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Association of serum calcium with level of blood pressure in type 2 diabetic patients

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ABSTRACT

Introduction: Hypertension and diabetes are two common diseases and they affect the same major target organs.

Objectives: In this study, we sought to investigate the probable association of serum calcium with levels of systolic and blood pressure in a group of type 2 diabetic (T2D) patients.

Patients and Methods: A total of 60 patients with T2D were enrolled to the study. To determine serum creatinine, calcium and hemoglobin A1c (HbA1c), venous blood samples were obtained in the fasting state.

Results: Among 60 participants, 56.7% were female. Mean of ages was 57 ± 8.3 years. Mean of systolic and diastolic blood pressure were 133 ± 13 mmHg and 84 ± 7.4 mmHg, respectively. Mean of serum calcium was 9.0 ± 0.4 mg/dl. In this study, there was no significant difference of serum calcium and HbA1c between males and females. A significant inverse correlation of serum calcium with level of diastolic blood pressure ($r = -0.261$, $p = 0.046$) was seen (adjusted for duration of diabetes). Moreover, a negative correlation of systolic blood pressure with level of serum calcium was existed, however, this correlation was not significant ($r = -0.232$, $p = 0.080$) [adjusted for duration of diabetes].

Conclusions: We found a significant inverse correlation of serum calcium with level of diastolic blood pressure. We propose to more attention to serum calcium during the treatment of hypertension in diabetic patients.

Implication for health policy/practice/research/medical education:

A significant inverse correlation of serum calcium with level of diastolic blood pressure in a group of diabetic patients in our study, imply to more attention to serum calcium during the treatment of hypertension in diabetic patients.

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1. Background

Hypertension and diabetes are two common diseases, which affect the kidneys (1). The combined presence of hypertension and diabetes concomitantly accelerates the decrease in kidney function, and also the development of diabetic kidney disease (1,2). The estimated prevalence of high blood pressure in adults with diabetes is about 20–60%, which is 1.5–3 times higher than that in age-matched individuals without diabetes (1,2). Hypertension may be present when type 2 diabetes (T2D) is diagnosed or may predate the onset of increasing blood sugar (2). T2D is frequently accompanied by advanced age or obesity, both of which increase the risk of hypertension. In addition, uncontrolled hypertension increases the risk of nephropathy (1,2). Hypertensive disease is associated with various abnormalities of calcium metabolism. Although, the relation of these abnormalities to the hypertension is remained unclear. Indeed, various data suggested a linkage between the regulation of calcium metabolism, renin system activity, and blood pressure in hypertension (3,4). It is possible that, alterations in extracellular calcium levels may influence intracellular calcium levels and possibly play an important role in the pathogenesis of essential hypertension (3-5).

2. Objectives

In this study we sought to investigate the probable association of serum calcium with levels of systolic and blood pressure in a group of type 2 diabetic (T2D) patients.

3. Patients and Methods

A cross-sectional analytical study was carried out among 60 patients (male and female) with T2D. Patients were between 41 and 81 years of

age. Their body weight was stable for at least 3 months before the study. Anthropometric measurements were obtained including height weight, and body mass index (BMI) which was calculated in kilograms per square meter (6). The diagnosis of hypertension in people with diabetes was made if the mean of two readings on at least two clinic visits was $\geq 130/80$ mmHg. The readings should be verified in the contralateral arm (7). Resting systolic blood pressures and fifth phase diastolic blood pressures were measured three times, while the subjects were seated, and the second and third measurements were averaged (7). Patients' history, current medications, insulin doses, tobacco use and family medical history were obtained. Venous blood samples were obtained in the fasting state for determinations of serum creatinine, calcium and hemoglobin A1c (HbA1c) [reference range 4–6%]. Results were expressed as mean \pm SD and were considered as statistically significant when two-sided $P < 0.05$. Independent-samples T test was used for comparison the variables between male and female. For correlations, partial correlation test was calculated. Exclusion criteria were cigarette smoking, taking calcium or vitamin D supplements. Also, patients who were under treatments of antihypertensive drugs, or drugs which affects the calcium or vitamin D metabolism, were excluded from the study.

4. Results

Of 60 participants, 56.7% were female. Mean of age was 57 ± 8.3 years. Mean of diabetic duration was 9.2 ± 4.9 years. Mean of HbA1c was $7.4 \pm 1.0\%$. Mean of serum creatinine was 0.98 ± 0.22 mg/dl. Mean of serum calcium was 9.0 ± 0.4 mg/dl. Mean of systolic and diastolic blood pressure was 133 ± 13 mmHg and 84 ± 7.4 mmHg, respectively. Table 1, summarizes the patients data. In this study, there was no significant

difference of serum calcium and HbA1c between males or females. Similarly, no significant difference of systolic or diastolic pressure between males and females was observed. A significant inverse correlation of serum calcium with level of diastolic blood pressure ($r = -0.261$, $p = 0.046$) was seen (adjusted for duration of diabetes). In addition, a negative correlation of systolic blood pressure with level of serum calcium was observed, however, this correlation was not significant ($r = -0.232$, $p = 0.080$) [adjusted for duration of diabetes].

5. Discussion

Diabetes and hypertension are well-known risk factors for cardiovascular mortality (1-3). Accumulating evidence has also shown that there is a close relationship between diabetes and hypertension (2-4). The prevalence of hypertension in patients with T2DM is known to be 1.5–3 times higher than in the age-matched non diabetic population. Also, patients with hypertension are at a two to three times higher risk for developing diabetes than those with normal blood pressure (2-5). Hypertension is multi-factorial disorders in which various physiological mechanisms participate to elevate blood pressure (1-5). Various hypotheses were proposed about the possible mechanisms underlying hypertension including

disturbances in serum electrolytes and water balance. One of the physiologically important ions in the serum is calcium (3-5). It is possible that, the alterations in extracellular calcium levels may influence intracellular calcium levels and possibly play a role in the pathogenesis of essential hypertension (5-8). In agreement with our finding, Reichel et al. in a study on essential hypertensive patients, measured parameters of calcium metabolism in groups of untreated male subjects with elevated diastolic blood pressure and age-matched male subjects with low diastolic blood pressure. They found that, individuals with high diastolic blood pressure had significantly lower total serum calcium (9). Similarly, Touyz et al. studied serum magnesium, calcium, sodium and potassium, and erythrocyte magnesium, sodium and potassium levels in hypertensive subjects. They showed a significant decrease in serum calcium in the hypertensive subjects. A significant inverse correlation was found between serum calcium and blood pressure (5). Accordingly, Sudhakar et al. studied serum calcium in 117 subjects with essential hypertension and their 77 first-degree relatives. Interestingly, the results showed that serum calcium levels were significantly decreased in both males and females with essential hypertension and their first-degree relatives when compared with the normotensive controls (10).

Table 1. The results of variables in type 2 diabetic patients

Variable	Min	Max	Mean ± SD
BMI (kg/m ²)	20.06	41.4	29.9 ± 4
Diabetic duration (years)	3	23	9.2 ± 4.9
Systolic BP (mmHg)	110	170	133 ± 13
Diastolic BP (mmHg)	70	100	84 ± 7.4
Serum creatinine (mg/dl)	0.7	1.9	0.98 ± 0.22
Serum calcium (mg/dl)	8.2	10	9.0 ± 0.4
Proteinuria (mg/day)	150	1170	389 ± 223
HbA1c (%)	4.8	9.5	7.4 ± 1.07

BP, Blood pressure; BMI, Body Mass Index

To assess the correlation between plasma and intracellular Ca^{2+} in normotensive and hypertensive subjects, Fu et al. conducted a study on 55 patients with essential hypertension and 32 normotensive controls. They found that, hypertensive group consistently demonstrated significantly lower plasma Ca^{2+} and higher cytosolic Ca^{2+} levels when compared with those in normotensive group. They concluded that, patients with essential hypertension have widespread depression of Ca^{2+} -ATPase activity with plasma Ca^{2+} depletion and cytosolic Ca^{2+} overload, which may reflect an underlying membrane abnormality in essential hypertension. The cellular abnormalities may be related to the defective transport mechanisms that in turn may be aggravated by plasma Ca^{2+} depletion (4). Few data published regarding the association of serum calcium and blood pressure in diabetic patients, and to the best of our knowledge this is the first study regarding calcium and blood pressure in T2D patients. We found a significant inverse correlation of serum calcium with levels of diastolic blood pressure. Thus, we propose to more attention to serum calcium during the treatment of hypertension in diabetic patients.

Authors' contributions

Main draft write up and editing by HN. SB designed and performed the research.

Conflict of interest

The authors declared no competing interests.

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