The Impact of Thiamine Treatment on Generalized Anxiety Disorder

Khanh vinh quóc Lương, Lan Thị Hoàng Nguyên

Vietnamese American Medical Research Foundation, Westminster, USA.
Email: Lng2687765@aol.com

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ABSTRACT

Objective: Patients with generalized anxiety disorder (GAD) are fearful. They constantly worry about minor matters, and they anticipate the worst. The GAD is diagnosed when a patient experiences excessive anxiety and worry for at least 6 months. The cause of GAD is unknown. In the present paper, we discuss patients with GAD who have low levels of thiamine in their bloods. We also discuss the role of thiamine in the pathogenesis and treatment of GAD.

Methods: We examined 9 patients (6 males and 3 females) who met the DSM-IV-TR diagnostic criteria for GAD. These patients had no history of alcoholism. Their ages ranged from 57 to 83 years old (mean age –72.8 ± 2.9 years). All of the patients had low blood thiamine levels (mean –25.1 nmol/L ± 6.0 nmol/L; normal level—70 nmol/L - 180 nmol/L). Participants completed the Hamilton Anxiety Rating Scale (HARS) for anxiety before and after thiamine treatments. All of the patients received daily thiamine 100 mg intramuscularly.

Results: Thiamine supplementation significantly improved HARS scores, increased both appetite and general well-being, and reduced fatigue in patients with GAD. Interestingly, these patients were able to discontinue taking anxiolytic and β-blocker medications.

Conclusion: Parental thiamine significantly affects patients with GAD.

Keywords: Thiamine, General Anxiety Disorder, Vitamin B₁, Anxiety

1. Introduction

Patients with generalized anxiety disorder (GAD) are fearful, they constantly worry about minor matters, and they anticipate the worst. A diagnosis of GAD is made when a patient experiences excessive anxiety and worry for at least 6 months, involving multiple events or activities. However, the National Comorbidity Survey Replication database has indicated that many people have GAD-like symptoms for less than 6 months. Kessler et al. [1] suggested that the reasons for not diagnosing people with GAD might need to be re-evaluated. An epidemiological study reported that patients with GAD exhibit high degrees of comorbidity with major depression (59%) and other anxiety disorders (56%) [2]. GAD is the most disabling and costly anxiety disorder seen in primary care [3,4]. Moreover, only 18% of patients with GAD who were followed over a 5-year period achieved full remission [5,6]. The cause of GAD is unknown. There are many biological theories concerning the etiology of GAD, such as the following: alterations in the structure and function of the amygdala [7], abnormalities of the γ-aminobutyric acid (GABA)-benzodiazepine receptor [8], noradrenergic activation [9], serotonergic deregulation [10], and modest genetic component [11]. Benzodiazepines are commonly used as a first-line GAD treatment. However, newer medications such as buspirone, serotonin and norepinephrine reuptake inhibitors (SNRIs) have begun replacing benzodiazepines in the treatment of GAD. Some patients may become dependent on benzo diazepines. In the meantime, the prevalence of mental health disorders has increased in developed countries in correlation with the Western diet [12]. Some investigators have reported that nutritional deficiencies are associated with some mental disorders [13]. Thiamine deficiency, common to alcoholism, can produce confusion and psychotic symptoms, in addition to neurological deficits. Low plasma thiamine levels have also been observed in cognitively impaired elderly patients [14].

Therefore, we examined patients with GAD who presented low levels of blood thiamine. This paper also discusses the role of thiamine in the pathogenesis and treatment of GAD.

2. Methods and Results

We examined 9 patients (6 males and 3 females) who met...
the DSM-IV-TR diagnostic criteria for GAD. Their ages ranged from 57 to 83 years old (mean—72.8 ± 2.9 years). All of the patients had low blood thiamine levels (mean, 25.06 nmol/L ± 6.0 nmol/L; normal level—70 nmol/L - 180 nmol/L). These patients had no history of alcoholism; however, they did present histories of hypertension, type 2 diabetes or both. Patients completed the Hamilton Anxiety Rating Scale (HARS) before and one week after thiamine treatment (the mean HARS scores were 27.33 and 5.8, respectively). The HARS has been used in numerous GAD treatment studies [15]. All of the patients received daily thiamine 100 mg intramuscularly for 2 - 4 weeks.

Thiamine supplementation improved HARS scores, increased appetite and general well-being, and decreased fatigue in patients with GAD. Interestingly, these patients were able to discontinue the use of anxiolytic and β-blocker medications.

3. Discussion

In the present study, all of the patients presented low blood thiamine levels. Thiamine is important to glucose energy-utilization pathways, particularly in the central nervous system, which needs a continuous supply of glucose. Thiamine deficiency is characterized by a selective loss of neurons in the hypothalamus, midbrain, brainstem and cerebellum of humans and animals [16,17]. Enccephalopathy due to thiamine deficiency may involve impairment of the function of cholinergic neurotransmitters. Thiamine is a coenzyme that is required for the synthesis of acetylcholine (ACh). The synthesis of ACh is impaired in the brains of thiamine deficient rats [18], which leads to a significant reduction of neural ACh levels [19]. Using biochemical analyses, Mair et al. [20] demonstrated that the concentration of norepinephrine was significantly reduced in the brain of rats’ (at both the cortex-hippocampus boundary and in the olfactory bulbs). Furthermore, this reduction in norepinephrine was accompanied by a concomitant decrease in learning and memory in the thiamine-deficient rats. Animal studies have suggested that thiamine is involved in the presynaptic release of ACh. Thiamine binds to nicotinic receptors and may exhibit anticholinesterase activity [21]. Moreover, thiamine deficiency induces an early central muscarinic cholinergic lesion [22]. The muscarinic cholinergic synaptic receptor densities were reduced by 30% in the homogenates of the hippocampus and by 40% in the homogenates of the temporal cortex of alcoholics [23,24]. Patients with GAD had fewer α2-adrenergic receptors than did control subjects [25]. A blunted growth hormone response to clonidine in patients with GAD indicated that these patients exhibit decreased postsynaptic α2-adrenergic receptor sensitivity [26].

Dicethiamine hydrochloride, an analogue of thiamine, improved performance in an animal model of complex fatigue [27]. Sulbutiamine, a highly lipophilic thiamine derivative, is an antiasthenic compound that can cross the blood brain barrier and selectively active on specific brain structures that are directly involved in asthenia [28]. Kreisler et al. [29] observed the effects of an induced vitamin B complex deficiency that caused severe primary mental changes or aggravations of pre-existing symptoms in psychotic patients. In a retrospective study, Mishra et al. [30] investigated the relationship between vitamin B intake in childhood and subsequent psychological distress in adulthood. They found that adult women who consumed less thiamine during childhood experienced more psychological distress; however, this relationship disappeared when the authors adjusted for smoking confound. In another study, a psychotic patient responded to intramuscular administration of thiamine 100 mg [31]. Gontzea et al. [32] assessed the thiamine status of patients with neurosis in a psychiatric department. They observed decreases in thiamine excretion and erythrocyte transketolase activity in patients with neurosis compared to healthy control participants, suggesting that the psychiatric patients had thiamine deficiencies. In a controlled trial, Benton et al. [33] demonstrated a significant association between improved thiamine status and enhanced performance across a range of cognitive function tests in women. They observed significant cognitive deteriorations when the subjects were deprived of thiamine using the psychoneurotic scales of the Minnesota Multiphasic Personality Inventory (MMPI); however, thiamine supplementation reversed these effects [34]. Smidt et al. [35] found that healthy elderly Irish women responded to thiamine supplementation with significantly increased appetites, energy intakes, and general well-being as well as decreased fatigue. Heseker et al. [36] noted that low levels of thiamine, ascorbic acid and folate associated with poor mood. Thiamine and other B vitamins augmented tricyclic antidepressants in the treatment of affective and cognitive disturbances in geriatric depression [37]. Thiamine supplementation improved the symptoms of neurotic patients [38]. Wilkinson et al. [39] noted that thiamine supplementation improved the quality of life of subjects with persistently low thiamine pyrophosphate levels. Students who took extra thiamine had more than doubled their scores on the clear-headedness and mood subscales of the Profile of Mood States (POMS) psychological test [40].

The intestinal absorption of thiamine is normally sufficient in young people but may decrease with age [41]. Schaller and Holler [42] reported that intestinal ALP is involved in the active thiamine absorption in the intestinal tract. Furthermore, Rindi et al. [43] found that intes-
tinal ALP can transphosphorylate thiamine to thiamine monophosphate during intestinal transport in rats. Without ALP, thiamine cannot be transported into the lumen of the gastrointestinal tract [44]. The decrease in intestinal ALP activity that is observed in older rats has been attributed to the reduction of enterocytes caused by the age-induced atrophy of intestinal mucosa [45]. The enzymatic activity of ALP in the duodenum was also found to be significantly higher in 5-month-old rats compared to the other age groups; these differences stark between the 2.5-week-olds and 23-month-olds [46]. The decrease in intestinal ALP activity of older rats has been attributed to the reduction of the number of enterocytes caused by the age-induced atrophy of intestinal mucosa [45].

In humans, single oral doses of thiamine above 2.5 mg are mostly unabsorbed [47,48]. Baker et al. [49] demonstrated that only the intramuscular administration of thiamine was able to correct thiamine deficiencies in subjects over 60 years-old. Sasaki et al. [50] reported a case study of a patient with a thiamine deficiency and psychotic symptoms. Only repeated intravenous administration thiamine ameliorated the condition of patients. In conclusion, parental thiamine affects the treatment of patients with GAD patients by improving anxiety, decreasing fatigue, and increasing appetite and general well-being.

REFERENCES


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