	11·4 years

The low dosage schedule was used (using 1·5 mg. tablets): ½ tablet daily for 4 days; ½ tablet b.d. for 4 days; 1 tablet b.d. for 4 days; 1 tablet t.i.d. for 4 days; 2 tablets b.d. for 28 days.

After the sixth week, dosage was cut to a maintenance level of one tablet (1·5 mg.) two or three times daily, for a further six weeks.

Laboratory tests (liver function, blood counts and urinalysis) were carried out before and at intervals of three weeks during the trial. Blood pressures and weights were recorded weekly—pulse and respiration daily. Before the trial began all treatment was stopped and patients were observed for a period of two weeks.

Ratings were simply "much improved" (discharged), "improved", "unchanged", "worse", or "much worse" (trial stopped because of mental deterioration), these were recorded weekly by one of us and by the nursing staff.

Two patients were withdrawn from the trial, one had a recurrence of a skin rash (he was eventually found to be on the placebo) and the other was found to have early pulmonary tuberculosis on routine chest X-ray. We were finally left with 50 patients (25 on drug and 25 on controls) who completed the trial.

Results

	Haloperidol	Control
Much improved	None	None
Improved	7 (28 per cent.)	4 (16 per cent.)
Unchanged	18 (72 per cent.)	16 (64 per cent.)
Worse	0	4 (16 per cent.)
Much worse	0	1 (4 per cent.)

No patient improved to such an extent that he could be discharged, neither did any patient on the drug get "worse" or "much worse". Of the seven patients who improved on the drug, three were hebephrenic, two paranoid and two simple schizophrenics.

Side-Effects

Side-effects were noted in 18 (72 per cent.) cases. Extrapyramidal side-effects appeared in 13 (52 per cent.) patients as follows:

Tremor	10 (40 per cent.)
Rigidity	10 (40 per cent.)
Akathisia	6 (24 per cent.)
Oculogyric crises	1 (4 per cent.)
Drooling	1 (4 per cent.)

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The dosage level which produced the above effects varied between 3 and 6 mg. daily. They were controlled by one of the anti-Parkinson drugs.

Jaundice appeared in one patient the day after the trial ended. Changes (increase in the serum bilirubin) were noted in her liver function tests in the final days of the trial. She had an uneventful recovery.

Vomiting occurred in two patients two days after completion of the trial and lasted twenty-four hours.

There were no significant changes in weight during the trial.

Summary

The results of a controlled study of haloperidol on twenty-five long-standing schizophrenics is reported. Haloperidol is moderately effective in the treatment of chronic schizophrenia. Side-effects (mainly extrapyramidal) appeared in almost 75 per cent. of the cases, although the low dosage schedule was used.

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