

Are There Schizophrenics for Whom Drugs May be Unnecessary or Contraindicated?<sup>1</sup>

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Abstract. This study reports that there are schizophrenics who do relatively well long term without the routine or continuous use of antipsychotic medication. Specially selected young males undergoing an acute schizophrenic episode were followed, after hospitalization, for up to three years. While hospitalized they were assigned randomly to either placebo or chlorpromazine treatment. Many unmedicated-while-in-hospital patients showed greater long-term improvement, less pathology at follow-up, fewer rehospitalizations and better overall function in the community than patients who were given chlorpromazine while in the hospital. Factors related to post-hospital outcome were good premorbid history and short-lived paranoid characteristics. Considerations which may have an effect on the successful management of acute schizophrenic patients not on medication are mentioned. The findings underline the need for further study of how to utilize antipsychotic medication more selectively in the treatment of schizophrenia.

For most patients diagnosed as schizophrenic, antipsychotic medication is the treatment of choice. Several reports have indicated, however, that some patients do better or get along quite well long term without the use of antipsychotic medication (Sullivan, 1953; Menninger, 1959; Perry, 1962, 1976; Dabrowski and Aronson, 1964; Goldberg et al., 1965; Lehman, 1967; Mosher et al., 1974; Silverman, 1974; Rappaport, 1978). Other reports indicate that phenothiazines may have less than helpful effects on some patients (Hartlage, 1964; Goldstein, 1970; Magaro and Vojtisek, 1971).

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In this study clinical outcome was examined in young hospitalized patients after the onset of an acute schizophrenic episode and for up to three years after discharge. Of particular interest was the examination of patients who were off antipsychotic medication at follow-up but who, while hospitalized, had been assigned randomly to either a placebo or chlorpromazine medication condition.

### *Subjects, Procedures and Measures*

Data are reported on 80 young male acute schizophrenics admitted to Agnews State Hospital (San Jose, California). Patients selected for the project met the following criteria: they were between 16 and 40 years old; they were referred from the community mental health program with a diagnosis of schizophrenia and also diagnosed independently as having an acute schizophrenic reaction at admission when examined by the hospital psychiatrist (who was not directly associated with the project) and by research personnel who evaluated patients using the Brief Psychiatric Rating Scale and a Global Assessment Scale; they had no serious adverse reaction to chlorpromazine; they had undergone no electroshock therapy within six months preceding admission; they had no gross organic impairment; they had no history of epilepsy; they had no known history of drug abuse immediately prior to admission; and they had no or few previous hospitalizations.

When a patient was accepted for the project he was assigned randomly to either a placebo or chlorpromazine condition. Over 80% were between 16 and 25 years of age, the two oldest patients were 38. Seventy-four percent had one or no previous hospitalization. Most were single and unemployed (83% and 57%, respectively).

### *Patient Assessment*

At admission a patient received a physical and mental status examination. On that day, or the following two, trained research personnel also interviewed each patient and completed a modified form of the Brief Psychiatric Rating Scale (BPRS) by *Overall and Gorham* (1962), a Global Assessment (GA) Rating Scale, a premorbid history form based upon *Kantor's Process-Reactive Criteria* (1966) and a paranoid-nonparanoid form based upon the *Venables and O'Connor* scale (1959). At discharge and at follow-up the administration of the BPRS and GA scales was repeated.

A composite measure based primarily on elements of the BPRS was designated as the experimental measure of severity of illness (SI). Elements of the BPRS were grouped to reflect thought disturbance, emotional disturbance, and functional disturbance. These three scores were combined with a global assessment rating (GA) to yield an overall SI score that ranged between 1 and 7 representing no disturbance to extremely severe disturbance.

A clinical change index (CI) was also used. It reflects change in clinical status over time obtained by recording improvement or worsening (as a plus or minus score respectively) that occurred between admission and discharge from the project as well as between admission and last follow-up contact. Direction of change was recorded for each measure and divided

by the number of measures available. This yielded scores ranging between +1.00 (improved on all items) through 0.00 (no change) to -1.00 (worse on all items).

#### Medication

All patients took nine tablets a day (three, three times a day). Those assigned to the chlorpromazine condition received a minimum of 300 mg a day. The physician could order up to 900 mg of chlorpromazine a day but he and the nursing staff remained blind as to whether the patient was receiving medication or placebo.

#### Follow-up

Follow-up measures consisted of BPRS and GA ratings obtained, whenever possible, at 1, 3, 6, 12, 18, 24, 30 and 36 months after discharge from the hospital portion of the project. Ratings were made by a trained research assistant who was unaware as to what the patient's medication condition was while he was hospitalized. A patient's medication status at follow-up was determined by asking the patient what medication he was on at the time he was being interviewed and also by checking his medication usage with a significant other if one was available.

#### Results

In this study it was not possible to control patient behavior or medication usage following discharge from the hospital. Since effect of medication was of paramount interest, patients were divided into four groups based on the medication condition randomly assigned while in the hospital and on the medication condition found at last follow-up contact. These four groups were designated as: PL-Off (i.e., *pl*acebo condition in the hospital and *off* anti-psychotic medication at last follow-up contact) and, similarly, CPZ-Off, PL-On, and CPZ-On, where CPZ refers to chlorpromazine.

These patient groupings reflected post-hospital medication utilization to the following extent: 39 (of 80) were found to be on major tranquilizer medication at last follow-up contact and reported being on such medication 65% of the time at previous contacts. Similarly, 41 patients found off medication at last follow-up contact reported they were off 71% of the time at previous contacts.

#### Admission

At admission SI scores were not significantly different for the four groups of patients. The four groups were similar in terms of age, education levels, marital status and employment status prior to admission.

## Discharge

All groups, except the PL-On group, showed significant clinical improvement, using the CI score, between admission and discharge. In addition, chlorpromazine patients showed significantly less severity of illness than placebo patients ( $t = 1.866$ ,  $p < 0.05$ , one-tailed). Analysis of functional disturbance scores did not reveal any significant differences.

Length of hospital stay also was not significantly different for patients assigned to chlorpromazine and placebo (means of 42.2 vs. 45.0 days respectively).

## Follow-up

PL-Off patients had significantly lower SI scores ( $M = 1.74$ ,  $SD = 0.863$ ,  $N = 25$ ) than did the CPZ-Off group ( $M = 2.79$ ,  $SD = 1.788$ ,  $N = 17$ ), the PL-On group ( $M = 3.54$ ,  $SD = 1.640$ ,  $N = 17$ ) and the CPZ-On group ( $M = 3.51$ ,  $SD = 1.640$ ,  $N = 17$ ).

Table I. Degree of improvement (CI scores<sup>1</sup>) between admission to the hospital project and last follow-up contact broken down by hospital/follow-up drug conditions, premorbid history and paranoid-nonparanoid status at admission

Drug status in hospital at FU	All pts.	Premorbid history		Diagnosis	
		good	poor	paranoid	nonparanoid
PL <sup>2</sup> - Off	M	0.92	0.92	0.98	0.85
	SD	0.164	0.177	0.055	0.205
	N	24	19	5	12
CPZ - On	M	0.48	0.74	0.53	0.45
	SD	0.668	0.460	0.743	0.566
	N	22	13	9	13
PL - On	M	0.29	0.26	-0.10	0.42
	SD	0.704	0.757	0.653	0.714
	N	17	8	9	4
CPZ - Off	M	0.52	0.57	0.47	0.64
	SD	0.669	0.687	0.607	0.639
	N	17	12	5	12

<sup>1</sup> CI scores based upon BPRS and Global Assessment changes between Day 2 and last follow-up contact. Scores ranged between -1.00 and +1.00, where -1.00 indicates worsening on all measures, 0.00 - no overall worsening or improvement and +1.00 indicates improvement on all measures.

<sup>2</sup> PL - placebo; CPZ - chlorpromazine.

Table II. t-test comparison between groups of schizophrenics shown in table I with different combined hospital/follow-up drug conditions

Drug group comparisons	All patients	Premorbid history		Diagnosis						
		df	good	df	poor	df	par.	df	non-par.	df
1. PL-Off vs. CPZ-On	3.040****	44	1.492	30	2.243*	12	2.606**	19	1.799	23
2. PL-Off vs. PL-On	4.090****	39	3.411****	25	1.884	12	4.875****	14	2.231*	23
3. PL-Off vs. CPZ-Off	2.755****	39	2.048*	29	1.692	8	2.676**	22	0.885	15
4. CPZ-On vs. PL-On	0.829	37	1.705	19	-0.604	16	1.576	11	0.110	24
5. CPZ-On vs. CPZ-Off	-0.162	37	0.710	23	-0.687	12	0.234	19	-0.479	16
6. PL-On vs. CPZ-Off	-0.921	32	0.883	18	-0.203	12	-0.567	14	-0.598	16

\*p < 0.05. \*\*p < 0.02. \*\*\*p < 0.01.

