Plasma and Erythrocyte Magnesium in Diabetes Mellitus: More on the Correlation and Regression Studies between several Variables

M. Speich[1], A. Murat[2], P. Arnaud[3] and A. Pineau[4]

Zusammenfassung

Die biologischen Zusammenhänge zwischen verschiedenen Variablen, die bei hospitalisierten Diabetikern oft erfaßt werden, angenommen werden, analysierten wir bei 19 insulinbedürftigen Männern sowie bei 22 insulinbedürftigen und 10 nicht-insulinbedürftigen Frauen die folgenden Größen unter biometrischen Aspekten: Plasma-Mg (Pl-Mg), Erythrocyten-Mg (Er-Mg), Plasma-Ca (Pl-Ca), Gesamt- und HDL-Cholesterin, Triglyceride, Albumin, Blutzucker, glycosyliertes HbA_1 sowie die Dauer der Behandlung.
Verglichen mit Kontrollen war das Pl-Mg bei insulinabhängigen Frauen signifikant erniedrigt ($p < 0{,}001$) und das Er-Mg bei insulinabhängigen Frauen und Männern ($p < 0{,}001$), während das Pl-Ca in allen 3 Gruppen signifikant erhöht war. — Auf Grund vermuteter Interaktionen zwischen den verschiedenen Variablen der Patienten, wurde auf einfache und multiple Korrelation geprüft, weiter wurden schrittweise Regressionen durchgeführt. Multiple Korrelationskoeffizienten waren signifikant ($p < 0{,}05$) zwischen Pl-Mg bei insulinabhängigen Männern oder Er-Mg bei insulinabhängigen Frauen und allen anderen normal verteilten Variablen. Mittels schrittweiser Regressionsgleichungen wurden die repräsentativen Variablen für Pl-Mg oder Er-Mg ermittelt. Die Studie bestätigt, daß man Diabetiker nach Geschlecht und Diabetestyp unterteilen soll.

[1] Laboratoire de Biochimie Pharmaceutique
[3] Laboratoire de Biophysique et Mathématiques
[4] Laboratoire de Toxicologie et Hygiène Industrielle, (1, 3, 4) Faculté de Pharmacie, 1, rue Gaston Veil, 44035 Nantes Cedex, France
[2] Hôpital de l'Hôtel-Dieu, Clinique Médicale B, 44035 Nantes Cedex, France

Summary

The biological relations assumed to exist between different variables often monitored in hospitalized diabetic patients led us to adopt the following criteria for statistical analyses: age, body mass index, plasma and erythrocyte magnesium (Pl-Mg, Erc-Mg), plasma calcium (Pl-Ca), total- and HDL-cholesterols, triglycerides, albumin, blood glucose, glycosylated hemoglobin A_1 and length of treatment of 19 insulin-dependent diabetic (IDD) men, 22 IDD women and 10 noninsulin-dependent women.
In comparison with reference subjects, Pl-Mg decreased significantly ($p < 0.001$) in IDD women, and Erc-Mg decreased in both IDD groups ($p < 0.001$), whereas Pl-Ca increased significantly in the 3 populations of diabetics. In view of the probable interactions between the different variables in these patients, simple and multiple correlations were searched for as well as stepwise regression equations. Multiple correlation coefficients were significant ($p < 0.05$) between Pl-Mg in IDD men or Erc-Mg in IDD women and all of the other 11 series of normally distributed variables. The stepwise regression equations selected the most representative variables of Pl-Mg or Erc-Mg. This study confirms that it is preferable to separate diabetic patients according to sex and type of diabetes.

Résumé

Les relations biologiques supposées entre différentes variables fréquemment demandées chez des diabétiques hospitalisés nous ont conduits à retenir pour les analyses statistiques: l'âge, l'index de corpulence, les magnésiums plasmatique et érythrocytaire (Pl-Mg, Erc-Mg), le calcium plasmatique (Pl-Ca), les cholestérols total et HDL, les triglycérides, l'albumine, la glycémie, l'hémoglobine glycosylée A_1 et la durée du traitement chez 19 hommes diabétiques insulino-dépendants (DID), 22 femmes DID et 10 femmes diabétiques non-insulino-dépendantes (DNID). Par rapport aux sujets de référence, Pl-Mg diminuait significativement ($p < 0{,}001$) chez les femmes DID et Erc-Mg dans les deux groupes DID ($p < 0{,}001$), tandis que Pl-Ca augmentait significativement dans les trois populations diabétiques.
Compte tenu des interactions probables entre les différentes variables de ces malades, les corrélations simples et multiples ont été recherchées ainsi que les équations de régression pas à pas. Les coefficients de corrélation multiple étaient significatifs ($p < 0{,}05$) entre Pl-Mg des hommes DID ou Erc-Mg des femmes DID et l'ensemble des onze autres séries de variables distribuées normalement. Les équations de régression pas à pas ont sélectionné les variables les plus représentatives de Pl-Mg ou Erc-Mg. Cette étude confirme qu'il est préférable de séparer les diabétiques selon le sexe et le type de diabète.

Introduction

Diabetes mellitus is the disease most often involving magnesium deficit [1; 3; 7]. The relations between the metabolism of magnesium (Mg) and carbohydrates are extremely close, and several recent publications [1; 3; 5] have attempted to treat this subject. However, analysis of the mechanisms of magnesium deficit in diabetes, as well as of the consequences in the physiopathology of diabetes and its complications, still raise serious problems.

The biological relations assumed to exist between different variables often monitored in hospitalized diabetic patients led us to adopt the following criteria for the present study: age, body mass index (BMI), plasma and erythrocyte magnesium (Pl-Mg, Erc-Mg), plasma calcium (Pl-Ca), total- and HDL-cholesterols, triglycerides (Tg), albumin (A), blood glucose (G), glycosylated hemoglobin A_1 (Hb A_1) and length of treatment. Plasma magnesium, Erc-Mg, Pl-Ca and total- and HDL-cholesterols were determined at the same time in reference subjects.

The means of the results for diabetic men and women as well as those for patients and controls of the same sex were compared. In view of the probable interactions between the different variables of the diabetic patients, simple and multiple correlations were searched for as well as stepwise regression equations.

Populations and Methods

Populations

The study concerned 51 hospitalized diabetics and 111 reference subjects, all residents of Nantes, France. The 51 patients, all free of acidoketosis or severe renal affections, diuretic agents and alcoholism, were divided into 3 groups: 19 insulin-dependent diabetic (IDD) men, 22 IDD women (not using oral contraceptives) and 10 noninsulin-dependent diabetic (NIDD) women. The controls (58 men, 53 women) were neither hospitalized nor blood donors, in good health and not under medication.

Assay Methods

Magnesium and Ca were measured by flame atomic absorption spectrometry in a Hitachi Model 180-80 with Zeeman effect (Skalar Analytique, 75015 Paris, France). HDL-cholesterol (after precipitation) and total-cholesterol were determined by the Boehringer enzymatic method, CHOD-PAP C-system (Boehringer, Mannheim, West Germany). Triglycerides were analyzed by the Boehringer enzymatic method. The blood glucose assay was performed using the glucose-oxidase method. Glycosylated hemoglobin was assayed according to the microchromatographic technique of Kynoch and Lehmann. Our methods have been previously described [7; 8].

Statistical Analyses of Results

The normality of distributions was searched for. Means were compared using appropriate parametric (Student's t-test, analysis of variances) or nonparametric (Mann and Whitney) tests. Simple (r) and multiple (R) correlation coefficients were calculated

Tab. 1: Summary of Results Obtained in 51 Diabetic Patients and 111 Reference Subjects (Means and S D of the Population).

Units	Age Years	Body mass index kg/m²	Plasma magnesium mmol/L	Erythrocyte magnesium mmol/L	Plasma calcium mmol/L	Total cholesterol mmol/L	HDL-cholesterol mmol/L	Triglycerides mmol/L	Albumin µmol/L	Blood glucose mmol/L	Hb A_1 %	Length of treatment Years
19 IDD men	40.0 (15.3)	21.2 (2.98)	0.74 (0.08)	1.82[b]*** (0.32)	2.28 (0.08)	4.70 (1.16)	1.14 (0.38)	1.18 (0.51)	638 (57.8)	10.3 (4.12)	11.9 (3.12)	7.42 (8.12)
58 reference men	42.8[a] (15.9)		0.77 (0.06)	2.12 (0.25)	2.20 (0.12)	5.23 (1.08)	1.21 (0.28)					
22 IDD women	34.8 (18.3)	20.9 (3.19)	0.71[b]**** (0.07)	1.71[b]**** (0.18)	2.26[b]** (0.12)	4.82 (1.09)	1.41[c]* (0.41)	1.06 (0.51)	603 (60.9)	12.7 (3.93)	12.0 (2.30)	11.7 (9.21)
							[d]**			[d]**	[d]****	
10 NIDD women	59.2 (9.04)	27.7[d]**** (5.36)	0.75 (0.11)	1.93[d]* (0.26)	2.30[b]*** (0.08)	4,97 (0.89)	0.96[b]**** (0.29)	1.94[d]** (0.99)	620 (51.0)	8.22[a] (3.81)	9.49 (2.37)	10.1 (11.9)
53 reference women	41.4 (13.1)		0.77[e]* (0.05)	2.03[e]**** (0.23)	2.18[e]** (0.10)	5.06 (0.97)	1.43[e]** (0.28)					

[a] Nonnormal distribution.
[b] Mean comparison with reference subjects of the same sex.
[c] Comparison of 19 IDD men with 22 IDD women.
[d] Comparison of 22 IDD women with 10 NIDD women.
[e] Analysis of variances (53 reference women/22 IDD women/10 NIDD women).
*p < 0.05, **p < 0.01, ***p < 0.005, ****p < 0.001.

between the normally distributed series. The Spearman correlation coefficient (r_s) was used for normally nondistributed series [8]. Stepwise regression equations were computed: Pl-Mg and Erc-Mg were selected as dependent variables, and the most representative variables had to show normal distribution [2].

Results

The results are summarized in Tables 1 and 2. Among the simple correlations, the following are the significant ones relative to Pl-Mg and Erc-Mg: in IDD men between Pl-Mg and age ($r = +0.70$, $p < 0.001$); in IDD women between Pl-Mg and albumin ($r = -0.49$, $p < 0,05$), Pl-Mg and Erc-Mg ($r = +0.63$, $p < 0.01$) and Erc-Mg and length of insulin treatment ($r = +0.69$, $p < 0.001$); in NIDD women between Erc-Mg and age ($r = +0.72$, $p < 0.05$), and Erc-Mg and albumin ($r = -0.88$, $p < 0.001$). In IDD men there was a significant multiple correlation between Pl-Mg and the other 11 series of variables ($R = 0.93$, $p < 0.05$), and in IDD women between Erc-Mg and the other 11 series of variables ($R = 0.90$, $p < 0.05$).

Tab. 2: Stepwise regression equations (same units as in table 1)

A) 19 IDD men (11 variables, exeluding length of insulin treatment)
Pl-Mg = 1.119 + 0.002 age − 0.005 G − 0.286 Pl-Ca + 0.071 HDL-ehol. + 0.061 Tg + 0.049 Erc-Mg ($\underline{R} = 0.908$)
Ere-Mg = 1.333 − 0.027 G + 0.035 Hb A_1 + 0.301 HDL-ehol ($\underline{R} = 0.574$)

B) 22 IDD women (same variables)
Pl-Mg = 0.274 − 0.007 A + 0.172 Pl-Ca + 0.207 Ere-Mg ($\underline{R} = 0.734$)
Ere-Mg = 0.347 + 0.012 BMI + 1.563 Pl-Mg ($\underline{R} = 0.664$)

C) 10 NIDD women (6 variables: age, BMI, Tg, G, Hb A_1, and length of insulin treatment being excluded)
Pl-Mg = − 8.125 + 1.966 Pl-Ca + 0.056 A − 0.069 total-chol. + 0.120 Erc-Mg ($\underline{R} = 0.965$)
Erc-Mg = 6.782 − 1.597 Pl-Ca − 0.048 A + 0.059 total-ehol. + 0.744 Pl-Mg ($\underline{R} = 0.996$)

Discussion

Out of all the correlated variables acting on a given phenomenon, the stepwise regression equation selects the most representative. This equation is admittedly less predictive than that of regression for all the variables measured, but it is simpler (only the essential factors are included), which accounts for its value. This study suggests that it is preferable to separate diabetic patients according to sex and type of diabetes [5; 7]. No significant correlations were found between Pl-Mg or Erc-Mg and blood glucose or Hb A_1, which both confirms or contradicts previous results [1; 5; 6]. Other studies are evidently required: correlations between calcium-phosphate parameters and their control factors, especially 1,25-dihydroxycholecalciferol, parathormone and calcitonin, or search for ionized, complexed and proteinbound fractions of Pl-Mg and Pl-Ca [7]. The Mg deficit of IDD subjects represents a typical form of Mg depletion induced both by direct effects such as osmotic diuresis [1] and indirect effects due to hormones, vitamins, ions and proteins. It cannot be considered as a simple deficit resulting solely from a reduction in Mg supply. Many unknown factors must still be investigated. As numerous variables are involved in diabetes mellitus, the study of a single variable is of little interest. Our team is currently carrying out more complete statistical studies relative to other variables.

References

[1] *Bachem, M. G.:* Hypomagnesiämie und zellulärer Magnesiummangel bei Typ — I — Diabetes-mellitus. Abhängigkeit von der Einstellungsqualität. In: *Lasserre, B.* (Ed). Magnesium — Physiologische Aspekte für die Praxis. Panscienta Verlag, Ch-Hedingen/Zürich (1987) 9 – 16.

[2] *Dagnelie, P.:* Analyse statistique à plusieurs variables. Presses Agronomiques de Gembloux. Gembloux, Belgium (1982) 75 – 126.

[3] *Durlach, J., P. Collery:* Magnesium and potassium in diabetes and carbohydrate metabolism. Magnesium **3** (1984) 315 – 323.

[4] *Durlach, J., Y. Rayssiguier:* Données nouvelles sur les relations entre magnésium et hydrates de carbone. I. Données physiologiques. Magnesium **2** (1983) 174 – 191.

[5] *Durlach, J., Y. Rayssiguier:* Données nouvelles sur les relations entre magnésium et hydrates de earbone. II. Données cliniques et thérapeutiques. Magnesium **2** (1983) 192 – 224.

[6] *Petri, M., R. Perry:* Cellular and plasma magnesium in diabetes. Mag.-Bull. **8** (1986) 271.

[7] *Speich, M., S. Gelot, P. Arnaud, A. Murat:* Plasma and erythrocyte magnesium in insulin-dependent and non-insulin-dependent diabetics: correlations between twelve variables. Mag.-Bull. **7** (1985) 140 – 145.

[8] *Speich, M., S. Gelot, P. Arnaud, N. Van Goc, N. Robinet, A. Pineau:* Multiple and simple correlations between magnesium, calcium, zinc, potassium, total- and HDL-cholesterol in 111 reference subjects. Mag.-Bull. **6** (1984) 137 – 141.

For the authors: Dr. *Michelle Speich*, Université de Nantes, Laboratoire de Biochimie Pharmaceutique, Faculté de Pharmacie, 1, rue de Gaston Veil, F-44035 Nantes Cedex, France