Chapter 5
Vitamin Deficiencies and Neuropsychiatric Disorders in Sub-Saharan Africa

Michael Ssonko

Abstract Deficiencies of vitamins are associated with psychiatric illnesses either by being the primary cause or an exacerbating factor. Psychiatric symptoms could also lead to poor nutrition. Vitamin deficiencies may play a role in compromising patient recovery. Vitamins are organic substances essential for several enzymatic functions. There are 13 known vitamins which are either fat soluble (4 vitamins i.e. KEDA) or water soluble (9 vitamins i.e. C, and the B group). For brain function, B-vitamins are essential in the maintenance of myelin, neuro-transmitter production and the methylation cycle. Fat-soluble vitamins are necessary in inflammatory regulation, regeneration of antioxidants and genetic modification. Vitamin deficiencies will, therefore, cause brain degeneration and will be associated with psychiatric symptoms. Few studies of vitamin deficiencies have been carried out in Sub-Saharan Africa. This chapter presents an overview of vitamins and their relation to neuropsychiatric disorders with the focus on Sub-Saharan Africa.

Keywords Vitamin deficiency • Psychiatric symptoms • Neurotransmission • Brain degeneration

Introduction

Deficiencies of vitamins are associated with psychiatric illnesses either by being the primary cause or an exacerbating factor. Psychiatric symptoms could also lead to poor nutrition. Vitamin deficiencies may play a role in compromising patient recovery.

Vitamins are organic substances essential for several enzymatic functions. There are 13 known vitamins which are either fat soluble (4 vitamins i.e. K, E, D, and A) or water soluble (9 vitamins i.e. C and the B group).

M. Ssonko, MBChB, MMED Internal Medicine (✉)
Department of Internal Medicine, Makerere University, Kampala 10681, Uganda
e-mail: mikssonko@gmail.com

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Regarding brain function, B vitamins are essential in the maintenance of myelin, neuro-transmitter production and methylation cycle. Fat-soluble vitamins are necessary in inflammatory regulation, regeneration of antioxidants and genetic modification. Vitamin deficiencies will, therefore, cause brain degeneration and will be associated with psychiatric symptoms. Few studies of vitamin deficiencies have been carried out in Sub-Saharan Africa. Below is an overview of vitamins and their relation to neuropsychiatric disorders with the focus on Africa.

Vitamin B1 Deficiency

Thiamine (Vitamin B1) is critical for glucose metabolism. It is a cofactor of α-ketoglutarate dehydrogenase and pyruvate dehydrogenase enzymes both within the citric acid cycle and transketolase enzyme in the pentose phosphate pathway. Severe B1 deficiency which may result from chronic alcoholism, diabetes or malnutrition is usually associated with Wernicke's encephalopathy (WE). WE is clinically characterised by confusion, ataxia, and nystagmus. It is an acute neuropsychiatric disorder which arises as a result of inadequate supply of thiamine to the brain. Confusion and disorientation stem from the brain's inability to oxidize glucose for energy because B1 is a crucial cofactor in glycolysis and the citric acid cycle. Deficiency leads to an increase in free oxygen radicals, cytokines, and alteration of the blood–brain barrier permeability [1].

The WE pathology involves micro-haemorrhages, loss of neurons and gliosis in the periaqueductal grey matter and in the mammillary bodies [2]. Inadequate treatment of WE can predispose a patient to permanent brain damage: the Korsakoff psychosis (confabulation, lack of insight, apathy, retrograde and anterograde amnesia). The amnesia of KS is probably due to the interruption of diencephalic-hippocampal circuits involving the thalamic nuclei and the mammillary bodies [3]. It is recommended that routine management of patients with alcohol-related disease should include thiamine even if neurological signs are absent as described in South Africa [4]. Other thiamine deficiency presentations have been described in Africa. Patients with tropical ataxic neuropathy usually on cassava diet showed evidence of improvement when treated with thiamine [5].

Vitamin B2 (Riboflavin) Deficiency

Riboflavin is important for the reproduction of glutathione, a known antioxidant. B2 is needed to create the essential flavoprotein coenzymes for synthesis of L-methylfolate and for proper utilization of B6. The majority of flavin coenzyme systems help regulate cellular metabolism, whereas the rest are specifically involved in carbohydrate or amino acid metabolism.

Low B2 levels are more prevalent in depressed patients, possibly because of B2's role in the synthesis and function of glutathione [6].

Vitamin B3 Deficiency

Vitamin B3, Niacin, is an essential component of coenzymes NAD/NADP. Niacin can be endogenously synthesized from its natural precursor, tryptophan, a process that requires vitamins B2 and B6.

Pellagra, described as a "3D" syndrome that includes diarrhoea, dermatitis, and dementia, results from niacin deficiency. The main aetiological factors of pellagra are: a deficient diet in niacin; chronic alcoholism; malabsorption; drugs like isoniazid, pyrazinamide, ehtionamide, 6-mercaptopurine, phenobarbital and chloramphenicol. Neuropsychologic manifestations of niacin deficiency include asthenia, depression, hallucinations, confusion, memory loss and psychosis [7].

Vitamin B6 Deficiency

Vitamin B6 (Pyridoxine) is crucial to glycolysis, the methylation cycle, and revitalising glutathione, which is an antioxidant in the brain. Pyridoxine is a coenzyme for the synthesis of neurotransmitters i.e. serotonin, dopamine and GABA. Lower levels of pyridoxal 5- phosphate (active form) as a result of low dietary and plasma B6 are significantly correlated with higher levels of depression with increased risk and severity of depression in geriatric patients [8, 9].

Vitamin B6 deficiency is common (24–56 %) among patients receiving haemodialysis [10]. Women who take oral contraceptives are at increased risk of vitamin B6 deficiency [11].

Vitamin B9 (Folate)

Folate is required in synthesis of neurotransmitters found in the brain and in phospholipid production. Dietary folate must be converted to L-methylfolate for use in the brain. Folate deficiency and insufficiency are common among patients with mood disorders and correlate with illness severity [12].

A meta-analysis of 11 studies of 15,315 persons found those who had low folate levels had a significant risk of depression [13]. In Tunisia, bipolar I patients with hyperhomocysteinemia were found to have reduced levels of folate [14].

Methylenetetrahydrofolate reductase polymorphism was associated with major depression and bipolar disorder [15]. Clinical trials have shown that several forms of folate can enhance antidepressant treatment [16].

Vitamin B12 Deficiency

An essential cofactor, B12 (cobalamin) is needed to produce monoamine neurotransmitters and maintain myelin. Psychiatric manifestations have been described to occur in the presence of low serum B_{12} levels but in the absence of the other well-recognized neurologic and haematologic abnormalities of vitamin B_{12} deficiency [17]. The psychiatric illnesses caused by vitamin B12 deficiency are depression, irritability, agitation, psychosis, and obsessive symptoms [18, 19]. Low B12 levels and elevated homocysteine increase the risk of cognitive decline and Alzheimer's disease and are linked to a 5-fold increase in the rate of brain atrophy [20].

Low levels of serum cobalamin were found among 23 % of the 34 patients in Tunisia with unexplained neurological symptoms without the presence of anaemia. Among the 82 individuals with isolated psychiatric disorders, 14 % of had low serum B12 levels [21]. Ranges of both Serum levels of folic and vitamin B12 levels in a young adult Ugandan population were found to be similar to those in the western countries [22].

The prevalence of low serum vitamin B12 levels among psychiatric patients admitted in Butabika mental hospital using Cobas E411 analyser for serum B12 assay was 28.6 %. The deficiency was 16.4 % [23]. Significant covariates independently associated with low serum vitamin B12 levels included having a DSM-IV diagnosis of Schizophrenia, duration of psychiatric illness $\geq$3 years and duration of hospitalization <3 weeks. The female population was significantly associated with protection from the low serum levels [23]. Irritable mood was a significant finding among HIV infected ART naïve adults in urban Uganda with suboptimal vitamin B12 [24].

Ascorbic Acid or Vitamin C Deficiency

Vitamin C has important biological functions that include carnitine and neurotransmitter biosynthesis, anti-oxidant protection and regeneration of folic acid and vitamin E respectively [25]. Vitamin C's primary role in the brain is as an antioxidant. Oxidative neuronal damage in the free radical theory was supported by plasma vitamin C levels being lower in older persons (aged 65 years and above) with dementia compared to controls [26].

Depression has been found to be a classic psychiatric symptom of vitamin C deficiency.

Ascorbic acid is a cofactor for dopamine beta-hydroxylase enzyme involved in the conversion of dopamine (DA) to norepinephrine. Vitamin C is also a cofactor for the tryptophan-5-hydroxylase enzyme which is required in the conversion of trypto-

phan to 5-hydroxytryptophan (5-HT). Dopamine, noradrenaline, and 5-HT, have important roles in the regulation of mood [27].

Vitamin C intake is significantly lower in older adults (age ≥60) with depression [28]. Some research has shown that patients with schizophrenia have decreased vitamin C levels and dysfunction of antioxidant defences [29].

Vitamin D Deficiency

Vitamin D is produced from cholesterol in the epidermis through exposure to sunlight. Calcitriol the active form of vitamin D is derived from dermal synthesis or ingestion of vitamin D. Increasing evidence reveals vitamin D's role in brain function and development [30]. The pathophysiology of depression is linked to glial and neuronal cells which possess vitamin D receptors [31].

Autism spectrum disorders (ASD) which suggest vitamin D deficiency is not well elaborated in Africa compared to the western industrialized countries with high technological development [32]. The prevalence of ASD among children with developmental disorders in Egypt and Tunisia was documented as 33.6 % and 11.5 % respectively [33]. Among the co-morbid disorders diagnosed in association with ASD among African children, intellectual disability was more common. Belhadj et al. documented co-morbid intellectual disability in over 60 % of cases that were studied [34].

Vitamin E Deficiency

There are 8 isoforms of vitamin E – 4 tocopherols and 4 tocotrienols – that function as fat-soluble antioxidants and also promote innate antioxidant enzymes. Neuronal membranes are protected from oxidation by vitamin E hence reducing inflammation of the brain. Tocotrienols are understood to mediate disease by modifying transcription factors in the brain, for instance glutathione reductase, and superoxide dismutase [35]. Depression has been associated with low plasma vitamin E levels, although other factors excluding dietary intake have been considered [36].

Ataxia with vitamin E deficiency (AVED) is a rare autosomal recessive neurodegenerative disease that occurs in North Africa [37]. Its early identification is essential in order to initiate therapeutic and prophylactic vitamin E supplementation before irreversible damage develops. In Uganda, 63 (30.3 %) of the 208 cases studied showed vitamin E deficiency. Among these, four of five patients with cerebrovascular accidents had vitamin E deficiency [38].

Conclusion

There is minimal or no publications in Africa concerning vitamin deficiencies of vitamins B_2, B_3, B_6, and C. Nonetheless the effect of vitamins on neuropsychiatric disorders is not well studied in Sub Saharan Africa. These deficiencies may ultimately lead to brain degeneration if not corrected as may be seen in none response to psychiatric treatment.

References

1. Page GL, Laight D, Cummings MH. Thiamine deficiency in diabetes mellitus and the impact of thiamine replacement on glucose metabolism and vascular disease. Int J Clin Pract. 2011;65(6):684–90.
2. Victor M, Adams RD, Collins GH. The Wernicke-Korsakoff syndrome. Philadelphia: F.A. Davis; 1971.
3. Thomson AD, Marshall EJ. The natural history of Wernicke's encephalopathy and Korsakoff's psychosis. Alcohol Alcohol. 2006;41:151–8.
4. Naidoo DP, Bramdev A, Cooper K. Wernicke's encephalopathy and alcohol-related disease. Postgrad Med J. 1991;67:978–81.
5. Adamolekun B, Adamolekun WE, Sonibare AD, Sofowora G. A double-blind, placebo-controlled study of the efficacy of thiamine hydrochloride in a seasonal ataxia in Nigerians. Neurology. 1994;44(3 Pt 1):549–51.
6. Naghashpour M, Amani R, Nutr R, et al. Riboflavin status and its association with serum hs-CRP levels among clinical nurses with depression. J Am Coll Nutr. 2011;30(5):340–7.
7. Pitche PT. Pellagre et érythèmes pellagroïdes, Sante 2005;15(3):205–8.
8. Hvas AM, Juul S, Bech P, Nexo E. Vitamin B6 level is associated with symptoms of depression. Psychother Psychosom. 2004;73(6):340–3.
9. Merete C, Falcon LM, Tucker KL. Vitamin B6 is associated with depressive symptomatology in Massachusetts elders. J Am Coll Nutr. 2008;27(3):421–7.
10. Corken M, Porter J. Is vitamin B(6) deficiency an under recognized risk in patients receiving haemodialysis? A systematic review: 2000–2010. Nephrology (Carlton). 2011;16(7):619–25.
11. Wilson SM, Bivins BN, Russell KA, et al. Oral contraceptive use: impact on folate, vitamin B6, and vitamin B12 status. Nutr Rev. 2011;69(10):572–83.
12. Coppen A, Bolander-Gouaille C. Treatment of depression: time to consider folic acid and vitamin B12. J Psychopharmacol. 2005;19(1):59–65.
13. Gilbody S, Lightfoot T, Sheldon T. Is low folate a risk factor for depression? A meta-analysis and exploration of heterogeneity. J Epidemiol Community Health. 2007;61(7):631–7.
14. Ezzaher A, Mouhamed DH, Mechri A, Omezzine A, Neffati F, Douki W, Bouslama A, Gaha L, Najjar MF. Hyperhomocysteinemia in Tunisian bipolar I patients. Psychiatry Clin Neurosci. 2011;65(7):664–71.
15. Gilbody S, Lewis S, Lightfoot T. Methylenetetrahydrofolate reductase (MTHFR) genetic polymorphisms and psychiatric disorders: a HuGE review. Am J Epidemiol. 2007;165(1):1–13.
16. Di Palma C, Urani R, Agricola R, et al. Is methylfolate effective in relieving major depression in chronic alcoholics? A hypothesis of treatment. Curr Ther Res Clin Exp. 1994;55(5):559–68.
17. Herrmann W, Lorenzl S, Obeid R. Review of the role of hyperhomocysteinemia and B-vitamin deficiency in neurological and psychiatric disorders: current evidence and preliminary recommendations. Fortschr Neurol Psychiatr. 2007;75(9):515–27.

18. Lindenbaum J, Healton EB, Savage DG, et al. Neuropsychiatric disorders caused by cobalamin deficiency in the absence of anemia or macrocytosis. N Engl J Med. 1988;318(26): 1720–8.
19. Bar-Shai M, Gott D, Marmor S. Acute psychotic depression as a sole manifestation of vitamin B12 deficiency. Psychosomatics. 2011;52(4):384–6.
20. Vogiatzoglou A, Refsum H, Johnston C, et al. Vitamin B12 status and rate of brain volume loss in community-dwelling elderly. Neurology. 2008;71(11):826–32.
21. Maktouf C, Bchir F, Louzir H, Elloumi M, Ben Abid H, Mdhaffer M, Elleuch N, Meddeb B, Mhiri C, Hassen Z, Makni F, Abid M, Cherif O, Rokbani L, Souissi T, Hafsia A, Dellagi K. Clinical spectrum of cobalamin deficiency in Tunisia. Ann Biol Clin. 2007;65(2):135–42.
22. Galukande M, Jombwe J, Fualal J, Baingana R, Gakwaya A. Reference values for serum levels of folic acid and vitamin B12 in a young adult Ugandan population. Afr Health Sci. 2011;11(2):240–3.
23. Ssonko M, Ddungu H, Musisi S. Low serum vitamin B12 levels among psychiatric patients admitted in Butabika mental hospital. BMC Res Notes. 2014;7:90.
24. Semeere AS, Nakanjako D, Ddungu H, Kambugu A, Manabe YC, Colebunders R. Sub-optimal vitamin B-12 levels among ART-naïve HIV-positive individuals in an urban cohort in Uganda. PLoS One. 2012;7(7):e40072.
25. Hathcock JN (2004) Vitamin and mineral safety, 2nd ed. Council for Responsible Nutrition (CRN).
26. Charlton KE, Rabinowitz TL, Geffen LN, Dhansay MA. Lowered plasma vitamin C, but not vitamin E, concentrations in dementia patients. J Nutr Health Aging. 2004;8(2):99–107.
27. DeSantis J. Scurvy and psychiatric symptoms. Perspect Psychiatr Care. 1993;29(1):18–22.
28. Payne ME, Steck SE, George RR, et al. Fruit, vegetable, and antioxidant intakes are lower in older adults with depression. J Acad Nutr Diet. 2012;112(12):2022–7.
29. Dadheech G, Mishra S, Gautam S, et al. Oxidative stress, α-tocopherol, ascorbic acid and reduced glutathione status in schizophrenics. Indian J Clin Biochem. 2006;21(2):34–8.
30. Berk M, Sanders KM, Pasco JA, et al. Vitamin D deficiency may play a role in depression. Med Hypotheses. 2007;69(6):1316–9.
31. Eyles DW, Smith S, Kinobe R, et al. Distribution of the vitamin D receptor and 1 alpha-hydroxylase in human brain. J Chem Neuroanat. 2005;29(1):21–30.
32. Bakare MO, Munir KM. Autism spectrum disorders (ASD) in Africa: a perspective. Afr J Psychiatry. 2011;14:208–10.
33. Seif Eldin A, Habib D, Noufal A, Farrag S, Bazaid K, Al-Sharbati M, et al. Use of M-CHAT for a multinational screening of young children with autism in the Arab countries. Int Rev Psychiatry. 2008;20(3):281–9.
34. Belhadj A, Mrad R, Halayem MB. A clinic and paraclinic study of Tunisian population of children with autism. About 63 cases. Tunis Med. 2006;84(12):763–7.
35. Sen CK, Khanna S, Roy S. Tocotrienol: the natural vitamin E to defend the nervous system? Ann N Y Acad Sci. 2004;1031:127–42.
36. Owen AJ, Batterham MJ, Probst YC, et al. Low plasma vitamin E levels in major depression: diet or disease? Eur J Clin Nutr. 2005;59(2):304–6.
37. Cavalier L, Ouahchi K, Kayden HJ, Di Donato S, Reutenauer L, Mandel JL, Koenig M. Ataxia with isolated vitamin E deficiency: heterogeneity of mutations and phenotypic variability in a large number of families. Am J Hum Genet. 1998;62:301–10.
38. Tulloch JA, Sood NK. Vitamin E deficiency in Uganda. Am J Clin Nutr. 1967;20(8):884–97.