

Role of Micronutrients in Psychiatric Disorders

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Abstract

Research evidences suggest about the association of deficiency of micronutrients with psychiatric disorders. The relation between micronutrient deficiency and psychiatric disorders are bidirectional. Identification of micronutrient deficiency in psychiatric disorder and psychiatric evaluation in patients with micronutrient deficiency are highly essential. Understanding this association will help the clinician for appropriate use of micronutrients in clinical practice.

Keywords: Micronutrients, Psychiatric disorder, Clinical Practice

Nutritional deficiency in psychiatric disorders can be the cause as well as the consequence. Deficiency of micronutrients and vitamins, which act as co-factors in cascade of steps of neurotransmitter synthesis may result in genesis of various psychopathology [1]. At the same time psychiatric illness may result in deficiency of micronutrients, which can be due to decreased intake or increased demand. Another potential reason may be mal-absorption. Patients using alcohol, nicotine, tea, coffee commonly interfere with the absorption of micronutrients like- iron and zinc [2]. Strict vegetarians are also vulnerable for deficiency of vitamins and micronutrients, which are abundantly found in animal sources. Patients taking antidepressants (selective serotonin reuptake inhibitors) and mood stabilizers (valproate, lithium and carbamazepine) frequently have gastric irritation and dyspepsia. Similarly, patients suffering from psychiatric disorders often experience drug induced gastritis for which they receive antacids for long time;

it also alter the gastric p^H. The change in gastric as well as intestinal biochemical milieu may cause impairment of absorption of micronutrients. Many patients with psychiatric disorders are prescribed calcium supplementation for several reasons, which interferes with the absorption of iron. Supplementation of iron orally, may not improve the body store of iron, if it is supplemented with calcium. Hence, careful dosing is required for an effective outcome. Deficiency of several nutritional elements may have overt manifestation (skin lesions, ulcers in mouth, Bitot's spot in eye, alopecia, etc) or covert manifestation (pica, irritability, lethargy). Globally, iron deficiency is one of the common micronutrient deficiency [3], which can have both overt manifestation (pallor, Koilonychia) and covert manifestation (lethargy, pica, breathlessness, restless leg syndrome; etc) [4,5]. Deficiency of iron, increases the risk of mood disorders, neurodevelopmental disorders, anxiety disorders as well as ADHD [6]. Low serum folate and vitamin B12 is associated with depression. Biotin deficiency may cause alopecia. S-adenosyl- methionine (SAME) is a donor of amino acid l-methionine, has an important role in treatment of depression. It has antidepressant properties and it also potentiates the effect of antidepressants [7]. Similarly patients with anorexia nervosa, need zinc supplementation for gaining weight [6]. Evidences suggest about possible implication of vitamin C and E in obsessive compulsive disorder (OCD). In studies on patients with OCD, the plasma level of Vitamin C and E was found to be lower than healthy controls [8, 9]. Vitamin D is found to be a useful augmenting agent in treatment of depression. In a 8 week trial, patients with depression receiving fluoxetine along with 1500 IU/day of vitamin D3 had shown significantly better response than patients receiving fluoxetine alone[10].

Low vitamin D concentrations were found to be associated with poorer executive function, processing speed and visuo-perceptual skills. Vitamin D may

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attenuate amyloid- β ($A\beta$) accumulation by stimulating the phagocytosis of the $A\beta$ peptide and by enhancing brain-to-blood $A\beta$ efflux transport at the blood-brain barrier, resulting in a decreased number of amyloid plaques. Maintaining vitamin D concentration in body may be helpful in preventing development of executive dysfunction, hippocampal atrophy and progression of vascular brain injury [11]. Severe vitamin D3 deficiency might be responsible for lack of inflammatory response and low mood in patients with long-term eating disorders like anorexia nervosa and bulimia nervosa. So vitamin D3 may be used as anti-inflammatory molecule for novel therapies in the treatment of long standing eating disorders [12]. High homocysteine level due to vitamin B12 deficiency may lead to increased oxidative stress and development of Autism spectrum disorder. These deficiencies can either play a role in the etiology of Autism or it can occur as a consequence of the disease [13]. Vitamin D level is found to be lower than normal in the children with autism. However, there are two possibilities—either children with ASD are born with lower vitamin D levels, or develop low levels due to less sun exposure than typically developing children [14]. Pyridoxine and magnesium deficiency is associated with Autism. Studies revealed that high dose pyridoxine and magnesium is helpful in the management of autism [15]. Low Omega-3 fatty acid is associated with depression and bipolar disorder as evidenced by deficits in erythrocyte docosahexaenoic acid (DHA) composition [16]. Consuming 1.5 to 2 gram/ day of eicosapentaenoic acid (having omega-3 fatty acids) has been shown to stimulate mood elevation in depressed patients. However, doses higher than 3 gram/day omega-3 fatty acids do not present better effects and may not be suitable for some patients, such as those taking anti-clotting drugs [17]. Vanadium levels are found to be elevated in patients with bipolar disorder, which attributes to the symptoms of mania, depression, and melancholy. A double-blind, placebo controlled study revealed the effectiveness of single dose of 3 gram vitamin C in decreasing manic symptoms in comparison to placebo by preventing the toxic effect of vanadium [18]. Disturbances in amino acid metabolism like serotonin and glycine have been implicated in the pathophysiology of schizophrenia. The negative symptoms of schizophrenia (socially withdrawn behaviour, apathy and emotional blunting) that do not respond to the existing conventional medication, have been shown to improve by 30 gram of glycine per day [17]. Deficiency of amino acids - tyrosine and tryptophan, which are the precursor of neurotransmitters dopamine and serotonin leads to depression and aggression. So, diets rich in these amino acids are

helpful in reducing depression and aggression. Low selenium intake is found to be associated with low mood and anxiety [8]. Vitamin B1 is a critical cofactor in glycolysis and the tricarboxylic acid cycle. Vitamin B1 (thiamine) deficiency have been reported in chronic alcoholics, protracted vomiting during pregnancy and chronic malnutrition. Vitamin B1 deficiency can result in Wernicke encephalopathy (Confusion, ataxia and nystagmus) and Wernicke-Korsakoff syndrome (confabulation and amnesia - both anterograde and retrograde) [19]. Vitamin B6 (pyridoxine) acts as co-enzyme for the synthesis of various neurotransmitter e.g. serotonin, dopamine and gamma aminobutyric acid (GABA). Deficiency of these neurotransmitters has been reported in the patients of depression. So vitamin B6 can be effective in the patients of depression. Vitamin B6 deficiency have been associated with seizure and mental retardation in infants [19]. Iodine deficiency can result in hypothyroidism which result in secondary depression [19]. Vitamin E (acting as antioxidants) deficiency have been associated with mild cognitive impairment, Alzheimer's disease and tardive dyskinesia [20].

Deficiency of micronutrients may cause treatment resistance; may the deficiency be the cause or consequence of psychiatric disorder. The patient may require addition of deficient micronutrient to replenish the body's store in order to get the desired therapeutic response.

To establish the association of micronutrient deficiency with psychiatric disorder, there should be evidences of low level of specific micronutrient in body, which correlate with the onset and progress of psychiatric disorders. Correction of the deficits of micronutrients in body should also result in improvement of symptoms of psychiatric disorders. But, it is often difficult to estimate the levels of most micronutrients in the routine clinical settings as the facility is limited to few advanced centers. The estimation of all micronutrients in body is also a costly affair; hence the health professionals need to evaluate the patient clinically for signs and symptoms of deficiency of micronutrients along with associated psychiatric disorder. Supplementation may be started, based on the deficiency manifestations and evidences regarding the association of the micronutrient with the specific psychiatric disorder along with specific treatment strategy for the psychiatric disorder. A non-response to addition of micronutrient may be considered a cue to evaluate for other possibilities.

Micronutrients may augment the action of various psychotropic medications, reduce the drug induced side effects and can also be effective in reducing the symptom of various psychiatric disorders [21]. So, a wholesome and balanced diet is very much necessary

to combat the manifestations of their deficiency; be it in the field of mental health or otherwise. In regard to prescribing micronutrients in the field of psychiatry, there are only few molecules, who withstand the burden of various researches and still proved to be fruitful in clinical background. Future research also needs to focus on determining the appropriate doses of nutritional supplements in various mental illnesses. In the cases of certain nutrients, psychiatrists can recommend doses of dietary supplements based on previous and current efficacious studies.

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