Vitamins Bl, B6, and B12 in the Adjunctive Treatment of Schizophrenia—Further Studies to Examine The Effect of Reduction of Chlorpromazine Dosage

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Summary

In a double blind placebo controlled randomized study, we have explored the possibility of reducing the drug requirement of acute schizophrenic patients who were given chlorpromazine along with injection Macrab-erin Glaxo, containing combination of vitamins Bl, B12 and B6 in the therapeutic doses of 100 mg, 1000 mcg and 50 mg respectively, or an identical placebo injection. No other drug or E.C.T. was administered to the patients.

We have observed that as the daily dose of chlorpromazine is reduced, the recovery in the vitamin therapy (active) group of patients is retarded to a greater extent than in the placebo group (Groups C and D), the difference becoming statistically significant ($p<0.05$) when the daily dose of chlorpromazine is at a subtherapeutic level i.e. less than 150 mg per day.

The possible reasons for this are discussed and a hypothesis is put forward that the vitamins are helping in the recovery process of these patients by decreasing the supersensitivity of postsynaptic neurones to a more normal level. But they act more slowly than the drugs which merely block the postsynaptic neurones. At the same time, the more normal postsynaptic neurones become less responsive to the blocking action of the drugs. Consequently, the recovery of the patients on vitamin therapy is slower than the recovery of those being given placebo injection. The slowing effect becomes more and more prominent as the dose of chlorpromazine is reduced until it reaches statistical significance when the dose of the drug becomes subtherapeutic.

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Introduction

In our previous study (Joshi and Eswaran, 1980) to assess the role of vitamins Bl, B6 and B12 in the adjunctive treatment of schizophrenia, it was found that the patients receiving the vitamin injection recovered with significantly ($p<0.05$) less number of modified ECTs (MECTs) than the patients

who received the placebo injection. A hypothesis was put forward that the psychotic symptoms of these patients are due to a biochemical lesion in brain metabolism relating to neurotransmitter formation and degradation. This lesion may be due to a relative deficiency of one or more of the neurotropic vitamins Bl, B6 and B12, a deficiency which, combined with environmental stress, can lead to psychotic symptoms in susceptible subjects. The vitamin injection corrects the deficiency and so helps in the recovery of these patients. Consequently their MECT requirement is reduced.

In this study, apart from MECTs and vitamin or placebo injection, the patients in both groups also received Tab. Chlorpromazine, Tab Trifluperazine and Tab. Trihexyphenidyl in therapeutic dosage as well as one Tab. Triclofos at night to promote sleep. The dosage of these additional drugs was the same in both the groups of patients. MECTs were, however, given only when found necessary and therefore the MECT requirement formed a dependent variable in this study.

In the present study, an attempt has been made to assess the therapeutic effect of these vitamins, on a double blind basis, with a reduced number of variables. It was therefore decided to dispense with the MECTs and other drugs entirely except chlorpromazine (CPZ) along with vitamins or placebo injection in a double blind manner, thus making CPZ administration as the sole variable.

Material and Method

Patients included in the trial were those suffering from untreated Acute Schizophrenic Psychosis. The trial was carried out on indoor basis in a double blind manner in four groups of patients, after obtaining due consent. Each patient received CPZ, the dosage of which varied according to the group the patient was in, along with a daily injection of vitamin preparation (active therapy)consisting of Macraberin-Glaxo: containing vitamins Bl, B6 and B12 in the doses of 100 mg, 50 mg, and 1000 mcg respectively or placebo injection according to a randomized and coded list.

The patients were grouped as follows:

Group A: No restriction on CPZ dosage, this drug being administered either orally or parenterally as per the needs of the patient. The CPZ dosage was generally between 50 and 100 mg t.d.s. orally plus parenteral CPZ to some patients.

Group B: CPZ dosage was restricted to 50 mg t.d.s. orally throughout the four weeks of the trial period.

Group C: CPZ dosage was 50 mg t.d.s. orally during the first week and 25 mg t.d.s. orally during the subsequent three weeks of the trial period.

Group D: CPZ dosage was 25 mg t.d.s. orally throughout the four weeks of the trial period.

The psychiatric ratings of these patients were quantified on the behavior scale devised by Rockland and Pollin (1965) which is particularly useful for assessing psychotics including non-communicative patients and is easy to administer and score. The assessments were made at the time of admission of the patients and at weekly intervals for four weeks. As the patients were on a restricted therapeutic regime, the trial was limited to four weeks duration for each patient.

Results

The results are given in Table 1 and are shown graphically in Figures 1, 2, 3, and 4.

Patients in both the active and placebo groups were found to be well matched in terms of age, sex, duration of illness and pretreatment scores on the Rockland scale. No serious side effects were encountered in either group during the entire period of study.

The most important finding in this study is that the patients in both the active and the placebo group show recovery which ranges from 64 percent to 91 percent (Table 1). But, as the dosage of chlorpromazine is reduced and the comparison between the active therapy (vitamin) and placebo group becomes clearer, it is seen that the rate of recovery generally slows down, more in the active than in the placebo group of patients (Figures 1,2, 3, and 4.)

This difference in the rate of recovery reaches statistical significance ($p<0.05$) in

TABLE 1

COMPARISON OF MEAN AND PERCENT REDUCTION FROM INITIAL SCORES AT THE END OF EACH WEEK OF THERAPY.

Percent Reduction at end 3rd week Percent Reduction at end 4th week

*Significant P<0.05

Test Applied: Mann-Whitney U.

MEAN SCORES

	Group A		Group B		Group C		Group D	
	Active	Placebo	Active	Placebo	Active	Placebo	Active	Placebo
Number of Patients	5	7	10	10	9	8	5	5
Mean Initial Score	100	86	89	77	77	78	77	79
Mean Reduction at end 1st week of therapy	49	26	36	31	18	28	15	25
Mean Reduction at end 2nd week of therapy	69	51	47	49	30	42*	35	51*
Mean Reduction at end 3rd week of therapy	83	70	56	56	43	52	43	58*
Mean Reduction at end 4th week of therapy	85	78	62	61	56	66	49	60*

PERCENTAGE REDUCTION

Percent Reduction at end 1st week	45	29	39	39	23	36	19	32
Percent Reduction at end 2nd week	65	57	52	63	40	52	44	65*
	81	81	62	74	57	65	55	73*
	84	91	70	80	74	84	64	76