

Vitamins B1, B6, and B12 In The Adjunctive Treatment of Schizophrenia

Dr. Vasant G. Joshi, M.B., D.P.M. (Eng.)¹, and Dr. S. Eswaran, M.D., D.P.M.²

Introduction

The evidence for a biochemical basis of schizophrenia appears to be strong at present. To quote Boyd, 1970, "there can be little doubt that such an apparently purely functional mental disease as schizophrenia, with its distressing delusions and hallucinations and split personality, has a biochemical lesion as its basis." Despite this, the overall attempts to elucidate the exact nature of the underlying biochemical lesion, have not met with much success so far. The possible role of vitamins in the etiology and therapy of schizophrenia too has been reviewed from time to time but only with conflicting results. (Hawkins, D. and Pauling, L, 1973; Walter Wolman, 1976).

Deficiencies of vitamins have been demonstrated mainly in chronic schizophrenics and this has been said to result from their poor dietary intake. As similar deficiencies are not usually encountered in acute schizophrenics with a short duration of illness, vitamins were not considered important in the aetiology of the illness. However, some authorities still maintain that vitamin deficiencies may play an

important role in the pathogenesis of schizophrenia and have claimed successful results by treating these patients with some vitamins. Particularly, Ascorbic Acid, Nicotinic acid, Pyridoxin and natural Vitamin- E have been employed in mega doses for this purpose. (Rimland, B., 1973).

The idea of using vitamins as a therapy in a condition where no deficiency of these substances has been clearly shown is not irrational, since some of the biochemical abnormalities demonstrated in schizophrenics appear to be correctable by certain vitamins. The reducing action of vitamin C inhibiting the formation of oxidation products of epinephrine (Angel, D., Leach, B.E., Martens, S., Cohen, M., and Heath, R.G., 1957) the role of vitamin B3 in regulating methyl transfer metabolism (Pauling, L, 1972) the role of vitamin B6 in the formation of NAD from Tryptophan (Hoffer, A. 1973) as well as the recent theoretical considerations linking vitamin B12 to acetyl choline and catecholamine metabolism in mental illness (Calzigna, L, 1970) may be mentioned in this regard. Further, in some persons a dietary vitamin intake within the accepted normal range may still be insufficient to satisfy their genetically determined requirements, and in such persons this subclinical deficiency can result in mental illness (Pauling, L, 1968; William, Z.J., 1959).

The role of neurotropic vitamins B1, B6 and B12 in the development of certain psychotic states too is well known; the deficiency of B12 in Wernicke-Korsakoff

¹ Hon. Professor of Psychiatry, J.J. Hospital and Grant Medical College, Bombay.

² Lecturer in Psychiatry, J.J. Hospital and Grant Medical College, Bombay.

All requests for reprints, etc. should be addressed to Dr. Vasant G. Joshi, 7 - Jitica Makarand Society, Sawakar Marg, Bombay 400 016, India.

psychosis (Freedman, A.M., Kaplan, H.I., Sadouc, B.J., 1975) deficiency of B¹² in the so called INH induced psychosis (Joshi, Vasant C, 1976) in childhood autism (Rimland, B., 1973) and some depressive states (Dickerson and Lee, 1978) and the possible implication of B¹² deficiency along with that of folic acid in the development of schizophrenia-like-psychosis seen in epileptics (Reynolds, E.H., 1967) may be cited as examples. Megaloblastic madness can be a presenting feature of B¹² deficiency even before the manifestation of its typical blood changes (Marks, J., 1975). Despite their importance, these neurotropic vitamins B¹, B₆ and B¹² do not appear to have been well tried in the therapy of schizophrenia. Hence the present study was undertaken to assess the usefulness of these vitamins in the management of acute schizophrenia.

Materials and Methods

Sixty acute schizophrenic patients presenting with a first episode of less than three months duration were taken up for the study after obtaining due consent. All the patients were admitted to the psychiatry ward after the diagnosis of both authors concurred, following an independent examination of each patient. Those with organic disorders and frank nutritional deficiencies were excluded. The psychiatric ratings of these patients were then quantified on a behavior scale devised by Rockland and Pollin, 1965. This scale has been devised particularly for assessing psychotics, including non-communicative patients, and is easy to administer and score.

The selected patients were allocated according to a randomised list to one of the two groups A or B, consisting of 30 patients each. Each patient was given either the vitamin injection (containing vitamins B¹, B₆ and B¹² in the therapeutic doses of 100 mg, 50 mg and 1000 mg respectively) or an identical placebo by intramuscular route, once daily for up to four weeks of their hospital stay, according to double blind code. The injectable therapy was used to ensure the certainty of administration and maintenance of optimum serum levels of

the vitamins.

Throughout the 4 weeks of the study, all 60 patients were also given:

Tab Trifluoperazine (TFP) — 5 mg thrice daily
 Tab Trihexyphenidyl — 2 mg thrice daily
 Tab Chlorpromazine
 (CPZ)-50 mg thrice daily
 Tab Triclofos — 1 tablet at night

(Triclofos is available in USA as Triclos and is phosphate ester of trichlorethanol. It is a hypnotic, having properties similar to chloral hydrate).

This combination was chosen because TFP is well suited for withdrawn patients while CPZ is useful in excited patients. Trihexyphenidyl is routinely used for the prevention of TFP, CPZ induced Parkinsonism. Further, this combination has been successfully used routinely for many years past in our hospital. The dose of all the above drugs was kept constant for all the patients throughout their indoor stay.

Besides the drugs, the patients were also given modified E.C.T. (MECT) whenever absolutely necessary for acute behavioral disturbances or for severe distress or whenever they failed to show adequate response with drug alone. However, it was decided to withhold MECTs during the first week of the study, whenever possible, giving time for the tranquillizers and vitamins to act. The patients were assessed at weekly intervals on the above mentioned behavioral scale (Rockland, L.H., Pollin, W., 1965), the study being terminated after the 4th week.

Results

Sixty patients entered the study over a period of one year. One of the patients absconded during the 2nd week of the study and hence was excluded from the analysis of the results. A comparison of the two groups shows that both the groups are evenly matched on age, sex and initial scores and duration of illness, and hence they are comparable for analysis. (Table 1).

VITAMINS B1, B6 and B12 FOR SCHIZOPHRENIA

TABLE I COMPARISON OF
THE TWO GROUPS OF PATIENTS

Total No. of patients No. of males No. of females Average age of patients in years	<table border="0" style="width: 100%; border-collapse: collapse;"> <tr> <td colspan="2">Average duration of illness in weeks</td> </tr> <tr> <td colspan="2">Mean initial score on behavior scale</td> </tr> <tr> <td style="text-align: left;">Group A (Active)</td> <td style="text-align: left;">Group B (Placebo)</td> </tr> <tr> <td>30</td> <td>29</td> </tr> <tr> <td>19</td> <td>20</td> </tr> <tr> <td>11</td> <td>9</td> </tr> <tr> <td>24.9</td> <td>26.0</td> </tr> <tr> <td>3.2</td> <td>2.5</td> </tr> <tr> <td>58.9</td> <td>65.8(P>0.10)</td> </tr> </table>	Average duration of illness in weeks		Mean initial score on behavior scale		Group A (Active)	Group B (Placebo)	30	29	19	20	11	9	24.9	26.0	3.2	2.5	58.9	65.8(P>0.10)
Average duration of illness in weeks																			
Mean initial score on behavior scale																			
Group A (Active)	Group B (Placebo)																		
30	29																		
19	20																		
11	9																		
24.9	26.0																		
3.2	2.5																		
58.9	65.8(P>0.10)																		

Thus both the groups were found to be comparable.

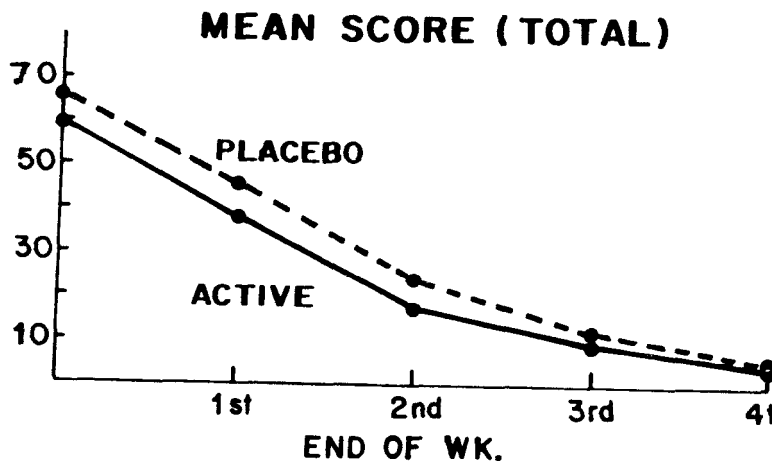


Figure 1

Weekly Comparison of Mean Scores

As may be seen from Figure 1, the mean total scores on behavior scale, show a definite tendency for patients in both groups to improve with treatment. All the patients were however brought to a near normal state by the end of the trial and hence a comparison of their scores does not show any difference between the two groups. It should, however, be recalled that MECTs were given only when found necessary and formed a

dependent variable in this study. The total number of MECTs required by Group A (on vitamin combination) was however lesser than the MECT requirement of Group B (on placebo) and this difference was statistically significant ($p < 0.05$). This is to say that for bringing about the same degree of improvement, significantly more MECTs were required with the placebo than with the vitamin combination. (Table II).

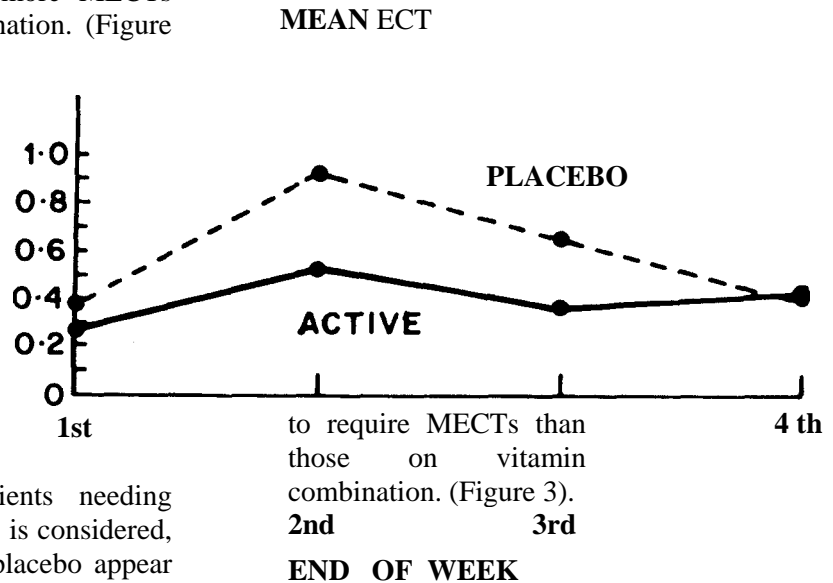
TABLE II
COMPARISON OF NO. OF MECTs PER PATIENT

Parameter No. of observations Total No. of MECTs required MECT - mean ±SE Value of t Value of P	<table border="0" style="width: 100%; border-collapse: collapse;"> <tr> <td style="text-align: left;">Group A (Active)</td> <td style="text-align: left;">Group B (Placebo)</td> </tr> <tr> <td>30</td> <td>29</td> </tr> <tr> <td>48</td> <td>70</td> </tr> <tr> <td>1.6</td> <td>2.4</td> </tr> <tr> <td>0.270</td> <td>0.274</td> </tr> <tr> <td></td> <td>2.081</td> </tr> <tr> <td></td> <td>p<0.05</td> </tr> </table>	Group A (Active)	Group B (Placebo)	30	29	48	70	1.6	2.4	0.270	0.274		2.081		p<0.05
Group A (Active)	Group B (Placebo)														
30	29														
48	70														
1.6	2.4														
0.270	0.274														
	2.081														
	p<0.05														

Thus the difference in MECT requirements of the "active" and the "placebo" group of patients is statistically significant, being lesser in the "active" group than in the "placebo".

A weekly break up of the mean number of MECTs in each group also shows that the patients on placebo needed more MECTs than those on vitamin combination. (Figure 2).

Figure 2 Weekly Comparison of Mean Number of MECTs



If the percentage of patients needing MECTs during different weeks is considered, once again more patients on placebo appear

% AGE OF PATIENTS NEEDING ECT
2nd

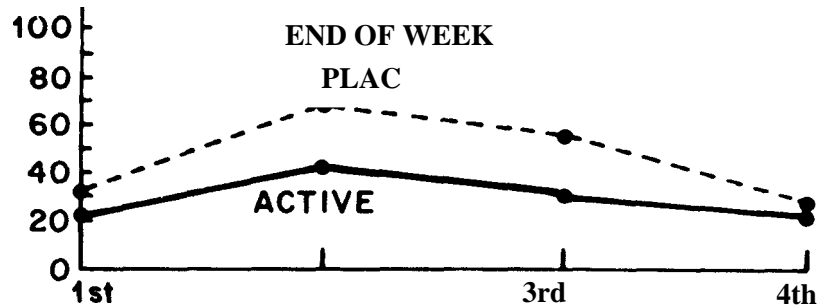


Figure 3 Weekly Comparison of the Percentage of Patients Needing MECT

No serious side effects were encountered in either group during the entire period of study.

Discussion

The difference between the two treatment groups whether assessed in terms of mean number of MECTs required by the group or the percentage of patients needing MECT in each group, establish clearly that Group A has shown more therapeutic benefits than

Group B. The only difference in the treatment received by the two groups is the vitamin combination and hence it is obviously inferable that the dependent variable (the requirement of MECTs) is favourably influenced by these vitamins.

A Possible Explanation

A battery of enzymes and coenzymes can be envisaged to be working in the brain during the course of mental activity. A disturbance or block in the action of one or more of these enzymes or coenzymes can lead to mental abnormality. It is known that vitamins B₁, B₆ and B₁₂ are importantly involved in neuronal metabolism. It is therefore, reasonable to assume that either deficiency or disturbed utilization of these vitamins coupled with increased need may result in mental abnormalities. The results of this trial seem to confirm this assumption.

It is possible that these neurotropic vitamins play an important role in the metabolism of neurotransmitters. In fact vitamin B₆ is needed for the metabolism of a whole group of brain amines including noradrenaline, adrenaline, dopamine and serotonin. These probably act as synaptic neurotransmitters in various brain areas. (J. Marks, 1975). Abnormal functioning of these neurotransmitters is therefore postulated as a possible cause for mental illness.

A relative deficiency of these vitamins may result in a biochemical lesion in brain metabolism relating to neurotransmitter formation and degradation. The inherent adaptability of the body may keep on adapting itself to the lesion until a time comes when the adaptive powers break down in toto. It is then that the acute psychotic symptoms appear. The vitamin combination is most likely correcting the biochemical lesion. Further research is needed to pin point the role of each of these vitamins in psychiatry.

Conclusion

It would thus seem that adjunctive therapy with vitamins B₁, B₆ and B₁₂ is useful in the management of acute schizophrenic psychosis, particularly in reducing the number of MECTs. It may therefore be suggested that a daily injection of vitamin combination be included as part of the treatment regimen of acute

psychotic patients of the schizophrenic type. It would be interesting to observe the efficacy of this combination in other mental illness as for example, chronic schizophrenia and depressive reactions of either psychotic or neurotic nature.

Summary

An injectable preparation, Macraberin-Glaxo, containing combination of vitamins B₁, B₆ and B₁₂ in the therapeutic doses of 100 mg, 50 mg and 1000 meg respectively was compared with an identical placebo in a double blind study involving sixty acute schizophrenic patients, and was found to be superior to the placebo. Each patient received a daily injection of either the vitamin combination or the placebo for 30 days, in addition to the usual therapy with phenothiazines in a fixed dosage, and modified ECTs (MECT) whenever necessary. It was found that the patients who received the vitamin combination, needed a lesser number of MECTs and this was statistically significant.

It is postulated that a relative deficiency of these vitamins in susceptible persons may result in a biochemical lesion in brain metabolism relating to neurotransmitter formation and degradation, leading to psychotic manifestations. The vitamin combination is most likely correcting the biochemical lesion. Further research is needed to pin point the role of each of these vitamins in psychiatry.

It is suggested that a daily injection of the vitamin combination be included as part of the treatment regimen in the management of acute schizophrenic patients, particularly because of its usefulness in reducing the requirements of MECTs. It would be interesting to observe the efficacy of the vitamin combination in other mental illnesses as, for example, depressive reactions of either psychotic or neurotic nature.

Acknowledgements

We wish to thank M/s. Glaxo Laboratories (India) Ltd. for the supply of the vitamin combination (Macraberin) and other assistance, and the Dean, J. J. Group of Hospitals, Bombay, for permission to carry out the trial.

REFERENCES

- ANGEL, C, LEACH, S.E., MARTENS, S., COHEN, M., and HEATH, R.G.: Serum Oxidation Tests in Schizophrenic and Normal Subjects. Arch. Neur. Psychiat. 78,500,1957.
- BOYD, W.: A Textbook of Pathology. 7th Ed., Lea and Febiger, Philadelphia, 1970.
- DICKERSON and LEE (Ed): Nutrition in the Clinical Management of Disease, p. 297, Edward Arnold (Publishers) Ltd., 25 Hill Street, London, 1978.
- FREEDMAN, A.M., KAPLAN, H.I., SADOUC, B.J.: Comprehensive Textbook of Psychiatry II, Vol. 1, p. 156,1975.
- GALZIGNA, L.: Complexes between Acetyl Choline and Catecholamines and their Tolerance to Mental Illness. Nature (London), 225:1058,1970.
- HAWKINS, D. and PAULING, L (Ed): Orthomolecular Psychiatry. Freeman and Co., San Francisco, 1973.
- HOFFER, A.: In: Orthomolecular Psychiatry. Ed. Hawkins, D. and Pauling, L., Freeman and Co., San Francisco, p. 241,1973.
- JOSHI, V.G.: Isoniazid (INH) in the Treatment of Depressive Syndrome: A Pilot Trial. Dis. Nerv. System, p. 106, Feb. 1976.
- MARKS, J.: A Guide to the Vitamins, their Role in Health and Disease. Medical and Technical Publishing Co. Ltd., St. Leonard's House, Lancaster, England, 1975.
- PAULING, L.: In: Orthomolecular Psychiatry. Ed. Hawkins, D. and Pauling, L., Freeman and Co., San Francisco, p. viii, 1973.
- PAULING, L.: Vitamin Therapy: Treatment for the Mentally III. Science, 160, p. 1181,1968.
- REYNOLDS, E.H.: Schizophrenia-like Psychosis of Epilepsy and Disturbances of Folate and Vitamin B12 Metabolism Induced by Anticonvulsant Drugs. Br. J. Psychiat. 113, 911,1967.
- RIMLAND, B.: In: Orthomolecular Psychiatry, Ed. Hawkins, D. and Pauling, L., Freeman and Co., San Francisco, p. 513,1973.
- ROCKLAND, L.H. and POLLIN, W.: Quantification of Psychiatric Mental Status (for use with psychotic patients). Arch. Gen. Psych. 12,23,1965.
- WILLIAM, Z.J.: Biochemical Individuality: The Basis for the Genotropic Concept, John Willy and Sons Inc., NY., 1959.
- WOLMAN, W.: J.A.M.A., 236,19, 2224,1976.