



Vitamin B₁₂ deficiency and depression in elderly: Cross-sectional study in Eastern Croatia

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ABSTRACT

Introduction: Vitamin B₁₂ deficiency occurs frequently among elderly patients and it has recently been connected with the occurrence of depressive symptoms in this population. The aim of this study was to determine the frequency of vitamin B₁₂ deficiency among elderly patients from Eastern Croatia and to evaluate whether there is a connection between this deficiency and the occurrence of depressive symptoms among them.

Methods: This cross-sectional study was conducted from April to June 2013, among 140 elderly patients from Vukovar-Srijem County (47.9%, 67/140 males and 52.1%, 73/140 females; mean age 71.0±6.7 years). The anonymous questionnaire was used to obtain demographic data, data regarding socio-economic status and personal history of diseases of study participants as well as data pertaining to the existence of depressive symptoms among them. The competitive immunoassay vitamin B₁₂ kit was used to determine serum levels of vitamin B₁₂.

Results: Among all study participants there were 7.1% (10/140) of them with B₁₂ deficiency and 70.0% (98/140) of them with the symptoms of depression. Depressive symptoms occurred in 100.0% (10/10) patients with the vitamin B₁₂ deficiency and 67.7% (88/130) of patients without it.

Conclusion: The study showed positive connection between the existence of depressive symptoms and vitamin B₁₂ deficiency among elderly patients. This finding points to the need for frequent vitamin status evaluation in this age group and its consequent correction that could improve overall health of this population subgroup.

Keywords: Croatia; depression; elderly; vitamin B₁₂

INTRODUCTION

Vitamin B₁₂ (cobalamin) is one of the water-soluble vitamins (1). It is found in meat, fish, milk, milk products and eggs. In fruits and vegetables it is found in negligible quantities. The dietary reference

intake for an adult is 3 µg per day, and the reserves in the human body are 2-5 mg. In the circulation vitamin B₁₂ is carried bound to proteins transcobalamines. Due to the relatively large reserves in the body, a disorder in the metabolism of vitamin B₁₂ can remain hidden for a long time (2).

In the human body, vitamin B₁₂ is a cofactor and coenzyme in many biochemical processes. Vitamin B₁₂ together with vitamin B₉ is involved in the biosynthesis of labile methyl groups, which are necessary

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for the biosynthesis of purine and pyrimidine bases, essential components of nucleic acids. Lack of these vitamins causes deterioration in cell division and changes in protein synthesis (2-6). Vitamin B₁₂ deficiency causes a decrease in the activity of methionine synthase, which inhibits the regeneration of tetrahydrofolate and folate remains in a form that human body cannot use. Therefore, the lack of folate and vitamin B₁₂ may interfere with DNA synthesis, due to the reduced amount of the active form of vitamin B₉. Disturbance in the DNA synthesis have a negative impact on the rapidly dividing cells, especially red blood cells, which results in the production of large and immature red blood cells. Such condition may result in megaloblastic anemia, and can occur with decreased number of leukocytes and platelets and with an increased number of hypersegmented neutrophils. The correlation between folate and vitamin B₁₂ explains why their deficiency results in morphologically identical anemia. Additionally taking folic acid restores sufficient amounts of this vitamin for normal red blood cell production. However, if the cause of anemia is vitamin B₁₂ deficiency, additional intake of folate may mask the condition, along with the successful treatment of anemia. Also, larger amounts of folate do not help reducing neurological symptoms caused by vitamin B₁₂ deficiency (2-7).

Neurological symptoms of B₁₂ deficiency can occur without anemia, in 75% to 90% of people who are lacking this vitamin. Those symptoms include numbness in hands and feet, difficulty in walking, exacerbated memory, disorientation, dementia, myelopathy, mood swings, irritability, mononeuropathy (optical or olfactory), autonomic neuropathy (impotence, urinary or fecal incontinence), problems with concentration and exacerbated hand coordination and legs. The most common symptoms in children are irritability, disrupted growth and development, apathy and anorexia. Generally, those symptoms can be cured by vitamin B₁₂ intake, but if you start treatment too late, part of the resulting damage is irreversible (8,9).

Vitamin B₁₂ deficiency in adults is considered the value of 150 pmol/L and below (10). According to a study conducted at the University Hospital of Strasbourg, Strasbourg, France, in 2004, vitamin B₁₂ deficiency was observed in more than 20% of

the elderly. The most common causes of deficiency of this vitamin according to this study were: malabsorption syndrome (in 60% of cases), followed by pernicious anemia and inadequate intake of this vitamin with food (10).

Depression is a mental illness which leads the patient in a state of helplessness and hopelessness. It always occurs as a reaction to a loss-physical or mental, real or imaginary. Older age, stress, alienation, disaffection, retirement, loss of a spouse, the departure of children, reducing the need and motivation for activities that used to be a normal part of life, are additional factors that can trigger depressive reaction in elderly people. Symptoms of depression are only worsened by the presence of somatic diseases, and it is very common in the elderly that depression develop as a side effect of medications. Depression can occur due to the lack of some essential nutrients in the diet or because of malnutrition (11). Typical symptoms of depression include depressed mood, loss of interest and enjoyment, and reduced energy (decreased activity and increased fatigue). Other common symptoms include reduced concentration and attention, reduced self-confidence and self-esteem, feelings of guilt and worthlessness, sleep disturbances, pessimistic and gloomy views of life, loss of appetite and suicidal or self-harm ideas. The diagnosis of depression is set based on the number of symptoms, duration of symptoms, the impact of depressive disorders in social, family and work functioning and the circumstances that led to the disorder. The literature states that depression comprises 10-15% of the elderly population, and according to some authors, even up to 40%. Although often occurs in elderly people, depression is a pathological process and certainly not part of normal aging (11).

Deficiency of vitamin B₁₂ has a well-established association with a wide variety of neurologic and psychiatric manifestations with depression being one of the most frequent of them (12). Considering the older age, it is especially important to emphasize that low serum vitamin B₁₂ level is one of the risk factors of geriatric depression (13). Study conducted in Norway confirmed that there is a connection between low serum vitamin B₁₂ level and occurrence of depressive symptoms in the group of 1935 study participants, aged 71 to 74 years (14) while the study conducted in Germany showed that taking

> 50 mg of vitamin B₁₂ per day could reduce the occurrence of vascular and neurological disorders and depressive symptoms in elderly persons (15).

The aim of this study was to determine the frequency of vitamin B₁₂ deficiency among elderly patients from Eastern Croatia and to evaluate whether there is a connection between this deficiency and the occurrence of depressive symptoms among them.

METHODS

This cross-sectional study was conducted in the County General Hospital Vukovar, Croatia during April to June 2013 period. Participation in the study was voluntary, and the study was approved by the Ethics Committee of the County General Hospital Vukovar. Elderly patients who performed blood tests in the Department of Laboratory Diagnostics of the County General Hospital Vukovar as an integral part of their preventive medical examination were asked to participate in this study. The convenience sample used in this study consisted of all elderly patients who performed blood tests in the Department of Laboratory Diagnostics of the County General Hospital Vukovar during April to June 2013 period. The self-administered anonymous questionnaire was used to obtain demographic data (age, gender, marital status, place of living), data regarding socio-economic status (way of living – living alone in one's own household, living in joint household with younger family members where those living alone were considered to be of lower socio-economic status than those living in joint household with younger family members), data regarding habit of taking vitamins and mineral as dietary supplements and personal history of diseases of study participants (presence of some sort of chronic disease) as well as data pertaining to the existence of depressive symptoms among them. The Anxiety and Depression Detector (the ADD), composed of five questions was used as the screening device for fast detection of depressive symptoms in study population (16). Total vitamin B₁₂ serum concentrations were determined using a competitive immunoassay vitamin B₁₂ kit with a measuring range between 22 and 1476 pmol/L (Roche Diagnostics GmbH, Mannheim, Germany) on a Cobas e601 immunoassay analyzer (Roche Diagnostics GmbH, Mannheim, Germany) (17).

Statistical analysis

Statistical analysis included data obtained by the laboratory analysis of participants' blood and by the anonymous questionnaire. Upon confirming normality of data distribution by Kolmogorov-Smirnov test, all data were processed by the methods of descriptive statistics. The proportions were calculated and compared by use of Fisher's exact test. $P < 0.05$ was considered statistically significant. Statistical analysis was done by the SPSS Statistical Package for Windows, version 13.0 (SPSS Inc., Chicago, IL, USA).

RESULTS

The study sample consisted of 140 elderly people from the Vukovar-Srijem County, 47.9% (67/140) males and 52.1% (73/140) females, mean age 71.0 ± 6.7 years. According to marital status, there were 65.0% (91/140) married and 35.0% (49/140) single (divorced or widowed) study participants. According to the place of living there were 28.6% (40/140) participants who lived in villages and 71.4% (100/140) participants who lived in town. Considering the chronic diseases, among all study participants there were 85.7% (120/140) of them who suffered from at least one chronic disease and 14.3% (20/140) participants who did not suffer from chronic diseases. When analyzing study population according to the habit of taking vitamins and mineral as dietary supplements, among all of them there were 35.7% (50/140) of those who took these supplements and 64.3% (90/140) participants who did not take them. According to the established presence of depressive symptoms among all study participants, there were 70.0% (98/140) of them with the existence of depression and 30.0% (42/140) of them without depressive symptoms.

According to the competitive immunoassay vitamin B₁₂ kit manufacturer the reference range of vitamin B₁₂ in serum was 141 to 489 pmol/L (17), and these values were used for the classification of the measured concentration of vitamin B₁₂ in serum samples of study participants. Accordingly, among all study participants there were 7.1% (10/140) of them whose measured serum concentrations of vitamin B₁₂ were below the reference range, 87.2% (122/140) of participants whose measured serum

concentrations of vitamin B₁₂ were within the reference range, and 5.7% (8/140) of participants whose measured serum concentrations of vitamin B₁₂ were above the reference range.

When analyzing the existence of depressive symptoms among study participants in relation to measured serum concentrations of vitamin B₁₂ it was established that depressive symptoms existed in 67.7% (88/130) of study participants whose measured serum concentrations of vitamin B₁₂ were within or above the reference range and in 100.0% (10/10) of study participants whose serum vitamin B₁₂ concentrations were below the reference range, and this difference in the existence of depression between the groups was statistically significant (Fisher's exact test; $p=0.033$) (Table 1).

Elderly patients with coexisted vitamin B₁₂ deficiency and depression mainly lived in town (90.0%, 9/10), alone in their own household (90.0%, 9/10) and were mainly married (60.0%, 6/10) living in one generation family. Majority of them suffered from some kind of chronic disease (90.0%, 9/10) and 30.0% (3/10) of them had been taking vitamins and minerals as dietary supplements.

DISCUSSION

This study revealed that 7.1% of elderly from Eastern Croatia had vitamin B₁₂ deficiency, which is in compliance with the majority of studies that found 5-15% prevalence of this deficiency among elderly (18-21) although there are studies that discovered even higher prevalence of vitamin B₁₂

deficiency in this age group (10). The explanation of determined prevalence of vitamin B₁₂ deficiency is probably connected with the fact that more than third (35.7%) of study participants were regularly taking vitamins and mineral as dietary supplements thus improved their vitamin B₁₂ status. This study also revealed extremely high prevalence (70.0%) of depression among study population that is much higher than the determined prevalence of depression among elderly in other studies in which the prevalence rates varies between 10 and 40% (11,22-24). A plausible explanation for this extremely high prevalence of depression in the studied population is the impact of recent history and past war events and the overall economic situation in the society, particularly in the Eastern Croatia, while it is known that war and poor economic situation leads to the increase in the prevalence of depression and all its disastrous consequences (25,26).

When analyzing the existence of depressive symptoms among study participants in relation to measured serum concentrations of vitamin B₁₂ this study established the statistically significant difference ($p<0.05$) in the existence of depression between group of study participants whose measured serum concentrations of vitamin B₁₂ were within or above the reference and the group of study participants whose serum vitamin B₁₂ concentrations were below the reference range. In the latter group all participants (100.0% of them) scored positive on the ADD regarding the existence of depressive symptoms, while the depression was detected in 67.7% of study participants whose measured serum concentrations of vitamin B₁₂ were within or above the reference range. This finding points to the positive connection between vitamin B₁₂ deficiency and depression confirming previously highlighted possibility that vitamin B₁₂ deficiency is a significant risk factor of geriatric depression (13,14). Considering the connection between vitamin B₁₂ and depression it is important to emphasize that the associations between vitamin B₁₂ status and cognitive function scores are stronger in patients with depression than in participants without depression (14,27,28). Decreased performance on visual memory and verbal fluency tests has been reported in depressed elderly people with low vitamin B₁₂ levels (28).

TABLE 1. The presence of depression among study participants according to the measured serum concentrations of vitamin B₁₂

Study participants according to the measured serum concentrations of vitamin B ₁₂	The presence of depression among study participants		Total
	Yes N (%)	No N (%)	
Below the reference range	10 (100.0)	0	10
Within and above the reference range	88 (67.7)	42 (32.3)	130
Total	98	42	140

However, several limitations should be taken into considerations. The study's cross-sectional design does not allow interpretation of causality and cannot demonstrate whether the observed association with vitamin B₁₂ status precedes or results from the depression. Furthermore, results for tests with relatively small sample sizes could be affected by selection bias and should be interpreted cautiously. Around 7.000 elderly people gravitate to this Hospital thus our sample represents 2% of the study population. Because elderly people are less prone to participate in such surveys we consider that this study is quite valuable despite such small sample size. Besides previously mentioned limitations there are limitations considering the convenience sample used in this study and the fact that we did not precisely measure the socio-economic status of study participants. The last mentioned is especially important knowing that there is a significant influence of socio-economic status on nutritional habits (for example meat availability) and also ability of study participants to obtain supplementation. Considering the fact that Eastern part of Croatia especially Vukovar-Srijem County is one of the least developed area in Croatia we did not specifically investigated this aspect but merely try to establish the actual situation in the field. Nevertheless this study can serve as a database for future studies related to this issue in Croatia, especially bearing in mind that the studies in the world pointed to a possible therapeutic use of vitamin B₁₂, which could reduce the occurrence of vascular and neurological disorders and depressive symptoms in elderly (15). This is especially important for the Croatia and the majority of EU countries that are considered to be old because they have more than 11% of population older than 65 years of age (11). The percentage of elderly persons in Croatia is 17.3% and it is considered that by 2050 it will go up to more than 20% (11). Older persons are able to function as very useful community members. They have usable potential for transmission of knowledge, skills, abilities and work experience to younger and other older generations, so that unnecessary mistakes would not be repeated (11). In order to elderly fulfill such an important societal role and to actively participate in social life of a community above all, it is important to prevent depression and other vascular and neurological disorders whose

occurrence can potentially be reduce with a vitamin B₁₂ supplementation. Further long-term trials in elderly patients with low vitamin B₁₂ status are required to assess the relevance of vitamin B₁₂ supplementation in that sense.

CONCLUSION

The study showed positive connection between the existence of depressive symptoms and vitamin B₁₂ deficiency among elderly patients. This finding points to the need for frequent vitamin status evaluation in this age group and its consequent correction that could improve overall health of this population subgroup and potentially reduce the occurrence of depression and other vascular and neurological disorders among elderly enabling them to more actively participate in social life of a community.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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