Serum magnesium levels in patients with diabetic retinopathy

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Abstract

Background: Diabetic retinopathy is one of the leading causes of blindness in the world. Hypomagnesemia has been reported to occur at an increased frequency among patients with type 2 diabetes compared with their counterparts without diabetes. Hypomagnesemia has been linked to poor glycemic control. Many studies have been undergone to find out the precipitated factors of retinopathy such as duration and type of diabetes, hyperglycemia, hypomagnesemia and increased urinary total protein levels. Aim: This study was carried out to study the correlation between serum magnesium levels, glycosylated hemoglobin and urinary total protein levels in diabetic patients with retinopathy. Materials and Methods: The study population comprised of 30 type 2 diabetic patients without retinopathy as Group 2, 30 type 2 diabetic patients with retinopathy as Group 3 in the age group 45-75 years as cases and 60 age and sex matched healthy individuals as controls (Group 1). Determination of Serum Magnesium (photometric xylidyl blue method), glycosylated hemoglobin, HbA1c (IFCC), fasting blood glucose, postprandial blood glucose (glucose oxidase method) and urine total protein (Pyrogallol red method) was carried out. The statistical software SPSS 11.0 and Systat 8.0 were used for the analysis of the data. Results: Hypomagnesemia was observed in cases compared with both Group 2 and Group 3. FBS, PPBS, HbA1c, Urine total protein levels were increased in cases (without retinopathy and with retinopathy) compared with controls. Conclusion: Hypomagnesemia and albuminuria individually or in conjunction serve as indicators for dysglycemia and could be used as marker for the risk of development of diabetic retinopathy.

Key words: Diabetic retinopathy, glycosylated hemoglobin, magnesium, urinary protein

INTRODUCTION

Type 2 diabetes accounts for approximately 90 to 95% of all diagnosed cases of diabetes. Multi-system effects of diabetes mellitus such as retinopathy, nephropathy, neuropathy and cardiovascular diseases are important public health concerns. Diabetic retinopathy is one of the leading causes of blindness in the world. Using new surgical and medical techniques, the incidence of blindness can be reduced up to 90%. Decrease in visual acuity in diabetic retinopathy is either associated with maculopathy or proliferative complications of it. Hypomagnesemia has been reported to occur at an increased frequency among patients with type 2 diabetes compared with their counterparts without diabetes. Despite numerous reports linking hypomagnesemia to chronic diabetic complications; attention to this issue is poor among clinicians. Hypomagnesemia has been linked to poor glycemic control. Although, it is generally believed that stringent metabolic control delays the development of late complications in diabetes mellitus, it has not been demonstrated conclusively that such control holds back the development of diabetic retinopathy. Many studies have been undergone to find out the precipitated factors of retinopathy such as duration and type of diabetes, hyperglycemia, hypomagnesemia and increased urinary total protein levels. Hence this study was carried out to study the correlation between serum magnesium levels, glycosylated hemoglobin and urinary total protein levels in diabetic patients with retinopathy.
MATERIALS AND METHODS

The study was conducted after obtaining usual permission from ethical committee and consent from subjects and controls were taken before commencing the study. The study population comprised of 30 type 2 diabetic patients without retinopathy as Group 2, 30 type 2 diabetic patients with retinopathy as Group 3 in the age group 45–75 years as cases and 60 age and sex matched healthy individuals as controls (Group 1). All the diabetic patients enrolled in the study were screened for the presence of retinopathy by direct and indirect ophthalmoscopy and fundus photography who attended the outpatient and inpatient department of Medical College. Non-diabetics, diabetics with other complications such as chronic diarrhoea, alcoholism, use of diuretics, cardiac disease and thrombotic stroke were excluded from the study. History and physical data were obtained from both cases and controls. Determination of Serum Magnesium (photometric xylidyl blue method), HbA1c (immuno-inhibition method). Fasting Blood Glucose (FBS), Postprandial Blood Glucose (PPBS) (glucose oxidase method) and urine total protein (Pyrogallol red method) was carried out.

Statistical analysis

Chi-Square test has been used to find the homogeneity of sex distribution between apparently healthy controls and diabetic cases. Student t-test (independent two tailed) has been used to find the significance of serum magnesium and other biochemical parameters between these two groups. The effect sizes due to Hedges (Bias Corrected) have been computed to find the effect of diabetes on biochemical parameters over the control group. The statistical software SPSS 11.0 and Systat 8.0 were used for the analysis of the data and Microsoft word and Excel have been used to generate tables and graphs.

RESULTS

Mean values of serum magnesium was found to be lower in cases, 1.38 ± 0.39 mg/dl with diabetic retinopathy (Group 3) compared with both the diabetic cases without retinopathy (Group 2), 2.02 ± 0.29 mg/dl and healthy controls (Group 1), 2.62 ± 0.36 mg/dl and was statistically significant.

The mean values of FBS, PPBS, HbA1c and urine total protein in diabetic cases with retinopathy (Group 3) were found to be higher from that of diabetic cases without retinopathy (Group 2), and healthy controls (Group 1), Group 3 versus group 1 P < 0.01 and Group 2 versus Group 1 P < 0.001. The values are depicted in Table 1. Pearson’s correlation showed that serum magnesium correlated negatively to both FBS (r = −0.527, P < 0.01) and HbA1c (r = −0.48, P < 0.01) and it was highly significant in cases with diabetic retinopathy, Figures 1 and 2.

DISCUSSION

Magnesium is the fourth most abundant cation in the human body and the second most abundant intracellular cation. It serves as a cofactor for all enzymatic reactions that require ATP and is a key component in various reactions that require enzymes (300 enzymes). It is also an essential enzyme activator for neuromuscular excitability, cell permeability and is a critical element in cellular proliferation and apoptosis. In addition Magnesium is a regulator of ion channels and mitochondrial function and is an important factor in both cellular and humoral immune reactions. Cellular Magnesium deficiency can alter the activity of membrane bound sodium-potassium ATPase that is involved in the maintenance of gradients of sodium, potassium and in glucose transport. It has been suggested that hypomagnesemia may induce altered cellular glucose transport, reduced pancreatic insulin secretion, defective post receptor insulin signaling, and/or altered insulin-insulin receptor interactions.

The present study revealed lower levels of serum magnesium in diabetic patients without retinopathy. More-over patients who had retinopathy were found to have lowest levels of serum magnesium. These observations are similar to other workers suggesting that hypomagnesemia is a possible risk factor in the

### Table 1: Mean±SD values of fasting blood glucose, postprandial blood glucose, Magnesium, HbA1c and urine total protein in controls and cases

| Group                  | FBS (mg/dl) | PPBS (mg/dl) | Mg (mg/dl) | HbA1c (%) | Urine protein total (mg/day) |
|------------------------|-------------|--------------|------------|-----------|-----------------------------|
| Group 1 control        | 94.52±9.50  | 140±10       | 2.62±0.36  | 4.68±0.88 | 41.56±5.89                  |
| Group 2 (Cases without | 165±18.50   | 201±19.50    | 2.02±0.29  | 7.56±0.59 | 307.42±28.90                |
| retinopathy)           |             |              |            |           |                             |
| Group 3 (Cases with    | 231±21.30   | 265±26.50    | 1.38±0.39  | 10.54±1.02| 458.05±30.47                |
| retinopathy)           |             |              |            |           |                             |

Group 2 versus Group 1 P < 0.001, Group 1 versus Group 3 P < 0.01
development and progression of diabetic retinopathy. The exact cause of hypomagnesemia is unknown but an increased urinary loss of magnesium may contribute to it. Some studies revealed that hyperglycemia contribute to hypomagnesemia by causing depression in the net tubular reabsorption of magnesium.\[11\]

In the present study mean HbA1c was significantly higher in type 2 diabetics with retinopathy (P < 0.001), indicating that higher level of HbA1c was associated with increased risk for development of microangiopathy in diabetics. This may be due to the fact that HbA1c has special affinity for oxygen thereby causing tissue anoxia and plays a role in causation of micro and macroangiopathy.\[12\]

We observed in our study that Urinary total protein was significantly higher in type 2 diabetics with retinopathy as compared with both type 2 diabetics without retinopathy and controls. Previous studies revealed that only small amount of protein is present in normal excreted urine (20-150 mg/day), and most of it is albumin. The remainder is entirely Tamm-Horsfall protein, secreted by distal tubules. Increased permeability of glomerular basement membrane is signaled first by increased amount of albumin in urine. The prevalence of microalbuminuria and macroalbuminuria in our study was 23% and 78% respectively.\[13\] Numerous studies were carried out to determine the prevalence of retinopathy and albuminuria in type 2 diabetics. These studies yielded different rates between 16 to 53.4% for retinopathy. The variation in rate could be as a result of different methods used in those studies, the population and or the races involved, or variation in controlling blood sugar level.\[14\] Parving et al. reported the incidence rate of 22% of microalbuminuria in type 2 diabetics\[15\] whereas Lunetta reported the incidence rate of 15%.\[16\] The above–mentioned studies show that there is significant relationship between the degree of retinopathy and albuminuria. However there are few studies opposing such relationship.

CONCLUSION

Hypomagnesemia and albuminuria individually or in conjunction serve as indicators for dysglycemia and could be used as marker for the risk of development of diabetic retinopathy. If longitudinal studies confirm these findings, diabetic patients with hypomagnesemia and albuminuria may benefit from close ophthalmologic follow up.

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