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Vitamin B_{12} Deficiency in Resistant Schizophrenia in Tropics

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Abstract

Vitamin B_{12} deficiency and hyperhomocysteinemia are common in tropical developing countries. In prevalence study, among Indian population by Yajnik and colleagues, 67% of men had low vitamin B_{12} concentration and 58% had hyperhomocysteinemia [1]. Here, we report two patients with vitamin B_{12} deficiency presented with symptoms of schizophrenia and required very high doses of antipsychotic medication surprisingly without any anticipated extra pyramidal side effects. The initial requirement of high dose of antipsychotic medication significantly came down after adding parenteral cobalamin supplementation.

Subject Areas

Psychiatry & Psychology

Keywords

B_{12} Deficiency, Schizophrenia, Hyperhomocysteinemia

1. Introduction

Vitamin B_{12} deficiency and hyperhomocysteinemia play important role in resistant schizophrenia. Low serum B12 level has been reported in resistant schizophrenia in literature [1]. Vitamin supplementation could provide therapeutic benefits through separate mechanisms of action than current medication regimens, which focus largely on monoamine and histamine signalling. The research indicates that taken in high doses, B vitamins—such as B-6, B-8, and B-12—can significantly reduce schizophrenia symptoms. Additionally, a combined dose of several vitamins was shown to have the same beneficial effect. However, low doses of the vitamins were revealed to be ineffective.

2. Case I

A 24 year old male, presented with an 8 month history suggestive of schizophrenia with normal cognitive and neurological functions. He was started on oral risperidone and the dose was gradually increased to 12 mg/day, due to poor response to treatment however no extra pyramidal side effects were noted. As the MCV was 98.4 [75 - 96 fl] he was evaluated for B_{12} and folic acid deficiency. Serum B_{12} was 159.5 pgm/ml (normal range: 220 - 900 pgm/ml), folic acid was 4.08 ng/ml (normal range: 3 - 17 ngm/ml) and homocysteine was 58.5 μM/L (normal range: 4.3 - 9.9 μM/L), confirming the possibility of vitamin B_{12} deficiency. Renal and hepatic indices were normal. Mr. A was started on a course of intramuscular vitamin B_{12} injections. After two months of treatment he developed extrapyramidal side effects and the dose of risperidone was reduced gradually to 6 mg daily without any worsening of psychotic symptoms. His homocysteine level has come down to normal limit at that time. He remained asymptomatic and was functioning well at 6 months follow up.

3. Case II

Mr. B, a 28 year old male, presented with a 2 year history suggestive of schizophrenia and his symptoms were uncontrolled over the preceding six months. At presentation he was on high doses of two typical antipsychotics (chlorpromazine and trifluoperazine) equivalent to 1400 mg daily dose of chlorpromazine with no manifestions of extrapyramidal symptoms. On examination, he had pallor, glossitis and angular stomatitis with normal cognitive and neurological functions. Mr. B was evaluated for B_{12} deficiency; his MCV was 112 [75 - 96 fl], serum B_{12} was 119 pgm/ml (normal range: 220 - 900 pgm/ml), folic acid was 4.5 ng/ml (normal range: 3 - 17 ngm/ml) and homocysteine was 49.5 μM/L (normal range: 4.3 - 9.9 μM/L). These results confirmed vitamin B_{12} deficiency. Serum electrolytes, renal and hepatic indices were normal. After a month of treatment with intramuscular vitamin B_{12} therapy, Mr. B developed severe extrapyramidal side effects and hence trifluoperazine was withheld and he was maintained on chlorpromazine 600 mg daily. His homocysteine and B_{12} levels were normalized after a month of treatment. Parenteral B_{12} administration was continued monthly. He remained asymptomatic and was functioning well at 3 months follow up.

4. Discussion

The role of one carbon metabolism in neuropsychiatric disorders is reviewed by Smythies *et al.* and Cohen *et al.* [2] [3]. While there are many reports of schizophrenia being associated with vitamin B_{12} deficiency, we would like to highlight two issues relevant to the above mentioned case scenarios [4].

1) Need for high dose antipsychotic therapy in the acute phase of treatment and lack of extrapyramidal side effects in this group of patients.

2) Evaluation for B_{12} and folate deficiency should be included in the assessment for treatment resistant psychosis.

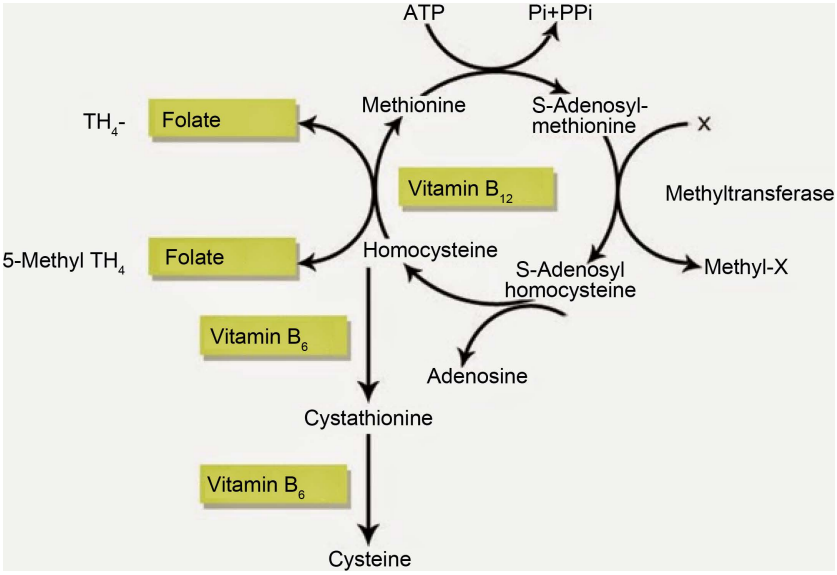

Figure 1. Role of vitamin B_{12} in homocysteine metabolic pathway.

When a person has B_{12} deficiency there is a possibility of dopamine accumulation which makes the psychosis resistant to antipsychotic therapy, and the patient may not develop extrapyramidal side effects and this can be reversed by vitamin B_{12} supplementation. Previous surveys have shown that a small but substantial number of psychiatric patients ranging from 6% - 15% have low serum B_{12} levels [5].

The methyl group of essential amino acid Methionine is activated by converting it to S-Adenosyl Methionine (SAM) by Adenosine Triphosphate (ATP) and Ethionine Adenosyl Transferase and SAM is the sole methyl donor in the central nervous system. S-Adenosyl Homocysteine (SAH), demethylation product of SAM is hydrolysed to Homocysteine (Hcy) in a reversible reaction. In the majority of tissues, Hcy is remethylated to Methionine by the Vitamin B_{12}-dependent enzyme Methionine Synthase (MS) (**Figure 1**). In Vitamin B_{12} or folic acid deficiency states this remethylation will be reduced, which in turn reduce the synthesis of SAM and results in decreased synthesis of Noradreranaline or accumulation of Dopamine [6].

In developing countries, underlying B_{12} deficiency should be considered in all the patients who are not responding to antipsychotic medications and before labelling them as treatment resistance or commencing on 2nd line therapies like clozapine. It is advisable to do B_{12} level during the initial evaluation because psychosis can precede anaemia. Homocystine assay is also to be considered in selected cases [7] in a view of early initiation of cobalamin supplementation.

Vitamin B_{12} deficiency and hyperhomocysteinemia was an etiological factor in our cases. Vitamin B_{12} therapy had a significant outcome in our cases. Low serum B_{12} levels have been reported in resistant schizophrenia [1] and Vitamin B_{12} therapy had good outcome in literature [5].

The informed consent was obtained from the patients to report this case in this journal.

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