Vitamin B12 Deficiency and Psychiatric Manifestations-A Consise Review

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Abstract

Vitamin B12 deficiency may contribute to the pathogenesis of neuropsychiatric disorders such as mental confusion, memory changes, cognitive slowing, mood disorder, violent behaviour, fatigue, delirium and paranoid psychosis. Vitamin B12 plays a crucial role in cell reproduction, normal erythropoiesis, nucleoprotein and myelin synthesis, normal growth, DNA synthesis, and one carbon metabolism. Vitamin B12 helps in synthesis of methionine from homocysteine and conversion of methylmalonylcoA to succinylcoA. Methionine is converted to SAM which donates its methyl group to myelin, membrane phospholipids and various neurotransmitters and free THF is liberated from N5 methyl THF which is used in synthesis of purine, pyrimidine and nucleic acid. An elevated level of Hcy as a neurotoxin was also shown to affect the redox signalling pathways in neurons through the generation of reactive oxygen species (ROS) and a decrease in endogenous antioxidants. If patterns of DNA methylation in redox-related genes can modulate cognitive impairment caused by vitamin B12 deficiency and hyperhomocysteinaemia is therefore of interest, low levels of vitamin B12 can cause serious cognitive dysfunction. Psychiatric symptoms attributable to vitamin B12 deficiency have been described for decades. The earlier studies are for the most part in accord with more recent ones, despite being diagnostically less precise in psychological and hematologic terms. These symptoms tend to fall into many clinically distinct categories: slow cerebration; confusion; memory changes; delirium, with or without hallucinations and/or delusions; depression; acute psychotic states; and more rarely) reversible manic and schizophreniform states. In conclusion, psychiatric disorders can be rare manifestations of vitamin B12 deficiency, which are reversible with therapy. Serum Vitamin B12 level should be checked in patients with psychiatric manifestations as it results in neuro psychiatric manifestations such as peripheral neuropathy, myeloneuropathy, cerebellar ataxia, optic atrophy, delirium, dementia, psychosis and mood disorders.

Keywords: *Depression, Schizophernia, Attention deficit hyperactivity disorder, Obsessive compulsive disorder.*

Introduction

Mental disorders, which are the same as psychiatric disorders, are clusters of syndromes which disturb an individual's cognition, emotion regulation or behaviour.

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Common mental disorders include bipolar disorders (manic disorder, depression, and manic-depression), dementia, schizophrenia, and panic disorder.[1] In India, one among every seven people who have a mental disorder, ranging from mild to severe. The proportional contribution of mental disorders to the total disease burden in India almost doubled from 1990 to 2017. Mental disorders were associated with a wide range of chronic illnesses, disability, and even mortality, particularly among elderly people.[2,3] Vitamin B12 is a group of physiologically active substance known as

Cobalamins or Corrinoids; composed of tetrapyrrole rings surrounding the central cobalt atom and nucleotide side chains attached to the cobalt atom. The cobalamin tetrapyrrole ring of cobalt and other side chain is called corrin, and the cobalt corrin complex is termed cobamide. Normal daily requirement is about 1 μg. Vitamin B12 is also known as cobalamin, extrinsic factor of castle and anti-pernicious anaemia factor. It is water soluble, heat stable and red colour and contains 4.35% cobalt by weight. Vitamin B12 is needed for cell replication, normal erythropoiesis, synthesis of nucleoproteins and myelin, normal development, DNA synthesis, and one-carbon metabolism. Dietary cobalamin binds to the R protein (glycoprotein) secreted by the salivary gland; it is a member of the Haptocorrins family. The R protein is hydrolyzed in the duodenum in an alkaline medium and pancreatic proteases, releasing Vitamin B12, which then binds to Intrinsic Factor (IF), a 50kDa glycoprotein. IF (gene on chromosome 11q13) is a protein that is immune to proteolytic digestion enzymes and is formed in the stomach. Vitamin B12 is released from the diet and changes from haptocorrin to IF in the duodenum as a result of pancreatic secretions raising the pH. Vitamin B12 binds to IF, preventing intestinal flora from using it. Vitamin B12-IF binds to a Cubilin receptor on the microvillus membrane of enterocytes in the ileum. After 2-3 hours of ingestion, Vitamin B12 enters the bloodstream and occurs in portal blood bound to Transcobalamin 2. Vitamin B12 is transported by transcobalamin 1 (TC-1) and transcobalamin 2 (TC-2). TC-1, also known as Haptocorrin, is produced from unique granules in neutrophils and is encoded by the TCN 1 gene. TC-1 is removed from the bloodstream by glycoprotein receptors. The TC-2 gene, which has a molecular weight of 43 kDa and is synthesized by the liver, macrophages, ileum, and vascular endothelium, is found on chromosome 22q11q13.1. Inactive TC-1 transports 80% of the vitamin in circulation, while active Transcobalamin 2 transports 20% of the vitamin (TC-2). The liver, bone marrow, and other essential cells actively take up the TC 2 complex, also known as Holo TC 2. The liver can store about 4-5mg of Vitamin B12, which is enough to satisfy the body's requirements for 4-5 years. At the age of five, the clinical signs of vitamin B12 deficiency are visible.[4-6]

Vitamin B12 and Depression

Depression gives the extensive burden on an individual's life and vast efforts have been made to explore the biological mechanisms of it.[7] Vitamin B12 plays a significant role in development of the neurology and DNA synthesis. Its deficiency has to do with hematology, neurology and psychological symptoms, the latter involving irritability, changes in personality, depression, dementia, and rarely psychosis. The linkages between deficiency of vitamin and depression have been established in recent literature. High serum B12 levels are blessed with improved treatment response, high levels of homocysteine typical of folate / B12 deficiency, and poor response to antidepressant therapy are associated with those with depression. Hyperhomocysteinaemia can have direct effects on depression-implied neurotransmitters.[8]

Vitamin B12 and Schizophernia

Single-carbon metabolism seems to be disrupted in schizophrenic patients. In this metabolic system, the intermediate metabolites methionine and homocysteine play a role. A majority of the patients in a case-control sample of the cerebrospinal fluid had elevated methionine, while a smaller subgroup had elevated homocysteine. Folate dependency caused by mutations in the methylenetetrahydrofolate reductase gene is a common cause of elevated homocysteine (MTHFR). The ability of single-carbon metabolism to be modified by natural means, such as B-vitamins and antioxidants, is a particularly encouraging feature.[9]

Patients with elevated homocysteine levels were given oral folic acid, B-12, and pyridoxine for three months, accompanied by a placebo in a randomized, double-blind, placebo-controlled crossover study. During the supplement phase of the study, homocysteine levels fell, which was linked to clinical changes in symptomatology and neurocognitive efficiency. As a result, adjunct treatment with B vitamins appears promising in people who have elevated homocysteine levels as well as those who have a genetic predisposition to irregular folate metabolism.[10]

Vitamin B12 and Attention deficit hyperactivity disorder

Attention-deficit/hyperactivity disorder (ADHD) is a common neurodevelopmental disorder characterized by symptoms of hyperactivity, impulsivity, and inattention.[11] The estimated prevalence of ADHD is 3.4% in children.[12] Recently, it has been reported that deficiencies of vitamins B12 and D can be present in attention deficit hyperactivity disorder and such deficiencies can be included among the risk factors .[13]

Vitamin B12 and Obsessive compulsive disorder

OCD (obsessive-compulsive disorder) is a neuropsychiatric disorder marked by obsessions and compulsions. OCD typically starts in infancy or adolescence, and patients with OCD often have comorbid disorders such as mood, anxiety, psychotic, and somatoform disorders. [14] There have been case reports of vitamin B12 deficiency in OCD patients in the literature. In addition, some research has looked into the connection between OCD and vitamin B12, folic acid, and homocysteine levels in both adult and child-adolescent patients. 30 patients with OCD, 30 patients with chronic schizophrenia, and 30 stable controls were contrasted by Hermesh et al. Vitamin B12 deficiency was found to be more common in OCD patients than in controls, but there was no substantial difference in vitamin B12 and folate levels between the three classes. [15 - 17]

Conclusion

Vitamin B12 deficiency is common in developing countries and its prevalence ranges up to 67% among Indian Population. It results in neuropsychiatric manifestations such as peripheral neuropathy, myeloneuropathy, cerebellar ataxia, optic atrophy, delirium, dementia, psychosis and mood disorders. Vitamin B12 deficiency or insufficiency and elevated homocysteine may contribute to the etiopathogenesis of depression. We recommend checking serum B12 and folate level in any case with psychiatric disorder such as OCD, even in the absence of anemia and other hematologic manifestations of B12 and/or folate deficiencies. B12 replacement therapy can resolve symptoms of psychiatric disorders in patients with B12 deficiency. Psychiatric symptoms of a B12 deficiency are common and can be severe. With an early diagnosis and treatment, further worsening of symptoms can be prevented. Present review article concludes that all patients old and young presenting with neuropsychiatric symptoms with or without anemia should be investigated for possible Vitamin b 12 deficiency and to determine its cause and whether it might be reversible. In all cases replacement therapy should be administered.

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References

1. Butola LK, Kanyal D, Ambad R, Jha RK. Role of Omega 3 Fatty acids, Vitamin D, Vitamin B12, Vitamin B6 and Folate in Mental wellbeing-A Short review of Literature. Indian Journal of Forensic Medicine & Toxicology. 2021 Apr;15(2):283.
2. Butola LK, Ambad R, Kacchwa K. Zinc and Psychiatric Disorders: A Review. 2020,11 (SPL4), 1505-1514 .
3. Jha RK, Kanyal D, Dhok D, Butola LK. NEED OF VITAMIN D BEYOND BONE: A CONSISE REVIEW. European Journal of Molecular & Clinical Medicine. 2021 Mar 16;8(3):1096-109.
4. Madhura TK, Kanyal L, Mujawar A. Effect of glycemic control on vitamin b12 status in type 2 diabetes mellitus. Indian Journal of Basic and Applied Medical Research. 2019 Dec;1(9):7-17.
5. Dhok A, Butola LK, Anjankar A, Shinde AD, Kute PK, Jha RK. Role of Vitamins and Minerals in Improving Immunity during Covid-19 Pandemic--A Review. Journal of Evolution of Medical and Dental Sciences. 2020 Aug 10;9(32):2296-301.
6. Lata Kanyal MT, Mujawar A. Status of vitamin b12 in type 2 diabetes mellitus patients taking metformin based oral hypoglycemic agent-a cross sectional study. Indian Journal of Basic and Applied Medical Research. 2019 Dec;1(9):18-26.
7. Ambad RS, Butola LK, Singh BR, Bankar N, Ghogare DA, Patil DR. A crosssectional comparison of minerals in psychiatric disorder. International Journal of Psychosocial Rehabilitation. 2020;24(06):5968-76.
8. Butola LK, Kute PK, Anjankar A, Dhok A, Gusain N, Vagga A. Vitamin B12-Do You Know

Everything?. Journal of Evolution of Medical and Dental Sciences. 2020 Oct 19;9(42):3139-47.

9. Regland B. Schizophrenia and single-carbon metabolism. Progress in Neuro-Psychopharmacology and Biological Psychiatry. 2005 Sep 1;29(7):1124-32.
10. Arroll MA, Wilder L, Neil J. Nutritional interventions for the adjunctive treatment of schizophrenia: a brief review. Nutrition journal. 2014 Dec;13(1):1-9.
11. Thapar A, Cooper M (2016) Attention deficit hyperactivity disorder. Lancet 387:1240–1250.
12. Polanczyk GV, Salum GA, Sugaya LS, Caye A, Rohde LA (2015) Annual research review: a meta-analysis of the worldwide prevalence of mental disorders in children and adolescents. J Child Psychol Psychiatry 56:345–365.
13. Bala KA, Doğan M, Kaba S, Mutluer T, Aslan O, Doğan SZ. Hormone disorder and vitamin deficiency in attention deficit hyperactivity disorder (ADHD) and autism spectrum disorders (ASDs). Journal of Pediatric Endocrinology and Metabolism. 2016 Sep 1;29(9):1077-82.
14. Adam Y, Meinlschmidt G, Gloster AT, et al. . Obsessive–compulsive disorder in the community: 12-month prevalence, comorbidity and impairment. Soc Psychiatry Psychiatr Epidemiol 2012;47:339–49.
15. Sharma V, Biswas D. Cobalamin deficiency presenting as obsessive compulsive disorder: case report. Gen Hosp Psychiatry 2012;34:578.e7–578.e8.10.
16. Valizadeh N, Valizadeh M. Obsessive compulsive disorder as early manifestation of B12 deficiency. Indian J Psychol Med 2011;33:203-10.
17. Hermesh H, Weizman A, Shahar A, et al. . Vitamin B 12 and folic acid serum levels in obsessive compulsive disorder. Acta Psychiatr Scand 1988;78:8–10.