Ionized Magnesium in Danish Children With Type 1 Diabetes

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I t is well known that type 1 diabetes is associated with magnesium deficiency (1), which may be followed by vascular complications (2–5). As a consequence, magnesium supplementation has been advocated to diabetic patients to minimize the risk of serious complications (6–8). The magnitude of hypomagnesemia in diabetic subjects is, however, difficult to establish because most studies have reported changes in total magnesium (i.e., ionized magnesium bound to albumin and other ligands), whereas only sparse information is available regarding ionized ion (9–11). Recently, a new electrode has been available for the measurement of ionized magnesium (12,13).

The aim of the present investigation was to test the hypothesis that the level of ionized magnesium was lower in diabetic children and related to poor glycemic control.

RESEARCH DESIGN AND METHODS

In total, 81 children with type 1 diabetes were included prospectively from September 1999 to May 2000. Inclusion criteria were age <18 years, duration of diabetes <3 months, and an equal distribution in the age-groups: 0–5, 6–11, and 12–17 years. All children were treated with diet and one to three daily injections of short- and intermediate-acting insulin. Exclusion criteria were conditions that could influence magnesium homeostasis, including other endocrine diseases aside from diabetes, serum creatinine >300 mmol/l, and C-reactive protein <50 mg/l.

Twenty children admitted to our outpatient pediatric clinic for observation served as control subjects. All were discharged within 2 h with the diagnosis of common cold. Exclusion criteria were similar to those in the diabetic group and also included no incidences of diabetes in a first-degree relative.

In seven diabetic and two control subjects, the analysis of blood samples failed because of calibrating or other technical problems, leaving 74 diabetic patients (37 girls and 37 boys) and 18 control subjects (8 girls and 10 boys), respectively.

An ion-selective analyzer (Nova 8; Nova Biomedical, Waltham, MA) was used to measure ionized magnesium, ionized calcium, and pH immediately after collection at 37°C. A capillary tube (55-μl volume) containing 50 IU/ml sodium heparinate (Clinitubes; Radiometer, Copenhagen, Denmark) was used for blood sampling. A plastic adapter between the capillary tube and the magnesium electrode was applied. Day-to-day coefficients of variation ranged from 2 to 4%. HbA$_{1c}$ was measured with a Tosoh automated glycohemoglobin analyzer. Vitrex end-to-end pipettes (10 μl) (Modulohm, Herlev, Denmark) were used.

The study was approved by the local ethics committee, registration number KA 99066m.

Statistical analysis

Analyses were performed using SPSS version 10.0 (SPSS, Chicago, IL). All values are expressed as median and range or mean ± SD. Differences between groups were assessed by paired Student's t test or the sign test. Correlation between variables was assessed using Pearson correlation coefficient. A P value of <0.05 was considered significant.

RESULTS

None of the children had hypertension, diabetic retinopathy, or nephropathy. The duration of diabetes ranged from 0.3 to 11.6 years (median 4.0). The daily insulin dose (in units per 24 h and units per kilogram) ranged from 12.3 ± 3.1 to 65.0 ± 25.9 units/24 h and 0.65 ± 0.10 to 1.03 ± 0.29 units/kg, respectively, and increased as expected with age and increasing BMI.

The age distribution of diabetic children appears in Table 1. HbA$_{1c}$ remained stable throughout the age span. We did not observe any relationship between HbA$_{1c}$ and ionized magnesium or any other variables.

The level of ionized magnesium at actual pH and corrected to pH 7.4 showed no change in relation to age in diabetic subjects (Table 1), and the level was comparable with that of control subjects (0.56 ± 0.05 vs. 0.55 ± 0.06 mmol/l, P = NS). There was no relationship between the levels of ionized magnesium at actual pH or at those corrected to pH 7.4 and any other variables.

Although the level of ionized calcium at actual pH tended to be slightly higher in diabetic children compared with that of control subjects, this difference disappeared when ionized calcium was corrected to pH 7.4.

CONCLUSIONS

Our study demonstrated that the level of ionized magnesium remained stable in relation to age, duration of diabetes, and insulin dosage and was comparable with the level in adults (0.55 ± 0.03 mmol/l) (13). These results are in agreement with the findings by Roffi et al. (14) but in contrast to those of others (15,16), who have reported significantly lower serum total magnesium levels in diabetic children. These earlier reports are probably of limited value because it is now generally accepted that the use of total magnesium is also of limited value in regard to the evaluation of magnesium metabolism; therefore, ionized magnesium should be measured instead. Recently, Husmann et al. (9) reported a

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Table 1—Demographic and biochemical data in 74 patients with type 1 diabetes and 18 control subjects

| | Control subjects | | Age-group | | | | | |
| | | | 0–5 years | | 6–11 years | | 12–18 years | |
	Girls	Boys	Girls	Boys	Girls	Boys	Girls	Boys
n	8	10	7	10	11	13	19	14
Age (years)	5.8 ± 4.4		4.9 ± 0.9	4.5 ± 1.3	7.9 ± 1.1	8.6 ± 1.5	13.8 ± 1.8	14.5 ± 2.0
Duration of diabetes (years)	—		2.2 ± 1.1	2.7 ± 1.5	3.9 ± 1.7	3.6 ± 1.8	5.0 ± 3.2	4.7 ± 3.5
BMI (kg/m^2)	17.8 ± 5.6		16.3 ± 1.2	16.5 ± 1.4	16.6 ± 1.5	17.6 ± 1.3	20.4 ± 2.7	21.4 ± 3.9
HbA$_{1c}$ (%)	—		8.6 ± 1.1	8.4 ± 0.6	8.1 ± 0.7	8.5 ± 0.9	8.8 ± 0.9	8.8 ± 1.3
IMg^{2+} (mmol/l)	0.55 ± 0.06		0.58 ± 0.06	0.55 ± 0.04	0.56 ± 0.04	0.56 ± 0.06	0.56 ± 0.05	0.54 ± 0.05
NMg^{2+} (mmol/l)	0.57 ± 0.07		0.60 ± 0.06	0.57 ± 0.04	0.58 ± 0.04	0.58 ± 0.06	0.57 ± 0.05	0.56 ± 0.05
ICa^{2+} (mmol/l)	1.25 ± 0.06		1.28 ± 0.03	1.27 ± 0.04	1.27 ± 0.03	1.27 ± 0.04	1.28 ± 0.04	1.28 ± 0.05
NCa^{2+} (mmol/l)	1.31 ± 0.06		1.34 ± 0.03	1.34 ± 0.05	1.33 ± 0.04	1.33 ± 0.04	1.33 ± 0.04	1.32 ± 0.05
pH	7.50 ± 0.03		7.49 ± 0.02	7.50 ± 0.02	7.49 ± 0.01	7.49 ± 0.02	7.48 ± 0.02	7.47 ± 0.02

Data are means ± SD. ICa^{2+}, ionized calcium at actual pH; IMg^{2+}, ionized magnesium at actual pH; NCa^{2+}, ionized calcium normalized to pH 7.4; NMg, ionized magnesium normalized to pH 7.4.

significantly lower level of ionized magnesium (0.50 mmol/l) in a diabetic population of children, which is lower than that observed in our study. Although the difference is remarkable, the explanation could be that our patients are well regulated, as indicated by HbA$_{1c}$ levels. Furthermore, we included three times as many subjects as Husmann et al., which may substantiate our findings.

Although our study does not substantiate the findings of hypomagnesemia in insulin-dependent diabetic subjects, recent findings (7,8,17) support the hypothesis that magnesium supplementation reduces the risk of developing diabetes and the complications associated with both type 1 and type 2 diabetes. The mechanism behind this phenomenon is not clear, but may be due to intracellular magnesium depletion in both types (17,18), which influences cellular insulin-mediated glucose uptake.

In conclusion, our study demonstrates that ionized magnesium and calcium are well regulated and within normal ranges in Danish children with type 1 diabetes. Furthermore, there appears to not be any relationship between these ions and glycemic control.

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