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STUDY TO REVEAL THE MEAN REDUCTION IN HOMOCYSTEINE LEVELS IN TYPE II DIABETES MELLITUS PATIENTS ON VITAMIN B12 THERAPY

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Abstract:

Objective: *To determine the mean decrease in homocysteine levels in patient of type II diabetes mellitus on vitamin B12 therapy.*

Study design: *A quasi experimental study.*

Place and Duration: *In the Medicine Unit II of Services Hospital Lahore for Six months duration from July 2018 to January 2019.*

Methods: *72 total patients were selected for the study during the six-month study period. Blood samples were taken for fasting blood glucose and homocysteine to evaluate inclusion criteria at the beginning of the study. Patients were given vitamin B12 500 mg / day for 6 weeks. Fasting homocysteine levels were determined again after 6 weeks. To ensure that bias is minimized, sample collection, transport and laboratory procedures are standardized. Using SPSS version 20.0 data analysis was done.*

Results: *The mean difference in homocysteine before and after treatment was 0.39 (95% CI 0.36 to 0.42) and a statistically significant p value of <0.001.*

Conclusion: *It was concluded that vitamin B12 have an important role in decreasing levels of homocysteine in patients with type II diabetes.*

Key words: *Homocysteine levels, vitamin B12, diabetes mellitus type II.*

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INTRODUCTION:

Diabetes mellitus is a syndrome with impaired metabolism and inadequate hyperglycaemia due to a combination of insulin secretion or insulin resistance and insufficient insulin secretion to compensate. Diabetes are of two types Type 1 and Type 2 [1]. The third group is labeled "another specific type" by the American Diabetes Association (ADA). Homocysteine is an amino acid produced by the liver by another amino acid methionine in the liver, animals and plant proteins [2]. Although it is 70% dependent on proteins, it is a potent toxin for endothelial cells [3]. Methyltetrahydrofolate and cobalamin play a role in metabolism, thus preventing their accumulation. In type 2 diabetic patients; one risk factor is Hyperhomocysteinemia for mortality for every increase of 5 hmol / L total serum homocysteine, 60% in non-diabetic and diabetic patients [4]. Various prospective studies have determined the association between total homocysteine and cardiovascular disease risk. Most, but not all, there is a positive relationship between hyperhomocysteinemia and cardiovascular disease [5]. This atherosclerotic effect is achieved by an increase in oxidative stress that can induce endothelial dysfunction. Homocysteine may also affect the extracellular matrix properties and smooth muscle cells proliferation. It is believed that oxidative stress in type 2 diabetes mellitus is increased and that the modification of the matrix is generally a distinct feature of diabetes, since both can make patients of diabetes more vulnerable to the negative effects of hyperhomocysteinemia [6]. Serum homocysteine levels are a risk factor for nephropathy without macroalbuminuria at the beginning of the study. Homocysteine may be a marker of hidden kidney damage or cause kidney damage on its own [7]. A suitable condition is required for vitamin B12 and folate to prevent the accumulation of homocysteine in the blood. Recent research, however, shows that a large proportion of the population, perhaps 40%, does not consume enough to keep plasma homocysteine levels low. Subjects who received daily vitamin B supplementation had a homocysteine concentration of 27% higher than the (> 15 µmol / l) reference range and above, whereas a lower homocysteine concentration than those not receiving them. 66% higher (> 10µmol / l) than suggested by the AHA for risk groups [8]. Reduction of homocysteine may reflect the use of different cobalamin derivatives in the intracellular metabolism of homocysteine [9]. Methylcobalamin is an essential cofactor for the methionine synthase enzyme, and 5'-deoxy-adenosylkobalamine is an essential cofactor for the methylmelonyl-CoA enzyme enzyme. If hyperhomocysteinemia is found in a patient with type 2 diabetes, there may be an increased risk of cardiovascular events[10]. In the case of demonstrating the effect of vitamin B12 on the reduction of homocysteine levels, it would be beneficial for physicians to recommend vitamin B12 in type 2 diabetes mellitus patients with high homocysteine and thus to avoid cardiovascular events.

MATERIALS AND METHODS:

This quasi experimental study was held in the Medicine Unit II of Services Hospital Lahore for Six months duration from July 2018 to January 2019.

A total of 72 patients were selected for the study. The patients having Type 2 diabetes ≥ 10 years were included from the OPD for participation in the Department of Medicine. The patients having less than 10 years of type 1 diabetes mellitus or type 2 diabetes and who received vitamin supplements 6 weeks before the study, patients with terminal diseases and patients with endocrine disease were excluded from the study. Blood samples were taken for fasting blood glucose and homocysteine to evaluate inclusion criteria at the beginning of the study. Tab. Vitamin B12 was administered to patients with 500 mg / day for 6 weeks. Fasting homocysteine levels were determined after 6 weeks. To minimize any bias, sample collection, transport and laboratory procedures will remain standard. The relevant information, including age, sex, fasting blood sugar and fasting homocysteine levels (before and after vitamin B12 uptake), has been recorded in a pre-approved form. Data entry and statistical analysis were entered and analyzed using SPSS version 18.0. Data were cleared prior to analysis by conducting frequencies. Categorical variables were presented as percentage; Continuous variables (age, FBS, homocysteine levels) were presented as mean + SD. The mean homocysteine levels were determined at the beginning of the study and six weeks after the administration of vitamin B12. To determine the average homocysteine levels in the serum, the previous and next measurements were compared in pairs. T-test and p-value were accepted as significant if less than or equal to 0.05.

RESULTS:

72 total patients were selected in the six-month study period. The participants mean age was 60.1 ± 7.3 years (Table 1), and 62.5% of the men and women were 1.7: 1 (Table 2).

Table 1: Age distribution of enrolled participants (n=72)

Age distribution	Frequency	%age
48-52 years	18	25.0
52.1-60 years	19	26.4
60.1-67 years	21	29.2
67.1-72 years	14	19.4

Mean age: 60.1±7.3 years

Table 2: Sex distribution of enrolled participants (n=72)

Sex	Frequency	%age
Male	45	62.5
Female	27	37.5

Male to female ratio: 1.7:1

Mean fasting blood glucose was 121.1 ± 6.4 mg / dL (Table 3).

Table 3: Frequency of fasting blood sugar in enrolled participants (n=72)

Fasting blood sugar	Frequency	%age
116.1-123 mg/dl	22	30.6
123.1-127 mg/dl	22	30.6
127.1-129 mg/dl	10	13.9

Mean fasting blood sugar: 121.1±6.4 mg/dl

The mean homocysteine level before treatment was 14.8 ± 3.1 µmol / L (Table 4) and the mean homocysteine level after treatment with vitamin B12 was 14.5 ± 3 µmol / L (Table 5).

Table 4: Frequency of homocystien level before vitamin B12 treatment in enrolled participants(n=72)

Homocystien level before treatment	Frequency	%age
<13 µmol/L	20	27.8
13-15 µmol/L	32	44.4
>15 µmol/L	20	27.8

Mean homocystien before treatment: 14.8±3.1 µmol/L

Table 5: Frequency of homocystien level after vitamin B12 treatment in enrolled participants(n=72)

Homocystien level after treatment	Frequency	%age
<13 µmol/L	26	36.1
13-15 µmol/L	29	40.3
>15 µmol/L	17	23.6

Mean homocystien after treatment: 14.5±3 µmol/L

The mean pre and post-treatment within the homocystine was 0.39 (95% CI 0.36 - 0.42) and a statistically significant p-value was <0.001 (Table 6).

Table 6: Mean difference in homocystien level before and after vitamin b12 treatment

	Mean	Std. deviation	95% CI of the difference	
			Upper	Lower
HCY* µmol/l (before)-HCY (after)	0.39	0.14	0.36	0.42

P value: <0.001, **HCY=Homocystien level*

DISCUSSION:

Hyperhomocysteinemia is a recently known modifiable risk factor that is independent of the main risk factors for cardiovascular disease such as hypertension, diabetes, smoking and hypercholesterolemia. The hyperhomocysteinemia prevalence (> 14 µmol / L) in the general population ranges from 5% to 30%. Meta-analysis showed that treatment with 0.5 to 5.0 mg of folic acid in a day could reduce total serum homocysteine (tHcy) by about 15% to 40% in about 6 weeks [11]. In addition, tHcy reduction in 5 µmol / L (i1 SD) is estimated to decrease the cardiovascular death risk by 10%. In general, hyperhomocysteinemia may be an important interchangeable risk factor for treatment to reduce homocysteine approved in randomized trials[12]. In a cross-sectional analysis, hyperhomocysteinemia appears to be a stronger risk factor for cardiovascular disease in patients with type 2 diabetes than non-diabetic patients. This interaction with cardiovascular risk between hyperhomocysteinemia and type 2 diabetes may be clinically important because it means that homocysteine reduction therapy can be effective in type 2 diabetes, in particular, the deficiency of vitamin B12 is traditionally diagnosed [13]. Laboratory findings of low vitamin B12 levels in serum, usually in the context of megaloblastic anemia. However, subclinical B12 deficiency usually occurs with normal B12 serum levels and hematological parameters. High levels of homocysteine and methylmalonic acid improve the diagnosis of B12 tissue deficiency and detect patients with deficiency at an early reversible stage [14]. Using these more specific diagnostic markers, we performed a cross-sectional study to know the degree of B12 deficiency in the diabetic population. The mean time to treatment was 14.8 ± 3.1 / mol / L and the mean homocysteine level after treatment with Vitamin B12 was 14.5 ± 3 / l. The mean difference in homocysteine before and after treatment was 0, 39 (95% CI: 0.36 to 0.42) and a statistically significant p value of <0.001 [15]. Vitamin B supplementation areas have a low homocystein17 concentration compared to those who did not have a 27% greater than the reference range (> 15 µmol / l) and greater than 66% homocysteine levels. For risk groups higher than recommended by AHA (> 10µmol / l).

CONCLUSION:

In this study, it was concluded that vitamin B12 supplementation significantly reduced homocysteine levels in type II diabetic patients. Hyperhomocysteinemia is a risk factor for noncommunicable diseases that can be changed in its entirety and with this simple and cost-effective measure.

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