

Magnesium and Intrauterine Growth Restriction

Naila O.E. Barbosa, MD, Thelma S. Okay, MD, PhD, Cléa R. Leone

Department of Pediatrics (N.O.E.B., C.R.L.), School of Medicine, Laboratory of the Children's Hospital "Prof. Pedro de Alcântara", Hospital das Clínicas (T.S.O.), University of São Paulo, São Paulo, BRAZIL

Key words: intrauterine growth restriction, term newborn, magnesium, ionized magnesium, total magnesium

Background: The presence of intrauterine growth restriction (IUGR), could potentially lead to imbalances of Mg homeostasis, which have not yet been fully clarified.

Objective: To describe, in term newborn (NB) without IUGR, ionized magnesium (iMg) and total magnesium (TMg) concentrations in umbilical cord blood, on the third and seventh days of life and to compare these values with those of term NB with IUGR.

Methods: A prospective study was performed on 70 term NB divided into two groups: Group I—30 NB without IUGR and Group II—40 NB with IUGR. TMg concentrations were determined in sera by a classical colorimetric end point method (Cobas-Mira, Roche), and iMg was determined in whole blood by means of the Stat Profile-M analyzer (NOVA Biomedical).

Results: We found that in term NB without IUGR, TMg concentrations increased during the first week of life and were lower than those of NB with IUGR in cord blood ($p < 0.05$). NB without IUGR had decreased iMg concentrations in comparison to NB with IUGR in all sampling times, i.e., cord blood, third and seventh days of life ($p < 0.001$). iMg concentrations remained unchanged during the study period. We also found that all NB enrolled in the study presented with low iMg concentrations (reference interval 0.4–0.6 mmol/L).

Conclusion: The presence of IUGR may influence neonatal levels of magnesium, suggesting an effect on the modulation of this ion homeostasis, during the perinatal period.

INTRODUCTION

Magnesium (Mg) is the 4th most abundant cation in the organism [1]. It has several metabolic functions: it is a cofactor in more than 325 enzyme systems in cells, activating several enzymes involved in the metabolism of phosphorous, mitochondrial oxidative phosphorylation and nucleic acids synthesis and degradation. It is also a component and activator of adenosine triphosphate (ATP) and adenylyl-cyclase [1,2].

Although Mg is predominantly an intracellular cation, due to technical difficulties in the determination of its cellular content in various tissues, its plasmatic dosage has been used as a clinical parameter [3].

The concentration of serum total magnesium (TMg), which includes that bound to the proteins, the complexes and the ionized, was the first and the most easily measured form of Mg

and is routinely used in clinical practice to access the circulating Mg [4,5]. The ionized fraction, however, is the physiologically active and presents a narrow normal range when compared to TMg, which contributes to its clinical relevance [1].

The recent development of an ion-selective electrode micro-method for iMg, has enabled a rapid determination of the iMg concentrations in small blood samples, which in turn has made possible to determine its fraction in the neonatal period and has contributed to clarify the action mechanisms of Mg [1].

There are few studies on Mg in the neonatal period, especially regarding the behavior of the ionized fraction. Furthermore, it is possible that nutritional factors, such as intrauterine growth restriction (IUGR), might lead to an imbalance of Mg homeostasis, which has not yet been fully explained.

The aim of this study was to describe the levels of iMg and TMg in term newborns (NB), without IUGR, in their 1st week

Address reprint requests to: Naila de Oliveira Elias Barbosa, M.D., Alameda Fernão Cardim n° 99 apartamento 11, Jardim Paulista, São Paulo—SP, CEP: 01403-020, BRAZIL. E-mail: naila@ajato.com.br.

This work was supported by a grant from FAPESP [Foundation to Aid Research of the State of São Paulo].

Abbreviations: iMg = Ionized magnesium, IUGR = intrauterine growth restriction, Mg = Magnesium, NB = newborn, TMg = total magnesium.

of life and to compare these data with those from NB with IUGR.

PATIENTS AND METHODS

A prospective study was performed on 70 term NB admitted to the Nursery Annex to the Maternity, Department of Pediatrics, University of São Paulo School of Medicine, from May 11, 2001 to June 10, 2003. Informed and written consent was obtained from the parents or legal guardian.

This research was approved by the Ethics Commissions of the Department of Pediatrics and by the Analysis of Research Projects, Clinical Directorship of the Hospital das Clínicas and University of São Paulo School of Medicine.

The exclusion criteria were: major malformations; genetic anomalies; congenital infections; twin births; exchange-transfusion within the first week of life; maternal disease liable to interfere in the metabolism of Mg, such as diabetes mellitus or gestational diabetes and hyperparathyroidism; and use of medications during the gestation or delivery that could affect the metabolism of Mg, such as magnesium sulfate.

NB with gestational age between 37 and 41 ⁶/₇ weeks were considered term. Gestational age at birth was based on the first day of the last menstruation period, whenever this differed by up to two weeks in relation to that indicated by the fetal ultrasound scan, if this had been performed by week 20 of gestation. In the absence of this exam or if it was accomplished after this gestational age, maternal information was used to indicate the definitive gestational age, if it differed to that given by the method of Capurro (1978) [6] by up to two weeks. When this difference was greater, the neonatal evaluation method was chosen.

The NB enrolled in the study were divided into two groups: Group I—without IUGR (n = 30); and Group II—with IUGR (n = 40).

The diagnosis of IUGR was based on birth weight <10th percentile for the gestational age and, besides this, a birth weight ratio (BWR), which is the ratio of the observed birth weight in a given infant to the 50th percentile for that infant's gestational age <0.85 [7]. The reference values for the 50th percentile, in complete weeks of gestation, were obtained from the study by Alexander *et al.* [8].

The umbilical cord blood was collected through venous puncture in the fetal face of the placenta, soon after its extraction, by the author herself. On days 3 and 7 of life, additional blood collections were performed by the author, from a superficial blood vessel with easy access. The collection was programmed to coincide with the venous puncture performed for routine laboratory tests in these NB.

The total volume of blood obtained in each collection was 2 ml. The first 1 ml was put in a heparinized syringe (S-Monovette® with 50 UI of lithium heparin/ml of blood, balanced with calcium; SARSTEDT) for gasometry, iMg and

iCa. This sample was sent to the laboratory cooled with ice, and the analysis was performed soon after sampling. The second 1 ml of blood was drained for dosage of TMg (dry tube with gel separator, BD Vacutainer). After retraction of clot at room temperature for 1 hour, serum samples were obtained after centrifugation at 3000 rpm for 10 minutes. Then, two aliquots of approximately 100 μ L of serum were stored at -20°C until the time of analysis.

The determination of iMg was performed by means of an ion-selective electrode microtechnique, using a NOVA Stat Profile-M Analyzer (NOVA Biomedical Corporation, Waltham, Massachusetts) at the Laboratory of the Children's Hospital, Hospital das Clínicas [9].

TMg was determined by an end-point colorimetric method in Cobas Mira Roche Diagnostic System Inc. equipment. The method is based on the reaction of magnesium with xylydil blue in alkaline solution containing EGTA to mask the calcium in the sample. Briefly, 50 μ L of each serum sample were added to 400 μ L of buffer 1 (Tris-(hydroxymethyl) aminomethane/6-aminocaproic acid, pH 11.25, 500 mmol/L and EGTA 90 μ mol/L). Then, buffer 2 containing xylydil blue 0.28 mmol/L was added. In alkaline solution Mg forms a purple complex with xylydil blue, a diazonium salt. TMg is thereafter measured photometrically via the decrease in the xylydil blue absorbance (wavelengths 600 nm and 505 nm). Tests were performed in duplicate thus requiring a minimum serum volume of 100 μ L [10].

Statistical Analysis

The sample size calculus was based on the presupposition that there was a difference of 30% between the means of iMg seric concentrations in the two groups. A pre-test was performed including 20 term newborns without IUGR, in which was obtained a mean iMg concentration of 0.23 mmol/L and a standard deviation of 0.08 mmol/L. These were considered the reference iMg concentrations. Based on these results, and an $\alpha = 5\%$ and a power of the test of 80%, the n calculated for each group was 20.

Mean values were compared by the Student's *t* test or with Mann-Whitney parametric test when suppositions for the test were not satisfied. Anova one-way or Kruskal-Wallis was used for analysis of the continuous variables. The comparison of proportions was carried out by Fischer's Exact Test or the Chi-square Test. Values of $p < 0.05$ were considered statistically significant.

RESULTS

From May 11, 2001 to June 10, 2003, a total of 3560 term newborn were admitted to the Nursery Annex to the Maternity and of these 70 were included in this investigation; all with an Apgar score >6 at the fifth minute of life.

All infants enrolled in the study were breast-fed.

Table 1. Characteristics of the Newborns according to Study Group

Characteristics	Without IUGR n = 30	With IUGR n = 40	p
Weight (grams)	3180.00 SD = 280.59	2287.75 SD = 177.50	<0.001
Gestational age (weeks)	39.65 SD = 1.23	38.20 SD = 0.97	<0.001
Male Gender	21 (70.0%)	22 (55.0%)	0.304
Length (cm)	48.62 SD = 1.42	44.69 SD = 1.79	<0.001
Head circumference (cm)	34.25 SD = 1.10	31.85 SD = 1.03	<0.001
BWR			
≥0.85	30 (100.0%)	—	<0.001
<0.85	—	40 (100.0%)	

Results are expressed as mean and standard deviation (SD) or frequency/relative frequency.
BWR = Birth weight ratio.

The frequency of tabagism among the mothers was evaluated and just 3 (10.0%) in the group without IUGR and 6 (15.0%) in the group with IUGR were light smokers (<10 cigarettes/day).

The NB were divided into two groups: Group I—NB without IUGR (n = 30, 42.9%); and Group II—NB with IUGR (n = 40, 57.1%).

There was no difference between the groups in terms of gender (Table 1).

The NB of group II, with IUGR, were more frequently delivered by Cesarean section (72.5%). Comparing groups I and II, the NB with IUGR were smaller in terms of: gestational age (p < 0.001); birth weight (p < 0.001); length (p < 0.001); head circumference (p < 0.001); and BWR <0.85 (p < 0.001) (Table 1).

Table 2 describes the mean and standard deviation of iMg and TMg concentrations in the two groups. TMg concentrations increased from 1.67 ± 0.25 mg/dL at birth to 1.86 ± 0.25 mg/dL in day 7 of life in the group without IUGR (p < 0.05) and remained unchanged in the group with IUGR. The mean value of 1.67 ± 0.25 mg/dL found in cord blood of NB without IUGR was lower than the value 1.83 ± 0.39 mg/dL in the group with IUGR (p < 0.05). iMg concentrations remained unchanged during the first week of life in both groups. NB without IUGR had lower iMg concentrations in comparison to NB with IUGR in all sampling times (p < 0.001).

Table 3 describes the iMg/TMg ratio in the two studying groups. In comparing the data, we found that the ratio in NB

without IUGR was significantly lower than the values in the group with IUGR (p < 0.001).

Table 4 shows the mean and standard deviation of iCa concentrations in the two groups. iCa concentrations decreased from birth to the third day of life and then, increased to the seventh day in both groups. The mean serum iCa levels, however, were significantly higher in NB without IUGR than in NB with IUGR in all sampling times (p < 0.05).

The iCa/iMg ratio was lower in NB with IUGR in relation to NB without IUGR during the first week of life (Table 5).

DISCUSSION

Magnesium is an ion common to several reactions of the organism. Therefore, variations in its concentrations, beyond those that could be considered as physiologic, can have important clinical repercussions. In order to identify these changes, it is necessary to have reference standards, especially in relation to the physiologically active ionized fraction. The presence of disturbs in intrauterine nutrition, such as IUGR can potentially lead to deviations in the homeostasis of Mg, which have not yet been fully explained.

Although the levels of TMg at various ages have already been established, these are not as useful clinically, as would be those for iMg, which reflect more closely the intracellular activity of the ion [1]. This is particularly so in the neonatal

Table 2. Mean Levels of Ionized Magnesium (iMg) and Total Magnesium (TMg) during the First Week of Life in NB with and without IUGR

Group	iMg (mmol/L)			TMg (mg/dL)		
	Umbilical cord	Day 3 of life	Day 7 of life	Umbilical cord	Day 3 of life	Day 7 of life
Without IUGR	0.23 (0.09)	0.22 (0.07)	0.20 (0.06)	1.67 (0.25)	1.80 (0.29)	1.86 (0.25)
With IUGR	0.33 (0.11)	0.34 (0.10)	0.31 (0.08)	1.83 (0.39)	1.80 (0.40)	1.96 (0.41)

Results are expressed as mean/standard deviation (SD).

iMg = ionized magnesium, TMg = Total magnesium.

p < 0.001: iMg without IUGR × with IUGR (umbilical cord, days 3 and 7 of life).

p < 0.05: TMg without IUGR (umbilical cord, days 3 and 7 of life).

p < 0.05: TMg without IUGR × with IUGR (umbilical cord).

Table 3. iMg/TMg Ratio during the First Week of Life in NB with and without IUGR

Group	iMg/TMg		
	Umbilical cord	Day 3 of life	Day 7 of life
Without IUGR	0.36 ± 0.17 (n = 26)	0.31 ± 0.17 (n = 19)	0.26 ± 0.08 (n = 18)
With IUGR	0.47 ± 0.16 (n = 33)	0.49 ± 0.26 (n = 32)	0.39 ± 0.11 (n = 19)

* $p < 0.001$, iMg/TMg without IUGR × with CIUR (umbilical cord, days 3 and 7 of life).

period, during which there are metabolic adaptations that increase the risk of disturbances occurring.

Studies into the evolution of the serum levels of TMg in the neonatal period during the first week of life, have presented conflicting results. Some authors have described a gradual increase in the levels of TMg up to 48 hours of life, with a stabilization until day 7 of life [11–13]. Other authors, however, have reported that there is no change in these values over the first one to 12 hours of life [14] or during the first week of life [15].

In the present study, a progressive and statistically significant increase was observed in the serum concentrations of TMg in the control NB (Group I), throughout the first week of life (Table 2).

Some authors, for instance Marcus *et al.* (1998) [1] and Cook; Mimouni (1997) [11] refer to a mean value for iMg 0.48 mmol/L (0.40 to 0.56), using the NOVA 8 machine. Dollberg *et al.* (2001) [16] found a mean value for iMg in umbilical cord blood of 0.28 mmol/L (0.12 to 0.40) and at 2 to 4 hours of life, of 0.30 mmol/L (0.20 to 0.40), this time using the NOVA M instrument. The electrode of the NOVA M is more specific and interacts insignificantly with other cations, thereby producing lower values than the NOVA 8. Therefore, the values for these levels should be interpreted carefully in function of the type of electrode used [16,9].

In this study, the measurement of iMg was done in NB, without risk factors and appropriate intrauterine growth,

Table 4. Mean Levels of Ionized Calcium during the First Week of Life in NB with and without IUGR

Group	iCa (mmol/L)		
	Umbilical cord	Day 3 of life	Day 7 of life
Without IUGR	1.25 ± 0.26 (n = 26)	1.10 ± 0.25 (n = 23)	1.23 ± 0.14 (n = 20)
With IUGR	1.03 ± 0.27 (n = 34)	0.95 ± 0.19 (n = 34)	1.06 ± 0.26 (n = 20)

* $p < 0.05$, iCa without IUGR × with CIUR (umbilical cord, days 3 and 7 of life).

Table 5. iCa/iMg Ratio during the First Week of Life in NB with and without IUGR

Group	iCa/iMg		
	Umbilical cord	Day 3 of life	Day 7 of life
Without IUGR	6.24 ± 2.93 (n = 26)	5.85 ± 2.37 (n = 20)	7.2 ± 2.86 (n = 18)
With IUGR	3.53 ± 1.95 (n = 34)	2.93 ± 0.86 (n = 34)	3.73 ± 1.88 (n = 20)

* $p < 0.001$, iCa/iMg without IUGR × with CIUR (umbilical cord, days 3 and 7 of life).

through the NOVA M machine and mean values of iMg obtained were within the normal range described previously and without significant variation during the first week of life [9] (Table 3).

It should be emphasized, however, that there have been few such studies into the course of the serum levels of iMg in the first week of life. In the first 24 hours of life, Cook; Mimouni (1997) [11] demonstrated that there is no alteration in the concentrations of iMg.

It has been well documented in the literature that disturbances in intrauterine nutrition can increase the risk of perinatal morbidity and mortality. IUGR, in turn, provides an outstanding example of such situations of deviation from normality, since it refers to fetuses that failed to reach their inherent growth potential, thus characterizing a pathological reduction in this parameter [17].

In clinical practice, the indicators of individual growth potential and of rate of intrauterine growth are not very well defined, consequently there are no standard parameters for diagnosing this condition [18].

In the present study, to increase the precision during the selection of those cases with IUGR, the authors used the criterion of birth weight <10th on the Curve of Alexander [8] and associated this to a second criterion of nutritional classification, namely a BWR ratio <0.85. In this way newborn which were small but nevertheless normal were excluded [7].

Several experimental studies have shown that fetus of severe Mg deprived mothers can maintain seric Mg levels equal or higher than their mothers [19]. The placenta active transport of Mg is seen as the main type of transport [20]. The study of Shaw *et al.* (1990), demonstrated the presence of an active transport of Mg from the mother to the fetus, against a concentration gradient [21].

In the presence of IUGR many placenta modifications are described, as an uncomplete adaptative remodeling of the spiral arteries that supply the intervillous space of the placenta with maternal blood, atherosclerosis-like lipid depositions and thrombotic infarctation [22]. As a consequence, the nutrients and oxygen transport to the fetus could be reduced, as well as the active transport of Mg, which is dependent of ATP.

The higher iMg/TMg relation observed in the IUGR group,

could be the result of a low TMg in these newborns. Considering Durlach study [23], in which TMg is appointed as the most reliable indicator of total body Mg, this one would be also reduced, and this would be in accordance to this smaller placental transport of nutrients in the presence of intrauterine growth restriction, resulting in nutritional deficiencies.

Nevertheless, the analysis of the results from the present research demonstrated statistically significant differences in the concentrations of umbilical cord TMg between groups I and II ($p < 0.05$). The group with IUGR presented higher values, which could indicate that IUGR did not reduce the placental transport of Mg, as reported by some authors [24].

Likewise, the mean levels of iMg detected in the three main collection times in the group with IUGR were higher than in the group without IUGR ($p < 0.001$) (Table 2). Therefore, the higher iMg/TMg relation observed was probably a reflex of a higher iMg concentration than TMg in the presence of intrauterine growth restriction. It is possible that unknown adapting mechanisms could be enhanced by the intrauterine situation of IUGR, protecting the fetus against the lower Mg offer.

The higher levels of iMg observed in these NB could also be explained by the presence of intrauterine oscillations in the oxygenation and pH, as elements in the process of nutritional restriction, which could lead to the deviation of Mg from the intracellular to the extracellular compartment [25,26]. Besides this, the reduction in the placental transfer of calcium, also due to this process, could also lead to the low iCa/iMg ratio observed in NB with IUGR (Table 5). As a consequence, a secondary elevation of the parathyroid hormone (PTH), with repercussions on these concentrations could occur. In addition to these factors, the smaller renal mass in NB with IUGR is associated to a lower production of 1.25-dihydroxyvitamin D (1.25-(OH)₂D and the “resistance” to PTH, with an even greater increase in the serum concentrations of this hormone, which could worsen the bone demineralization and lead to an elevation in the plasmatic concentration of Mg [24,27].

CONCLUSION

This study has demonstrated that in term NB there were no changes in iMg concentrations during the first week of life, in spite of the significant increase in the concentrations of TMg. The presence of IUGR lead to higher serum levels of iMg, in relation to NB without IUGR, thus demonstrating the influence of intrauterine nutrition on the homeostasis and on the serum levels of this ion.

The determination of values of TMg and iMg in the neonatal period, in the presence and absence of IUGR, can be used as a reference for further studies that investigate the behavior of this ion in other situations involving deviation from the normal levels.

REFERENCES

1. Marcus JC, Valencia GB, Altura BT, Cracco RQ, Jean-Baptiste D, Sinha K, Altura B: Serum ionized magnesium in premature and term infants. *Ped Neurol* 18:311–14, 1997.
2. Altura BM: 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, 1994.
3. Fiser RT, Torres A, Butch AW, Valentine J: Ionized magnesium concentrations in critically ill children. *Crit Care Med* 26:2048–2052, 1998.
4. Munoz R, Laussen P, Palacio G, Zienko L, Piercey G, Wessel DL: Whole blood ionized magnesium: age-related differences in normal values and clinical implications of ionized hypomagnesemia in patients undergoing surgery for congenital cardiac disease. *J Thorac Cardiovasc Surg* 119:891–898, 2000.
5. Sasaki S, Oshima T, Matsuura H, Ozono R, Higashi Y, Sasaki N, Matsumoto T, Nakano Y, Ueda A, Yoshimizu A, Kurisu S, Kambe M, Kajiyama G: Abnormal magnesium status in patients with cardiovascular diseases. *Clin Sci* 98:175–181, 2000.
6. Capurro H. A simplified method for diagnosis of gestational age in the newborn infant. *J Pediatr* 93:120–122, 1978.
7. Kramer MS, Mclean FH, Olivier M, Willis D, Usher R. Body proportionality and head and length “sparing” in growth retarded neonates: a critical reappraisal. *Pediatrics* 84:717–23, 1989.
8. Alexander GR, Himes JH, Kaufman RB, Mor J, Kogan M: A United States national reference for fetal growth. *Obstet Gynecol* 87:163–8, 1996.
9. Nova Biomedical: “Stat Profile M Reference Manual.” Waltham, MA: Nova Biomedicals, 1998.
10. Wills MR, Sunderman FW, Savory J: Methods for estimation of serum magnesium in clinical laboratories. *Magnesium* 5:317–327, 1986.
11. Cook LA, Mimouni FB: Whole blood ionized magnesium in the healthy neonate. *J Am Coll Nutr* 16:181–183, 1997.
12. Hillman LS, Rojanasathit S, Slatopolsky E, Haddad JG: Serial measurements of serum calcium, magnesium, parathyroid hormone, calcitonin, and 25-hydroxy-vitamin D in premature and term infants during the first week of life. *Pediatr Res* 11:739–744, 1977.
13. Geven WB, Monnens LAH, Willems JM: Magnesium metabolism in childhood. *Miner Electrolyte Metab* 19:308–313, 1993.
14. David L, Salle BL, Putet G, Grafmeyer DC: Serum immunoreactive calcitonin in low birth weight infants. Description of early changes; effect of intravenous calcium infusion; relationships with early changes in serum calcium, phosphorus, magnesium, parathyroid hormone, and gastrin levels. *Pediatr Res* 15:803–808, 1981.
15. Bajpai CP, Sugden D, Ramos A, Stern L: Serum magnesium levels in the newborn and older child. *Arch Dis Child* 41:424–427, 1966.
16. Dollberg S, Bauer R, Lubetzky R, Mimouni FB: A reappraisal of neonatal blood chemistry reference ranges using the Nova M electrodes. *Am J Perinatol* 18:433–40, 2001.
17. Pollack RN, Divon MY: Intrauterine growth retardation: definition, classification, and etiology. *Clin Obstet Gynecol* 35:99–107, 1992.
18. Larsen T: Intrauterine growth restriction. *Danish Med Bull* 4:256–274, 2001.
19. Handwerker SM, Altura BT, Jones KY, Altura BM: Ionized serum magnesium and potassium levels in pregnant women with pre-eclampsia and eclampsia. *J Reprod Med* 40:201–208, 1995.

20. Nandakumaran N, Dashti HM, Al-Zaid NS: Maternal-fetal transport kinetics of copper, selenium, magnesium and iron in perfused human placental lobule: in vitro study. *Mol Cell Biochem* 231:9–14, 2002.
21. Shaw AJ, Mughal MZ, Mohammed T, Maresh MJA, Sibley CP: Evidence for active maternofetal transfer of magnesium across the *in situ* perfused rat placenta. *Pediatr Res* 27:622–625, 1990.
22. Henriksen T, Clausen T: The fetal origin hypothesis: placental insufficiency and inheritance versus maternal malnutrition in well-nourished populations. *Acta Obstet Gynecol Scand* 81:112–114, 2002.
23. Durlach J, Pagès N, Bac P, Bara M, Guiet-bara A: Importance of the ratio between ionized and total Mg in serum or plasma: new data on the regulation of Mg status and practical importance of total Mg concentration in the investigation of Mg imbalance. *Magnes Res* 15:203–205, 2002.
24. Tsang RC. Neonatal magnesium disturbances. *Amer J Dis Child* 124:282–293, 1972.
25. Soothill PW, Nicolaidis KH, Campbell S: Prenatal asphyxia, hyperlacticaemia, hypoglycaemia, and erythroblastosis in growth retarded fetuses. *Brit Med J* 294:1051–1053, 1987.
26. Wicks TC: AANA Journal Course: Update for nurse anesthetists—Magnesium homeostasis and deficiency. *AANA J* 67:171–179, 1999.
27. Namgung R, Tsang RC, Specker BL, Sierra RI, Ho ML: Reduced serum osteocalcin and 1,25-dihydroxyvitamin D concentrations and low bone mineral content in small for gestational age infants: Evidence of decreased bone formation rates. *J Pediatr* 122:269–275, 1993.

Received August 25, 2003; revision accepted March 18, 2004.