STUDY OF VITAMIN B12 DEFICIENCY AND ITS RELATION WITH METFORMIN TREATMENT AMONG DIABETICS IN PRINCE RASHID HOSPITAL

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Abstract

Introduction: Vitamin B12 has important functions in physiology and pathology of human body. It can help against diseases through improving immune system. The role of Its deficiency with metformin treatment is still subjecting to diabetes. **Objectives:** 1. To investigate the prevalence of Vitamin B12 deficiency among diabetics visiting internal medicine clinics in Prince Rashid Hospital. 2. To explore the association of Vitamin B12 deficiency with metformin treatment among the same sample. **Methods and subjects, *Study design*:** A retrospective design was employed to collect data from files of diabetic patients. ***Study sample:*** A total of 447 files of diabetic patients were accessed if inclusion criteria were met. ***Inclusion criteria:*** Diabetic patient. Vitamin B12 status is mentioned. Metformin treatment is recorded in files of diabetic patients. **Data collection:** data will be collected for each patient and entered into excel sheet for further analysis. **Statistical analysis:** SPSS version 20 was used for data analysis. Data was presented as frequency and percentage for numerical variables, whereas the association between variables was tested using Chi-Square test. Significance was tested at alpha level < 0.05. **Results:** The prevalence of vitamin B12 deficiency was 7.2%. The mean age of study participants was 55.70+10.13 years. Metformin intake was reported by approximately 84% of diabetics. About 76% of participants had cardiac diseases. No significant association was observed between metformin and

vitamin B12 deficiency (p=0.269). **Conclusion:** The prevalence of vitamin B12 deficiency among diabetics was 7.2%. No significant association was observed between treating diabetics with metformin and vitamin B12 deficiency. **Recommendation:** Lacking the association between treatment of metformin and vitamin B12 deficiency may due to small participants included in other studies, and we recommend to include larger numbers of participants in future studies.

Keywords: Diabetes type 2, vitamin B12, metformin

Introduction

Diabetes mellitus is considered a chronic disease with metabolic nature. Furthermore, Type 2 diabetes has been reported to affect approximately 382 million persons on global level (Cho, 2013).

Vitamin B12 deficiency

In a study by Howard et al (1998), it has been reported that the deficiency of vitamin b12 among elderly individuals is not due to dietary low supplementations, whereas other studies showed that vitamin B12 deficiency is due to pathological conditions that are associated with ageing (Andres et al.,2007; Herrmann and Obeid, 2008).

Metformin and diabetes

According to a recent study by Niafar et al (2015), metformin is considered the only biguanide oral hypoglycemic drug of choice to treat patients with type-2 diabetes. According to American Diabetes Association (2014), several considerations about the use of metformin treatment including its efficacy, safety, and cardiovascular benefits have made it as the first choice to treat diabetes type 2.

The effect of metformin treatment on vitamin B12

Niafar et al (2015) conducted a study to investigate the effect of metformin treatment on vitamin B12 deficiency. This study was a meta-analysis review. The authors came with the following conclusion: treatment by metformin leads to increased incidence of VB12 deficiency and reduced serum VB12 levels.

Yazdanpanah (2014) conducted a study to investigate the impacts of metformin on the concentration of vitamin B12 among diabetics. Patients were categorized into two groups: metformin treated patients group, and a group treated with other anti-diabetic drugs. Study findings showed that there was no significant differences in the level of vitamin B12 between two

groups. The results did not show significant association between age and gender with vitamin B12.

According to findings of two studies, using the treatment of metformin leads to decreased levels of serum vitamin B12 (Wulffele et al., 2003; Reinstatler et al., 2012). Furthermore, it has been emphasized that compared with diabetic patients not treated with metformin, or non-diabetics, treating diabetics with metformin caused lowering levels of vitamin B12 (Reinstatler et al., 2012).

Two studies focusing on the evaluation of diabetics with metformin have shown that vitamin B 12 deficiency is in the range of 5.8 to 33 % (Pflipsen et al., 2009; Reinstatler et al., 2012).

Study objectives

The main objectives of the present study were: to investigate the prevalence of vitamin B12 deficiency among diabetic patients, and to examine a proposed association between metformin treatment and vitamin B12 deficiency.

Methods and subjects

***Study design*:** A retrospective design was employed to collect data from files of diabetic patients.

Study sample: A total of 447 files of diabetic patients were accessed if inclusion criteria were met.

Inclusion criteria:

- Diabetic patient.
- Vitamin B12 status is mentioned.
- Metformin treatment is recorded in files of diabetic patients.

Data collection: data was collected for each patient and entered into excel sheet for further analysis.

Statistical analysis: SPSS version 20 was used for data analysis. Data was presented as frequency and percentage for numerical variables, whereas the association between variables was tested using Chi-Square test. Significance was tested at alpha level < 0.05.

Results

As seen in table 1, study sample included 447 patients. The mean age is 55.70 ± 10.13 years. A total of 210 (47%) participants were males. The mean intake of metformin is 1473 ± 937 mg/day. Family history of cardiac disease was shown among 280 (62.6%) of participants. About 31% of participants had positive history of diabetes. Metformin intake was reported

among 84% of participants. The prevalence of vitamin B12 deficiency among diabetics was 7.2%.about 76% of diabetics had cardiac diseases.

Table 1: general characteristics of participants

Variable	
Age (M±SD) years	55.70±10.13
Gender (N, %)	
- Male	210 (47%)
- Female	237 (53%)
Metformin (M±SD) mg/day	1473±937
Family history of CD (N, %)	
- Yes	280 (62.6%)
- No	167 (37.4%)
Family history of diabetes (N, %)	
- Yes	137 (30.6%)
- No	310 (69.4%)
Metformin intake (N, %)	
- Yes	374 (83.7%)
- No	73 (16.3%)
Vitamin B12 deficiency (N, %)	
- Yes	32 (7.2%)
- No	415 (92.8%)
Cardiac disease (N, %)	
- Yes	339 (75.8%)
- No	108 (24.2%)

The relationship between metformin intake and study variables

As it can be seen in table 2, there were no significant association between metformin intake and other variables under study. As an example, metformin intake was not associated significantly with vitamin B12 deficiency (p=0.269), gender (p=0.228), cardiac disease (p=0.315), family history of cardiac disease (p=0.258), and family history of diabetes (p=0.199).

Table 2: The relationship between metformin intake and study variables

Variable	Metformin				P value
	Yes		No		
	N	%	N	%	
Vitamin B12					0.269
- Deficiency	29	90.6	345	83.1	
- No deficiency	3	9.4	70	16.9	
Gender					0.228
- Male	171	81.4	39	18.6	
- Female	203	85.7	34	14.3	
Cardiac disease					0.315
- Yes	287	84.7	52	15.3	
- No	87	80.6	21	19.4	
Family history of cardiac disease					0.258
- Yes	230	82.1	144	86.2	
- No	50	17.9	23	13.8	
Family history of diabetes					0.199
- Yes	110	80.3	264	85.2	
- No	27	19.7	46	14.8	

Discussion

In the present study, the prevalence of vitamin B12 deficiency among diabetics was 7.2%. This finding is consistent with other studies in which vitamin B 12 deficiency among diabetics receiving metformin was reported to range from 5.8 to 33 % (Pflipsen et al., 2009; Reinstatler et al., 2012).

We have examined the association of metformin with vitamin B12 deficiency. Our results did not support the existence of such an association (p=0.269). However, the presence of significant association between the use of metformin and vitamin B12 deficiency is subjecting to debate in literature. One of the important studies in this regard is the study of Niafar et al (2015) who conducted a meta- analysis review and concluded that treatment by metformin leads to increased incidence of VB12 deficiency and reduced serum VB12 levels. The same findings have been confirmed by other studies such as the studies of Wulffele et al (2003) and Reinstatler et al (2012) in which it was reported that vitamin B12 deficiency was associated with the treatment of metformin. On the other hand, our findings agree with the study of Yazdanpanah (2014) who did not find a significant association between metformin treatment and vitamin B12 deficiency.

Conclusion

The prevalence of vitamin B12 deficiency among diabetics was 7.2%. No significant association was observed between treating diabetics with metformin and vitamin B12 deficiency.

Recommendations

Lacking the association between treatment of metformin and vitamin B12 deficiency may due to small participants included in other studies, and we recommend to include larger numbers of participants in future studies.

References:

American Diabetes Association (2014). Standards of medical care in diabetes–2014. Diabetes Care 37(Suppl 1):S14–S80. doi:10. 2337/dc14-S014.

Cho NM (ed) (2013) Diabetic atlas, 6th edn. International Diabetes Federation, Bruccel.

E. Andres, J. Vidal-Alaball, L. Federici, N.H. Loukili, J. Zimmer, G. Kaltenbach (2007). Clinical aspects of cobalamin deficiency in elderly patients. Epidemiology, causes, clinical manifestations, and treatment with special focus on oral cobalamin therapy, Eur. J. Intern. Med. 18, 456-462.

J.M. Howard, C. Azen, D.W. Jacobsen, R. Green, R. Carmel (1998). Dietary intake of cobalamin in elderly people who have abnormal serum cobalamin, methylmalonic acid and homocysteine levels, Eur. J. Clin. Nutr. 52, 582-587.

L. Reinstatler, Y.P. Qi, R.S. Williamson, J.V. Garn, G.P. Oakley Jr (2012). Association of biochemical B(1)(2) deficiency with metformin therapy and vitamin B(1)(2) supplements: the National Health and Nutrition Examination Survey, 1999- 2006, Diabetes Care 35, 327-333.

Leila Yazdanpanah (2014). Comparison of vitamin B12 and folic acid serum levels in diabetic patients under metformin and other therapeutic regimens. J Diabetes Metab, 5:10, 148.

M.G. Wulffele, A. Kooy, P. Lehert, D. Bets, J.C. Ogterop, B. Borger van der Burg, A.J. Donker, C.D. Stehouwer (2003). Effects of short-term treatment with metformin on serum concentrations of homocysteine, folate and vitamin B12 in type 2 diabetes mellitus: a randomized, placebo-controlled trial, J. Intern. Med. 254, 455-463.

Mitra Niafar, Faizi Hai, Jahan Porhomayon, Nader Djalal Nader (2015). The role of metformin on vitamin B12 deficiency: a meta-analysis review. Intern Emerg Med, 10:93–102.

Pflipsen MC, Oh RC, Saguil A, Seehusen DA, Seaquist D, Topolski R (2009). The prevalence of vitamin B(12) deficiency in patients with type 2 diabetes: a cross-sectional study. J Am Board Fam Med JABFM, 22(5):528–534.

Reinstatler L, Qi YP, Williamson RS, Garn JV, Oakley GP Jr (2012). Association of biochemical B(1)(2) deficiency with metformin therapy and vitamin B(1)(2) supplements: the National Health and Nutrition Examination Survey, 1999-2006. Diabetes Care 35(2):327–333.

W. Herrmann, R. Obeid (2008). Causes and early diagnosis of vitamin B12 deficiency, Dtsch. Arztebl. Int 105, 680-685.