Plasma and Erythrocyte Magnesium, Total Calcium, Phosporus, Copper and Zinc at Birth in Premature Dizygotic Twins and Two Brothers from Diabetic Mothers

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Zusammenfassung

Die Konzentrationen an Magnesium (Mg), Gesamtcalcium (Ca), Phosphor (P), Kupfer (Cu) und Zink (Zn) wurden im Plasma (Pl) bzw. in den Erythrocyten (Ery) bei prämaturen, dizygoten, weiblichen Zwillingen sowie bei zwei Söhnen diabetischer Mütter kurz nach der Geburt gemessen. Bei den Zwillingen ergaben sich beachtenswerte Konzentrationsunterschiede, besonders für Pl-Mg, Pl-Ca und Pl- P.

Der Zwilling mit dem höheren Pl-Mg (1,11 gegenüber 0,79 mmol/l) hatte auch höheres Pl-Ca (2,55 gegenüber 2,06 mmol/l) und Pl-P (2,20 gegenüber 1,87 mmol/l). Ery-Zn war recht niedrig, vor allem bei einem Zwilling mit transientem Atem-Distress (12,2 gegenüber 15,2 µmol/l).

Von den zwei Söhnen hatte der ältere eine Makrosomie (die Mutter hatte einen Schwangerschaftsdiabetes und erhielt Insulin) – er wies niedriges Pl-Mg (0,75 mmol/l), Ery-Mg (1,57 mmol/l) und Pl-Ca (1,56 mmol) auf, die Cu- und Zn-Werte waren normal.

Beim jüngeren Bruder, der multiple Mißbildungen hatte (die Mutter verweigerte eine Insulin-Therapie), lagen die Elektrolytkonzentrationen größtenteils im Normbereich (Pl-Mg: 0,85, Ery-Mg 1,98 mmol/l); nur Pl-Ca war erhöht (2,93 mmol/l).

Für die zweieiigen Zwillinge wird eine genetische Kontrolle des Mineralmetabolismus diskutiert.

Summary

Plasma (Pl) and erythrocyte (Erc) concentrations of magnesium (Mg), total calcium (Ca), phosphorus (P), copper (Cu) and zinc (Zn) were investigated at birth in two premature female dizygotic twins and two brothers from diabetic mothers. Differences in values between the twins were especially noteworthy for Pl-Mg, Pl-Ca and Pl-P. The twin with the highest concentration of Pl-Mg (1.11 vs 0.79 mmol/l) also had the highest concentrations of Pl-Ca (2.55 vs 2.06 mmol/l) and Pl-P (2.20 vs 1.87 mmol/l). Erc-Zn concentrations were quite low, particularly in the twin with transient respiratory distress (12.2 vs 15.2 mmol / l). The older brother, born with macrosomia (mother with gestational diabetes and on insulin), had low Pl-Mg (0.75 mmol/l), Erc-Mg (1.57 mmol/l) and Pl-Ca (1.56 mmol /l) but normal Cu and Zn. Most mineral results for the younger brother, born with multiple malformations (mother then refusing insulin), were normal (Pl-Mg 0.85 mmol/l, Erc-Mg 1.98 mmol/l). Only Pl-Ca (2.93 mmol/l) was elevated. Genetically controlled regulation of mineral metabolism would seem likely in the case of the dizygotic twins.

Résumé

Les concentrations plasmatiques (Pl) et érythrocytaires (Erc) du magnésium (Mg), du calcium total (Ca), du phosphore (P), du cuivre (Cu) et du zinc (Zn) ont été déterminées à la naissance chez deux jumelles dizygotes prématurées et deux frères de mères diabétiques. Les différences étaient particulièrement importantes entre les jumelles pour Pl-Mg, Pl-Ca et Pl-P. La jumelle avec la concentration la plus élevée de Pl-Mg (1,11 vs 0,79 mmol/l) était aussi celle qui présentait les concentrations les plus élevées de Pl-Ca (2,55 vs 2,06 mmol/l) et Pl-P (2,20 vs 1,87 mmol/l). La concentration de Erc-Zn était très basse chez ces jumelles, particulièrement chez l'enfant présentant une détresse respiratoire transitoire (12,2 vs 15,2 µmol/l). Le frère le plus âgé, né avec une macrosomie (mère avec un diabète gestationnel, recevant de l'insuline), avait des valeurs basses de Pl-Mg (0,75 mmol/l), Erc-Mg (1,57 mmol/l), Pl-Ca (1,56 mmol/l) et des résultats normaux de Cu et Zn. Chez le frère le plus jeune, présentant de multiples malformations (mère refusant l'insuline), la plupart des résultats minéraux étaient normaux: Pl-Mg (0,85 mmol/l), Erc-Mg (1,98 mmol/l). Seulement Pl-Ca était élevé (2,93 mmol/l). Une régulation du métabolisme minéral sous contrôle génétique est suggérée après l'étude des jumelles dizygotes.

Introduction

Metabolic modifications induced by maternal diabetes have an effect on fetal development. It has also recently been recognized that congenital malformations, more frequent in babies from diabetic mothers than in the general population, may result from disturbances in mineral metabolism [1, 2]. Although the prognosis for diabetic pregnancy has improved considerably in recent years as a result of early care provided in specialized centers, certain constraints have not proved acceptable to all future mothers, particularly those socially disadvantaged.

The purpose of this study was to compare the results of plasma (P1) and erythrocyte (Erc) concentrations in venous cord blood or heel blood (day 2) for magnesium (Pl- Mg, Erc-Mg), total calcium (Pl-Ca), phosphorus (Pl-P), copper (Pl-Cu, Erc-Cu) and zinc (Pl-Zn, Erc-Zn) in 4 abnormal infants with those of 66 reference newborns and 44 healthy newborns from diabetic mothers studied thoroughly in previous publications [3, 4]. Our work on the lat-

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ter group led us to differentiate results for the 4 abnormal cases (premature female twins and two brothers) from the others.

Subjects and Methods

The dizygotic twins were born to a 32-year-old diabetic woman who had been insulin-dependent for 13 years. Delivery was by cesarean section in emergency conditions (rupture of the bag of waters) at 30.5 weeks of gestation. The first twin weighed 1.600 kg at birth and the second 1.560 kg. Both cried immediately after birth and had Apgar scores of 10 at 5 min. However, after 10 min the second twin presented transient respiratory distress and was transferred to the neonatal intensive care unit of the Nantes University Hospital, whereas the first twin was immediately placed in an incubator in the neonatology ward of the same hospital. After simple deobstruction and several days of infusion, the second twin improved rapidly and was then, like her sister, fed with special milk for the premature. The twins' growth and weight increase were satisfactory relative to their head circumference of 29.5 cm at birth. Presently, they are 2 years old and in fine health.

The mother's previous pregnancy 8 years before had been terminated at 17 weeks of gestation because of notable fetal malformations, particularly anencephaly. This second pregnancy, after a long period of sterility, proceeded normally until the day of emergency delivery when normochromic, normocytic anemia was noted and the following concentrations determined: glucose 6.60 mmol/l, sodium 141 mmol/l, potassium 4.20 mmol/l, chlorine 110 mmol/l, calcium 2.20 mmol/l, bicarbonates 20 mmol/l, total proteins 58 g/l, urea 3.00 mmol/l and creatinine 70 µmol/l.

The mother's diabetic problem had been quite effectively controlled during the 3 preceding years by use of a portable insulin pump with two basic rates of 1.6 U/h during the day and 0.9 U/h at night, together with boluses of 15 U in the morning, 8 U at noon and 13 U in the evening. During delivery, the insulin pump was left in place but the doses reduced. Two months before delivery, total glycohemoglobin was within the upper limits of normal (8.80%). The most recent ophthalmic examination showed no signs of retinopathy. There was a weight increase of 14 kg during pregnancy (54 kg before). Arterial blood pressure was normal, and no clinical signs of electrolyte deficiency were noted at any time.

The two brothers were the ninth and tenth children of a 33-year-old Moroccan woman living in France with gestational diabetes who refused to practice contraception. She was persuaded to receive insulin treatment beginning at 33.5 weeks of gestation for the ninth child. Her eighth child, a girl weighing 5 kg, had been stillborn. For the tenth child, she refused insulin, accepting only to diet.

The first brother (ninth child), born by breech delivery after 38 weeks of gestation, presented macrosomia, weighed 3.780 kg, was 51 cm in height and had a head circumference of 37 cm. On the day of delivery, the mother had low concentrations of Pl-Mg (0.60 mmol/l), Erc-Mg (1.63 mmol/l) and Pl-Ca (1.38 mmol/l). The Mg concentration in 24-h urine (dU) was normal (4.71 mmol/24 h), and dU Ca was slightly elevated (9.09 mmol/24 h).

The second brother (tenth child), born 3 years and 3 months later by breech delivery after 39 weeks of gestation, was considerably more handicapped. He was cyanotic, had Pierre Robin syndrome, cardiac malformation and only 4 fingers on the left hand. His birth weight was not determined. Mineral analyses were not performed for the mother who never presented any tetanic signs.

Magnesium, calcium and zinc concentrations were measured by the specific (and reference) method of flame atomic absorption spectrometry, and copper was analyzed by flameless atomic absorption spectrometry (the reference method) with Zeeman effect. Phosphorus was determined by ultraviolet detection (340 nm) of ammonium phosphomolybdate. All these protocols were described previously [3, 4].

Results and Discussion

Results for normal infants and the dizygotic twins are reported in tab. 1. Differences between the twins were especially noteworthy for Pl-Mg, Pl-Ca and Pl-P, the second twin having the highest Pl-Mg concentration as well as the highest concentrations of Pl-Ca and Pl-P. The two infants thus regulated these elements differently, even though both had received appreciably the same minerals from their mother and had lived in nearly identical conditions. It is conceivable that in such cases intrinsic regulation of the individual takes place, perhaps through genetic control of mineral metabolism depending on different hormones (parathormone, calcitonin, insulin, etc.). At day 2, Pl-Mg and Pl-Ca decreased without tetanic signs, while Pl-P increased. Erc-Zn concentration was low for both, particularly for the second twin who experienced respiratory distress, but increased at day 2. Such low values in neonates correspond to relatively low concentrations of carbonic anhydrase (EC 1.4.2.1). This situation could be explained by the fact that the twins were not yet ready to breathe normally when born. These infants, who were to develop normally and survive, showed a considerable increase in Erc-Zn from bone or liver reserves as early as day 2. This increase was particularly notable in the second twin and coincided with an improvement in respiratory capacity. An especially low Pl-Cu concentration (determined twice in one twin only) is normal at this stage of life as it is associated with a low fetal ceruloplasmin rate [4, 5].

The results for the two brothers, who had the same Moroccan father, were quite different. The first brother born with macrosomia had, as in the case of his mother who was on insulin, low concentrations of Pl-Mg (0.75 mmol/l), Erc-Mg (1.57 mmol/l) and Pl-Ca (1.56 mmol/l) and normal Cu and Zn. Apparently, this infant drew heavily on blood Mg and Ca in developing macrosomia since only his Pl-P concentration was elevated (2.28 mmol/l). His mother, however, had low blood Mg and Ca results at delivery, except for

Tab. 1: Mineral results in plasma and erythrocytes of premature twins of a diabetic mother compared to healthy infants (mean and SD).

		Pl-Mg	Erc-Mg	Pl-Ca	Pl-P	Pl-Cu	Erc-Cu	Pl-Zn	Erc- Zn
		mmol/l					µmol/l		
66 reference newborns (cord blood)		0.85 (0.08)	1.76 (0.15)	2.48 (0.22)	1.57 (0.25)	5.58 (2.14)	12.9 (3.00)	16.0 (3.02)	40.4 (13.6)
44 healthy newborns from diabetic mother (cord blood)		0.82 (0.14) n=37	1.71[a] (0.17) n=44	1.96[b] (0.32) n=37	1.99[b] (0.40) n=33	5.15 (1.92) n=25	10.9[b] (2.41) n=39	16.8 (5.66) n=23	33.0 (18.3) n=44
1st dizygotic twin girl from ID[c] diabetic mother (birth weight: 1.600 kg)	day 1	0.79	2.08	2.06	1.87	1.08	12.8	19.6	15.2
	day 2	0.63	2.05	1.53	2.15	0.71	ND[d]	18.8	20.2
2nd dizygotic twin girl from ID diabetic mother (birth weight: 1.560 kg)	day 1	1.11	1.91	2.55	2.20	ND	11.3	ND	12.2
	day 2	0.90	1.98	1.92	2.55	ND	10.2	ND	22.0

[a], [b] Significantly different by analysis of covariance (adjustment for duration of gestation): [a] $P < 0.05$; [b] $P < 0.001$.
[c] ID = Insulin-dependent.
[d] ND: Not determined.

Pl-P (1.23 mmol/l), probably due to a depletion of these cations which may have made it difficult to transfer to the fetus elements which had previously been supplied in abundance. For the other brother (mother not on insulin), who had multiple malformations, mineral values were normal (Pl-Mg 0.85 mmol/l, Erc-Mg 1.98 mmol/l, Pl-P 1.75 mmol/l, Pl-Cu 4.49 µmol/l, Erc-Cu 15.3 µmol/l, Pl-Zn 17.3 µmol/l, Erc-Zn 44.3 µmol/l), except for elevated Pl-Ca (2.93 mmol/l). However, his Pl-Zn/Pl-Cu ratio was higher (3.85) than that of reference newborns (2.87). This ratio, when elevated in childhood, can be an indicator of atherogenesis occurrence later in life [4, 6].

There are few studies on this subject. In hyprotrophic newborns, *Nagel* et al. [7] found elevated Pl-Mg and Pl-Zn concentrations and decreased Pl-Cu values in cord blood. Pl-Zn, analyzed twice in one of the twins in our study, was elevated both times. This result is in agreement with the findings of *Arumanayagam* et al. [8] who showed that cord blood Pl-Zn, beginning at 35 weeks of gestation, decreases slightly with gestational age. This may be due to demands of the growing fetus since it gains weight near term. On the contrary, *Bro* et al. [9] found no difference in serum Zn concentrations in preterm infants but noted lower serum Cu concentrations than in reference infants. Moreover, these authors point out that serum Zn and Cu in malformed infants did not differ from concentrations in reference infants [9]. In preterm appropriate-for-gestational-age infants, *Nelson* et al. [10] found a significant decrease in Pl-Mg and no variation in Pl-P.

The present study of 4 abnormal infants (a pair of twins and two brothers) from 2 diabetic mothers shows that there were great variations in mineral concentrations and that changes in values sometimes occurred very rapidly during the first 24 hours of life. Two conclusions may be drawn: 1. Regulation of mineral metabolism under genetic control occurs very early in life, as suggested by the study of the dizygotic twins; 2. Macrosomia plays a role in lowering Pl-Mg, Erc-Mg and Pl-Ca concentrations. For the brother with multiple malformations, whose mother refused insulin treatment, most mineral results were normal. However, further studies are required before firm conclusions can be reached since the field of perinatal mineral research and genetic factors regulating mineral concentrations is still at the pioneer stage [11–13].

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