

Original Research Article

Vitamin B 12: the hidden ingredient of stroke

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ABSTRACT

Background: Study aimed to evaluate the relationship between vitamin B12 and acute cerebral stroke in this study.

Methods: Blood samples drawn within 24 hours after the stroke from hospitalized patients (n=100) and from 100 control cases matched for age, sex and other modifiable risk factors of stroke were analyzed. With a competitive, ECLIA, serum levels of vitamin B12 were measured. The quantitative data of the groups was compared using Analysis of Variance and Tukeys HSD post hoc test for comparison. Chi-square tests were used.

Results: Median serum vitamin B12 levels were significantly lower in the patients than in the control subjects, 188.71 and 256.25 pg/ml respectively (p=0.0001). This difference was independent from other risk factors. The mean age in case group was 62.49 (SD: 12.45 years) and 56.62 (SD: 13.05 years) in control group with p=0.001. Therefore, prevalence of stroke is more between 6th and 7th decade of life. Mean serum vitamin B12 levels were lower in males (201.8pg/ml) than the females (268.pg/ml) in the case group.

Conclusions: Low vitamin B12 is associated with an increased risk of stroke, and its relationship is independent from the other known modifiable stroke risk factors.

Keywords: Stroke, Transient Ischemic Attack, Vitamin B12 deficiency

INTRODUCTION

Hyperhomocysteinemia (HH) has been observed in arterial and venous thrombotic diseases. Vitamin B12 is an integral part for metabolization of homocysteine. HH is known to lead to the production of free oxygen radicals. It also stimulates the development of smooth muscles and inhibits intracellular methylation processes, alters anticoagulation pathways within endothelium via inhibition of thrombomodulin.

HH is suggested to be an independent risk factor for atherosclerotic cerebrovascular diseases aside from classical vascular risk factors such as hypertension, smoking, hyperlipidemia, hyperglycemia and hyperfibrinogenemia.¹ Decreases in circulating vitamin B12 and folate levels reveal an increase in the risk of atherothrombosis.^{2,3}

An analysis of 13 different studies performed between 1969 and 1998 revealed that HH associated with vitamin B12 and folate deficiency increases the risk of stroke (Engman 1998). Verhoef et al, found a correlation between lower serum B12 levels and cardiovascular diseases independent of total HH levels. Yilmaz et al, evaluated serum vitamin B12 and folate levels in cases of stroke and found statistically significant correlations among cerebrovascular stroke, serum B12 and folate levels. HH becomes more prominent in older age groups and in the presence of the risk factors. Dalery et al, Selhub et al, Verhoef et al, found that homocysteine levels in healthy women were lower than in their male counterparts.²⁻⁴

In this study, evaluated the effects of vitamin B12 levels on acute cerebrovascular stroke, which is an important cause of morbidity and mortality worldwide. The present

study searched for an answer to an issue: “Is deficiency of vitamin B12 deficiency, the hidden ingredient in pathogenesis of stroke?”.

METHODS

The study was completed between January 2016-January 2017. Blood samples were drawn within 24 hours after the stroke from hospitalized patients (n=100) with the diagnosis of acute cerebrovascular disease and also blood samples from 100 similarly age, sex and modifiable risk factor matched control subjects without any CVA were analyzed. Before each analysis, the objective of the study was described, and informed consent was obtained from all patients. The diagnosis of stroke was made by a neurologist according to the criteria of World Health Organization defining stroke as rapidly developing clinical symptoms lasting more than 24 hours or leading to death without any other etiology other than a vascular abnormality (Hatano 1976). The following inclusion criteria were used for the diagnosis of stroke: clinical evidence of stroke and computed tomography (CT) evidence of cerebral infarction without demonstrable source of embolism. Patients were evaluated with cranial CT and cranial magnetic resonance imaging (MRI) whenever indicated to define stroke. People were excluded with a history of vitamin complex tablets intake within last three months. The modifiable risk factors were noted. Hypertension was considered to be present if at the time of diagnosis the subjects had a systolic blood pressure >160 mmHg or a diastolic pressure >95 mmHg, and if treatment for high blood pressure was administered previously. Hypercholesterolemia was considered present if subjects had serum total cholesterol >200 mg/100 ml. Hyperglycemia was considered present if subjects had a serum glucose level >115 mg/100 ml, or if treatment for diabetes was started previously. Routine hematological, biochemical and microbiologic analyses were performed. Serum levels of vitamin B12 was measured in blood samples taken within 24 hours after the stroke. Intergroup differences and correlations were tested using Analysis of Variance and Tukeys HSD post hoc test. Chi-square tests were used. All analyses were made using the SPSS 10.0 version statistical software package, and probability value of less than 0.05 was accepted to be statistically significant.

RESULTS

The study group consisted of 100 patients and 100 control subjects with similar distribution of gender, age and other risk factors like hypertension, diabetes, alcohol consumption and smoking. Descriptive features of patients are shown in (Table 1). Mean ages of cases and controls was 62.49(SD 12.45 years), 56.62 (S.D.: 13.05 years) respectively. In a similar study by Kocer et al, the mean age in the case group was 64.46 (SD 11.1 years) and 60.28(SD 12.96 years). So, the prevalence of stroke is more in the 6th and 7th decade of life. The correlation between serum vitamin B12 levels and patients ages was

statistically non-significant with $p=0.068$ in control group and 0.081 in the case group. Cohort of cases was evaluated and found mean vitamin B12 values to be 207.8pg/ml for males and 268.6pg/ml in females. In the study by Kocer et al, these values were 207.13pg/ml in males and 283.6pg/ml in females in the case group. Median values for vitamin B12 in cases was 188.71pg/ml and 256.25pg/ml in the case and control group respectively. Thus, the serum vitamin B12 level was significantly lower in cases than controls ($p=0.0001$). There were similar conclusions by Kocer et al.

Table 1: Descriptive characteristics of patients and control group.

	Case	Control	p value
No of patients	100	100	
Male	60	65	0.170
Female	40	35	
Mean age	62.49 (12.45)	56.62 (13.05)	0.001
S vitamin B12 Median	188.71	256.25	0.0001

DISCUSSION

the mean age in case group was 62.49 (SD 12.45 years) and 56.62 (SD 13.05years) in the control group. Results are comparable to those obtained by Kocer et al, where the mean ages in case group was 64.46 (SD 11.1 years) and 60.28 (SD 12.96 years) in the control group.⁸ But unlike in the parent study, the correlation between vitamin B 12 deficiency and age was not statistically significant($p=0.081$). In the same study the mean vitamin B12 levels in the case group was 207.13 pg/ml for males and 283.6 pg/ml in females. It was 201.8 pg/ml and 268.6 pg/ml in males and females respectively. Out of 64 cases 71.9% were deficient in Vitamin B12 levels. Out of the 36 patients who were on a mixed diet, 58.3% were deficient; the correlation was non-significant ($p=0.205$).⁹ The study has parallel results in regards to correlation between age, smoking, alcohol intake, dietary type and incidence of stroke as other studies by Biswas et al, Kocer et al, and Engman et al.⁹⁻¹¹ Vitamin B 12 is a potentially correctable risk factor for development of stroke.

CONCLUSION

The majority of cases of strokes and controls in the study group were in the age group of 51 to 70 years with the mean age of 59.57(SD:13.06 years).

There was no significant difference found in serum vitamin B12 level between <60 years of age and >60 years of age. Age is a confounder so that needs to be considered. B12 is decreased with an increasing age in the present study confirming previous papers.

Mean vitamin B12 level was found to be lower in males than in females as against the findings of Dalery et al, Selhub et al, Verhoef et al, who found that serum Vitamin B12 levels in healthy women were lower than in their male counterparts.

Mean serum Vitamin B12 level was significantly lower in cases than that in controls. Yilmaz et al, evaluated serum vitamin B12 and in cases of stroke and found statistically significant correlations among cerebrovascular stroke, serum B12 and folate levels.

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Ethical approval: The study was approved by the Institutional Ethics Committee

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