Chapter 65

Abnormalities of Serum Ionized Magnesium in Type 2 Diabetes Mellitus

K. Yokota[*], M. Kato,[**] M. Shiraishi,[***] T. Yamada,[****] S. Kageyama,
T. Sakurai, K. Ishibashi, J. Yamamoto, A. Mimura, K. Aihara,
T. Yokose and N.Tajima

*Department of Internal Medicine, **Dept. of Clinical Laboratory, ****Division of Clinical Pharmacology
& Therapeutics, Jikei University School of Medicine, *Kato Medical Clinic, ***SRL Inc. Tokyo, Japan*

Summary

In order to clarify the relationship between clinical status of type 2 diabetes mellitus in Japanese patients and abnormalities of magnesium metabolism, the serum ionized magnesium (iMg) levels were measured using the ion-selective electrodes. The subjects were 21 male patients diagnosed as having type 2 diabetes without any complications and 18 age-matched healthy male as control group. The serum total magnesium (TMg) and the iMg levels were significantly lower in the diabetes group. Although there was no relationship between the iMg levels and the HOMA-R index, there was a significant negative correlation between iMg and HbA1c ($r = -0.66$, $P < 0.01$). Both diastolic (D) and mean(M) blood pressure (BP) were significantly higher in the diabetes group compared with the control group and there was a significant negative correlation between iMg and DBP ($r = -0.48$, $P < 0.05$) or MBP($r = -0.43$, $P < 0.05$), although the patients with overt hypertension were excluded. These findings suggest that the abnormalities of iMg may have a close relationship with the status of type 2 diabetes and that the clinical usefulness of measurements of iMg.

Key words: Ionized magnesium, ion-selective electrodes, type 2 diabetes mellitus, HbA1c, blood pressure.

Introduction

Magnesium, the fourth most abundant mineral in the body, plays an important role in various cellular functions. A high prevalence of hypomagnesemia has been documented in diabetes.[1,2] The aim of this study was to clinically investigate the relationship between clinical status of type 2 diabetes and serum ionized magnesium (iMg) levels using the ion-selective electrodes (ISEs).[3]

Patients and methods

Twenty-one male type 2 diabetes with a mean age of 48.6 ± 1.2 (mean ± SE) years without any diabetic complications are included. Individuals with hypertension, hyperlipidemia or being treated with insulin, arrhythmias, ischaemic heart diseases, heavy drinkers, using magnesium-containing drugs or diuretics were excluded. Eighteen healthy male matched for age (46.4 ±

1.7 years) were also studied as the control group. Routine biochemistry tests, fasting plasma glucose (FPG), serum immunoreactive insulin (IRI), total Mg (TMg) and calcium (TCa) were measured using serum obtained while fasting. The iMg and iCa levels were measured in the same sample using a CRT8 (Nova Biomedical Co.). The homeostastis assessment (HOMA-R) index was used as an indicator of insulin resistance. Statistical analysis of the data was conducted using Student's t-test, and differences of $P < 0.05$ were considered significant.

Results

There was no significant difference in body mass index between the two groups. Systolic blood pressure (BP) was slightly higher in the diabetes group (123.4 ± 2.3 vs. 117.8 ± 2.4 mmHg, n.s.), but the difference was not significant. However, diastolic BP (78.2 ± 1.6 vs. 68.0 ± 1.7 mmHg, $P < 0.01$) and mean BP (93.3 ± 1.8 vs. 84.6 ± 1.8 mm Hg, $P < 0.01$) were significantly higher in the diabetes group than in the control group. FPG and HbA_{1c} were significantly higher in the diabetes group (FPG, 149.3 ± 6.7 vs. 99.4 ± 1.5 mg/dl; HbA_{1c}, 7.0 ± 0.4 vs. 5.0 ± 0.1 per cent, $P < 0.01$) but there was no significant difference of fasting IRI levels (6.3 ± 0.7 vs. 6.1 ± 0.6 μU/ml, n.s.).

As shown in Table 1 both the TMg and iMg levels were significantly decreased in the diabetes group ($P < 0.01$). As for the TCa and iCa levels, there were no significant differences between the two. The iMg/TMg rate did not differ significantly, but the TCa/TMg ratio ($P < 0.01$) and the iCa/iMg ratio ($P < 0.01$) were significantly higher in the diabetes group than in the control group.

Table 1. Mg and Ca levels along with other parameters

	Diabetes	Control	P value
N	21	18	
iMg (mmol/l)	0.53 ± 0.01	0.58 ± 0.01	< 0.01
TMg (mg/dl)	2.09 ± 0.03	2.28 ± 0.03	< 0.01
iCa (mmol/l)	1.28 ± 0.01	1.27 ± 0.01	n.s.
TCa (mg/dl)	9.40 ± 0.07	9.43 ± 0.11	n.s.
(TCa/TMg) ratio	4.55 ± 0.08	4.14 ± 0.05	< 0.01
Ionization ratio (iCa/iMg)	2.41 ± 0.04	2.19 ± 0.03	< 0.01
Mg ionization rate (iMg/TMg)	0.62 ± 0.01	0.62 ± 0.01	n.s.

iMg, Serum ionized magnesium; TMg, Serum total magnesium;
iCa, Serium ionized calcium; TCa, Serum total calcium. Mean ± SE.

No significant correlation was seen between iMg and FPG levels. However, a significant negative correlation (r = –0.66, $P < 0.01$) was seen between iMg and HbA_{1c} (Fig. 1). On the other hand, no significant correlation was evident between TMg and FPG or HbA_{1c}. There was also no significant correlation between the iMg and the HOMA-R index and between TMg levels and each blood pressure values in either group. However, there was a significant negative correlation between iMg and diastolic BP (y = –114.7X+139.5, r = –0.48, $P < 0.05$) as well as mean BP (y = –109.0X+151.5, r = –0.43, $P < 0.05$).

Discussion

The recent development of the ion-selective electrodes has led to a focus of attention on the kinetics of magnesium in various diseases.[4] Diabetes is one of the diseases associated with a high prevalence of hypomagnesemia. Mather et al.[2] have reported a significant decrease in the
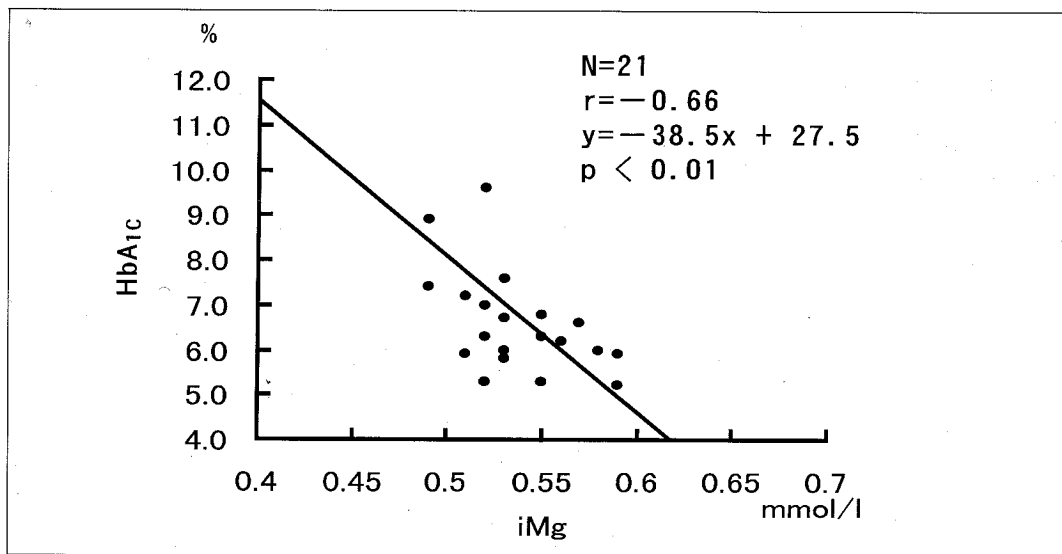
%

N=21
r=−0.66
y=−38.5x + 27.5
p < 0.01

HbA$_{1C}$

12.0
11.0
10.0
9.0
8.0
7.0
6.0
5.0
4.0

0.4 0.45 0.5 0.55 0.6 0.65 0.7
iMg   mmol/l

Fig. 1. Correlation between iMg and HbA$_{1C}$.

plasma concentration of TMg in diabetes, with 25 per cent of patients exhibiting levels below the lower limit found in normal subjects. The present study also demonstrated that 43 per cent of type 2 Japanese diabetics had serum TMg levels were below the lowest value found in the non-diabetics. Serum iMg levels were also significantly lower in the diabetic group, with more than 60 per cent of the patients exhibiting levels below the lowest value found in the control group. The TCa/TMg ratio and the iCa/iMg ratio were significantly higher in the diabetes group reflecting a reduction of magnesium levels. There was a significant negative correlation between iMg and diastolic BP as well as mean BP, even the patients with overt hypertension were excluded. Although there was no significant correlation between TMg and HbA$_{1c}$, there was a significant negative correlation between iMg and HbA$_{1c}$. These findings suggest that the iMg concentration may have a close relationship with the status of type 2 diabetes and that the iMg measurements may be clinically more useful rather than TMg measurements.

References

1. Jackson, C.E. & Meier, D.W. (1968): Routine serum magnesium analysis:correlation with clinical state in 5100 patients. *Ann. Int. Med.* **69,** 743–748.

2. Mather, H.M., Nisbet, J.A., Burton, G.H., Poston, G.J., Bland, J.M., Bailey, P.A. & Pilkington, T.R.E. (1979): Hypomagnesaemia in diabetes. *Clin. Chem. Acta* **95,** 235–242.

3. Altura, B.M., Burack, J.L., Cracco, R.Q., Galland, L., Handwerken, S.M., Markell, M.S., Mauskop, A., Memon, Z.S., Resnick, L.M., Zisbrod, Z. & Altura, B.M. (1994): Clinical studies with the NOVA ISE for IMg^{2+}. *Scand. J. Clin. Lab. Invest.* **54** (Suppl. 217), 53–67.

4. Altura, B.M. (1994): Introduction:Importance of Mg in physiology and medicine and the need for ion selective electrodes. *Scand. J. Clin. Lab. Invest.* **54** (Suppl. 217), 5–9.