Original article

There is a positive association between vitamin B12 deficiency and serum total cholesterol in Iranian type 2 diabetic patients on Metformin

Il existe une association positive entre la carence en vitamine B12 et le cholestérol total plasmatique des patients iraniens diabétiques de type 2 sous Metformine

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Abstract

Introduction. – Considering the low level of vitamin B_{12} in diabetic patients on Metformin and also the importance of this vitamin in lipid metabolism, the aim of the present study was assessing the possible relationship between vitamin B_{12} deficiency, lipid profile and atherogenic indices in Iranian diabetic patients.

Method. – In the present cross-sectional study, a sample of 200 patients with type 2 diabetes was selected. Serum level of lipid profile was measured using enzymatic colorimetric method. LDL-C was calculated by Friedewald equation and atherogenic indices including total cholesterol to HDL-C and Log Triglyceride to HDL-C ratio were calculated. Serum level of vitamin B_{12} was measured photometrically using commercial kit.

Results. – The prevalence of vitamin B_{12} deficiency was about 14%. There was a significant difference between normal participants and vitamin B_{12} deficient subjects in the case of total cholesterol ($P = 0.04$). The results of the regression analysis showed that in adjusted model, there was significant association between total cholesterol and vitamin B_{12} deficiency (OR: 16.46 [95% CI: 0.27, 33.19], $P = 0.04$).

Conclusion. – The results of the present study showed the relatively high prevalence of the vitamin B_{12} deficiency in type 2 diabetic patients who were on Metformin. Moreover, there was a significant association between vitamin B12 deficiency and total cholesterol level in diabetic patients. Further studies with larger sample size and considering dietary information and duration of Metformin consumption are needed to confirm these preliminary results.

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Keywords: Vitamin B_{12}; Lipid profile; Type 2 diabetes; Metformin

Résumé

Introduction. – Considérant le faible taux de vitamine B_{12} chez les patients diabétiques sous Metformine et l'importance de cette vitamine dans le métabolisme lipidique, le but de cette étude était d'évaluer la relation possible entre la carence en vitamine B_{12}, le profil lipidique et les indices athérogènes chez les diabétiques iraniens.

Méthodes. – Un échantillon de 200 patients atteints de diabète de type 2 était sélectionné. Le profil lipidique était évalué en utilisant la méthode colorimétrique enzymatique. Le LDL-C était calculé par l'équation de Friedewald et les indices athérogènes incluant le rapport cholestérol total/HDL-C et le rapport Log Triglycéride/HDL-C étaient mesurés. Le taux sérique de vitamine B12 était mesuré par photométrie en utilisant un kit commercial.

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Résultats. – La prévalence de la carence en vitamine B_{12} était d'environ 14 %. Il y avait une différence significative entre les participants normaux et les sujets déficients en vitamine B_{12} dans le cas du cholestérol total ($p = 0,04$). Les résultats de l'analyse de régression montraient que dans le modèle ajusté, il y avait une association significative entre le cholestérol total et la carence en vitamine B_{12} (OR : 16,46 [IC à 95 % : 0,27, 33,19], $p = 0,04$).

Conclusion. – La prévalence de la carence en vitamine B12 était relativement élevée chez les patients diabétiques de type 2 sous Metformine. De plus, il existait une association significative positive entre la carence en vitamine B_{12} et le taux de cholestérol total chez les patients diabétiques. D'autres études avec une population plus large et tenant compte des informations nutritionnelles et de la durée de la consommation de Metformine sont nécessaires pour confirmer ces résultats préliminaires.

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Mots clés : Vitamine B_{12} ; Profil lipidique ; Diabète de type 2 ; Metformine

1. Introduction

Diabetes, one of the most common non-communicable diseases (NCDs), is the health challenges facing the world today [1]. Diabetes is accompanied with macro and microvascular diseases [2]. The risk of cardiovascular disease is shown to be higher in patients with diabetes [2] that may be due to higher prevalence of hyperglycemia, hypertension and dyslipidemia [3]. Although the aims of prescribing glucose lowering medication among people with type 2 diabetes are to reduce the symptoms of hyperglycemia and the risk of microvascular and macrovascular complications [4], these drugs may have adverse effects that are not commonly considered. Recently, it has been shown that Metformin, the common drug used as a glucose lowering drug, has effects on absorption of vitamin B_{12}. The rate of serum vitamin B_{12} deficiency was between 5.8 to 33% in Metformin consumers [5–7]. Today, vitamin B_{12} deficiency and consequently higher level of homocysteine is suggested as a risk factor for CVD in diabetic patients. Limited studies assessed the relationship between vitamin B_{12} deficiency and cardiovascular disease in diabetic patients and providing conflicting results. In a study conducted in European and Indian diabetic populations [8], vitamin B_{12} deficiency was positively correlated with triglyceride and TG/HDL-C. In another study, Ahmed et al. showed a significant positive association between serum level of vitamin B_{12} and total cholesterol in diabetic patients [9].

Considering the low level of vitamin B_{12} in diabetic patients on Metformin and importance of this vitamin in lipid metabolism, the aim of the present study was assessing the possible relationship between vitamin B_{12} deficiency, lipid profile and atherogenic indices in Iranian diabetic patients on Metformin.

2. Materials and methods

The present cross-sectional study was conducted in an outpatient center for diabetic patients in Tabriz University of medical sciences in 2017. A sample of 200 patients with type 2 diabetes was selected according to inclusion and exclusion criteria. Volunteer patients aged between 18–70 years who consumed Metformin as a glucose lowering agent were included. Diabetic patients who were pregnant or breastfeed and the subjects with chronic liver disease, renal failure, thyroid disorders, taking lipid lowering agents and other major systemic and infectious disease were excluded. The ethics Committee of Tabriz University of Medical Sciences approved the present study (registration number: IR.TBZMED.REC.1396.537) and informed consent form was obtained from all individual included in the present study.

For biochemical analysis, about 5 ml blood sample was collected after an overnight fast. The samples were immediately centrifuged and the serum samples were separated. Enzymatic colorimetric method (by commercial kit of Pars Azmoon, Tehran, Iran) was used for measuring the serum level of total cholesterol, high-density lipoprotein and triglyceride. LDL-C was calculated by Friedewald equation [10] and atherogenic indices including Total cholesterol (TC) to HDL-C and Log triglyceride (TG) to HDL-C were calculated. Vitamin B_{12} was measured photometrically using commercial kit (Azmoon, Kit). The values less than 200 pg/ml were considered as deficiency [11].

The covariates for regression analyses were age, sex, Body Mass Index (BMI), Fasting Blood Sugar (FBS), HbA1 C, drug consumption, duration of the disease, vitamin B_{12} supplement use. The socio-demographic characteristics were collected through questionnaire. For BMI calculation, the body weight (by Seca scale to the nearest 0.1 kg) and height (to the nearest 0.5 cm) were measured according to standard protocols. BMI was calculated as weight (kg) divided by height^2 (m^2). FBS concentration was measured by the enzymatic method using an Abbot Model Alcyon 300 (USA) auto-analyzer with a kit from Pars-Azmoon (Tehran, Iran) and glycated hemoglobin was measured using chromatography method.

3. Statistical analysis

SPSS v18 Statistical computer software was used for all statistical analyses. Normal distribution was assessed using Kolmogorov Smirnov test. Participants' characteristics were described using means, standard deviations, and percentages whenever appropriate. Independent *t*-test and chi-square test were used for comparison between group analyses. For the correlate analyses, linear regression models were used for investigating the association between serum level of vitamin B_{12} (categorical variable: Normal or deficient) and lipid profile (as