A comparison of serum alpha-1-antitrypsin and vitamin B12 levels in patients with vitamin B12 deficiency

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Abstract

Aim: Alpha-1-antitrypsin (A1AT) loses its antiprotease activity as a result of oxidation of the methionine in its structure. Vitamin B12 plays an active role as a co-factor during methionine synthesis. Thus, we think that vitamin B12 deficiency may lead to decreased A1AT. Material and Method: The research was planned as an observational study. One hundred eighty patients were enrolled. The levels of serum A1AT and vitamin B12 were compared based on demographic characteristics of the patients. Twenty-seven patients' -who have accomplished therapeutic protocol and who have come to control visits- A1AT levels were controlled after treatment and compared with the before treatment levels. Results: The levels of serum A1AT could not be found statistically significantly different according to the level of vitamin B12. However, in patients using any medication because of a chronic disease, the levels of serum A1AT were found higher in the group with high level of vitamin B12, than the group with the low level of vitamin B12. Serum A1AT levels were found significantly lower in obese than non-obese participants. Following treatment with vitamin B12, the levels of serum A1AT (pre-treatment 121.67±13.884, post-treatment 138.04±16.922, P=0.001) were found to be increased. Discussion: This study's results suggest that the level of vitamin B12 may have a significant role in the synthesis of A1AT.

Keywords

Vitamin B12; Alpha 1-Antitrypsin; Obesity

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Introduction

A1AT acts as an antioxidant due to its methionine content, and its deficiency causes chronic diseases such as emphysema. It is the main inhibitor of the serine protease in human plasma and inhibits trypsin and other proteases such as elastase [1]. It is synthesized by hepatocytes, macrophages, and intestinal and bronchial epithelial cells, and it has a plasma half-life of five days [2-4]. It is estimated that the ratio of development of emphysema in patients with genetic A1AT deficiency is approximately 5%, but autopsy studies reveal that there is significant lung injury in approximately 70% of the patients with the genetic deficiency [3]. It is highlighted that the risk of developing emphysema is increased when serum level of A1AT falls below 80 mg/dl [5]. The mechanisms of the environmental factors that play a role in the development of Chronic Obstructive Pulmonary Disease are suggested to be secondary to their action as free radicals oxidizing A1AT. The oxidation by free radicals of the methionine sulfide groups at the 351st and 358th amino acids of the peptide chain lead to loss of the antiprotease activity of A1AT [3,6]. A1AT deficiency may be seen particularly in pulmonary involvement with diseases such as emphysema, bronchiectasis, and chronic bronchitis, and also in liver involvement in clinical situations such as neonatal cholestasis, chronic hepatitis, and cirrhosis and hepatocellular carcinoma. It is reported that in the deficiency of A1AT the risks of necrotizing panniculitis and multisystem vasculitis are increased [7,8].

Vitamin B12 mainly acts as a cofactor in two enzyme systems in the body. There is methylmalonyl-CoA-mutase which converts methylmalonyl-CoA to succinyl-CoA. On the other hand, there is methionine synthase which converts homocysteine, a methionine residue formed by methylation reactions back to methionine where vitamin B12 transfers the methyl group taken from folate [9]. Epidemiological studies point out that cobalamin deficiency ranges between 5% and 60% and this difference is correlated with age [10,11]. Framingham reported that prevalence of cobalamin deficiency among elderly is 12% [12]. Interestingly, a significant deficiency of vitamin B12 is observed in smokers and alcohol users. There are several studies reporting an association between cigarette as a free radical source and reduced vitamin B12 serum levels [13,14].

The amino acid methionine is one of the building stones of A1AT, and since it is not synthesized in the body, it should be taken from the environment. One of the principal functions of methionine is to participate in methylation reactions by S-adenosyl methionine molecules [15]. A large part of homocysteine produced by methylation reactions is converted to methionine by the enzyme methionine synthase which has vitamin B12 as a cofactor. A stable level of methionine in the body is provided by the maintenance of this transformation in an uninterrupted manner. To evaluate this relation, we investigated whether serum A1AT levels were affected by the level of vitamin B12.

Material and Method

This study was designed as an observational study. The study was approved by Dokuz Eylul University (DEU) Ethical Committee. The sample size was calculated to be at least 144 according to the formula n = t2pq / d2. In determining the sample size the values were accepted as follows: p = 0.12, the q = 0.88, d = 0.05, α error level = 0.05 and t = 1.96 according to error level, respectively.

A total of 5743 serum samples for vitamin B12 tests ordered between April and July 2011 by DEU Hospital outpatient and inpatient clinics were examined with the help of the central laboratory operating system. The serum samples of the 180 patients who accepted to participate in the study and have inclusion criteria were stored. The serum levels of vitamin B12 were categorized into two groups; the high group was up to 220pg/ml, and the low group was below 220pg/ml. The levels of serum A1AT and vitamin B12 were compared based on demographic characteristics of the patients.

Exclusion criteria: Pregnant women, children, patients whose folate levels were not measured or detected to be higher or lower than normal, the ones with iron deficiency anemia, liver disease, kidney failure, infection, trauma history, and tissue necrosis pathologies.

Among one hundred eighty patients, only twenty-seven patients -who have accomplished therapeutic protocol and who have come to control visits- A1AT levels were controlled after treatment and compared with the before treatment levels.

Windows SPSS statistical software package (PASW Statistics for Windows, Version 16.0 Chicago: SPSS Inc.) was used in analyzing the data. Chi-square test was used to compare percentages. In the comparison of the mean values of the two groups, the independent-samples t-test was used for independent variables, and paired samples t-test was used for dependent variables.

Results

Of the 180 patients enrolled in the study; 101 (56.1%) were females, and 79 (43.9%) were males. There were no significant differences between the two vitamin B12 groups, regarding weight, height, age, gender, and use of cigarette, alcohol, and drugs.

The levels of serum A1AT could not be found statistically significantly different according to the level of vitamin B12. However, in patients using any medication because of a chronic disease, the levels of serum A1AT were found higher in the group with high level of vitamin B12, than the group with the low level of vitamin B12 (Table 1).

Table 1. The comparison of A1AT levels in patients by according to vitamin B_{12}

		B_{12} groups	n	Mean ± SD*	p
A1AT levels	All patients	Low level group	112	129.12 ± 18.10	0.168
		High level group	68	132.93 ± 17.01	
	Using any medication	Low level group	35	120.11 ± 10.19	0.012
		High level group	28	128.00 ± 13.92	

*SD: Standard Deviation

Serum A1AT levels were found significantly lower in obese participants than non-obese. In addition, vitamin B12 levels were lower in obese than non-obese (Table 2).

The mean serum A1AT level before treatment was 121.67 ± 13.884 mg/dl, and the post-treatment mean level was 138.04 ± 16.922 mg/dl. A statistically significant increase was observed in the A1AT levels after Vitamin B12 replacement therapy (P = 0.001) (Table 3).

Table 2. The comparison of A1AT levels and vitamin B_{12} in patients by according to obesity

		n	Mean ± SD*	p
A1AT levels	Non obese	67	134.25 ± 20.78	0.036
	Obese	113	128.31 ± 15.78	
Vitamin B_{12} levels	Non obese	67	218.30 ± 60.12	0.116
	Obese	113	204.62 ± 51.16	

*SD: Standard Deviation

Table 3. Analysis of pre-treatment and post-treatment with data

		n	Mean ± SD*	P
A1AT levels	Pre-treatment	27	121.67 ± 13.884	0.001
	Post-treatment	27	138.04 ± 16.922	
Vitamin B_{12} levels	Pre-treatment	27	208.78 ± 43.292	0.001
	Post-treatment	27	489.00 ± 127.599	

*SD: Standard Deviation

Discussion

The levels of serum A1AT could not be found statistically significantly different according to the level of vitamin B12. Serum A1AT level is affected by many genetic or individual-related physiological factors. However, in patients using any medication because of a chronic disease, the levels of serum A1AT were found higher in the group with high level of vitamin B12, than the group with the low level of vitamin B12. These data indicate that there is a relation between serum A1AT and vitamin B12 levels in some certain conditions, and in groups that have certain specifications. It was mentioned in one study that hepatocellular carcinoma risk increases in A1AT deficiency, and in another study, it was stated that using S-adenosyl-methionine is beneficial for treating hepatocellular carcinoma [16,17]. This brings in to mind the thought that there might be a relationship between A1AT and S-adenosyl-methionine, and this relationship can be related to vitamin B12.

Serum A1AT levels were found to be lower in obese participants. Serum A1AT levels were found significantly lower in obese participants than non-obese. In addition, vitamin B12 levels were lower in obese participants than non-obese. There are studies claiming an increased obesity frequency in subjects with vitamin B12 deficiency [18,19]. Since there are no accessible studies citing the relationship between serum A1AT level and obesity, we may claim that our results mentioned a relationship may be a new data. The demonstrated decrease in serum A1AT levels in obese individuals may account for the obesity, which is observed more frequently in vitamin B12 deficiency. Both vitamin B12 and A1AT play roles in the etiopathogenesis of obesity, either independently, or A1AT synthesis affected by serum vitamin B12 levels.

In this study, acceleration was detected on serum A1AT levels on participants who attended the therapy protocol and showed up at control visits. This finding suggests that owing to a steady plasma methionine level provided by vitamin B12 treatment, A1AT synthesis is accelerated.

Conclusion

As a conclusion; this study's results suggest that the level of vitamin B12 may have a significant role in the synthesis of A1AT. However, further studies are needed to support our results.

Competing interests

The authors declare that they have no competing interests.

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