The Turkish Journal of Pediatrics
Volume 19 / Nos. 3-4 / July-October 1977 / pp. 89 - 96

Serum Magnesium Levels in Children with Vitamin D Deficiency Rickets

Şinasi Özsoylu, M.D. / Necla Hanioğlu, M.D.*****

Magnesium is second only to potassium in abundance as an intracellular cation.[1] Like calcium, it is absorbed from the small intestine, which is under the influence of vitamin D and parathormone.

In vitamin-D-deficiency rickets, calcium absorption from the proximal part of the intestine is decreased, and as a result the serum calcium level tends to decrease, but with stimulation of the parathyroid glands its level is in general normal or low normal. At the same time, the stimulation of osteoblasts causes serum alkaline phosphatase activity to rise, but tissue alkaline phosphatase stays normal, or decreases, with exception of bone activity.[2-4] A decrease in the serum phosphorus level has also been known as a characteristic findings of vitamin-D-deficiency rickets, but changes in serum magnesium level has only been studied in a few patients with this condition.[5]

In this study the serum magnesium level was determined in patients with rickets due to vitamin D deficiency, and compared with that of normal, age-matched controls.

Materials and Methods

Serum calcium (Ca++), phosphorus (P), alkaline phosphatase (AP), total protein and magnesium (Mg++) levels were determined from 15 children, two and a half to 24 months of age, who had no evidence of rickets on clinical or radiological examination, and who were free of

* From Hacettepe University, Faculty of Medicine, Department of Pediatrics and Hacettepe Children's Medical Center Ankara, Turkey, (This study was partly presented in the 1st International Symposium on magnesium deficit in human pathology 1971 Vittel).
** Prof. of Pediatrics and Head of the Hematology and Hepatology Sections.
*** Pediatrician.

apparent infections. The same determinations were made on 60 patients who showed clinical evidence of rickets, and whose diagnoses were confirmed by X-ray examination of the wrists (58 patients) and costochondral junctions (two patients). The ages of these patients ranged from four to 24 months.

Serum Mg++, Ca++, protein, P, and AP levels were determined using the titan yellow,[6] Ferro-Ham,[7] and Bodansky[9] methods respectively.

Results

Although the serum magnesium and total protein values of rachitic and control children did not differ statistically ($P < 0.05$, for both determinations), the lowest magnesium values were observed in the rachitic children. Calcium and phosphorus values were significantly decreased in the rachitic group compared to the controls ($P < 0.001$ and $P. < 0.01$ respectively), and alkaline phosphatase was found to be significantly increased in the former, as expected ($P < 0.001$) (Table I).

When the rachitic group was separated into two sub-groups according to their calcium values, 20 hypocalcemic patients (below 8 mg per cent) and non-hypocalcemic patients, a marked difference between their respective Mg++ values was found (Table II) Figure 1. The ranges and statistical evaluation of the determinations are shown in the Tables.

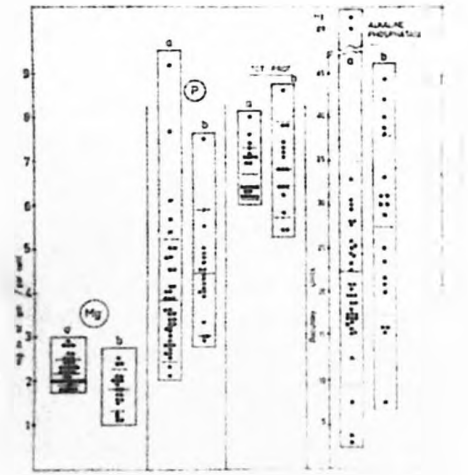

Figure 1

Magnesium (Mg), phosphorus (P), total protein (TOT.PROT) and alkaline phosphatase values of rachitic children without (a) and with hypocalcemia (b) are shown.

TABLE I

THE COMPARISON: OF THE SERUM MAGNESIUM (Mg++), CALCIUM (Ca++), PHOSPHORUS (P), ALKALINE PHOSPHATASE (AP) AND PROTEIN VALUES OF PATIENTS WITH VITAMIN-D-DEFICIENCY RICKETS AND THOSE OF CONTROL CASES (UNDERLINED NUMBERS INDICATE THE RANGE)

		Rickets (60 Cases)	Controls (15 Cases)	P (Values
Mg++	(mg %)	2.095 ± 0.050 (S.D.: 0.388) 1.1–2.92	2.153 ± 0.082 (S.D.: 0.317) 1.8–2.7	> 0.05
Ca++	(mg %)	8.443 ± 0.224 (S.D.: 1.741) 4.2–11.2	10.232 ± 0.257 (S.D.: 1) 8.9–11.4	< 0.001
P	(mg %)	4.055 ± 0.176 (S.D.: 1.364) 2.1–9.2	5.1 ± 0.217 (S.D.: 0.843) 4.1–7	< 0. 01
AP	(U)	25.288 ± 2.163 (S.D.: 16.77) 4.1–113	9.353 ± 0.482 (S.D.: 1.871) 6.8–13.9	< 0.001
Protein	(gm %)	(41 cases only) 6.753 ± 0.104 (S.D.: 0.671) 5.4–8.6	6.873 ± 0.169 (S.D.: 0.656) 5.8–8	> 0. 05

TABLE II

THE COMPARISON OF THE SERUM Mg++, P, AP, AND PROTEIN VALUES OF NON-HYPOCALCEMIC (40 PATIENTS) AND HYPOCALCEMIC (20 PATIENTS) SUB-GROUPS OF RACHITIC CHILDREN (UNDERLINED NUMBERS INDICATE THE RANGE.)

	Non-Hypocalcemic	Hypocalcemic	P (Values)
Mg++ (mg %)	2.235 ± 0.057 (S.D.: 0.361) 1.8–2.92	1.815 ± 0.113 (S.D.: 0.510) 1.1–2.72	< 0.001
P (mg %)	3.89 ± 0.234 (S.D.: 1.485) 2.1–9.2	4.42 ± 0.323 (S.D.: 1.45) 2.9–7.5	> 0. 05
AP (U)	22.3 ± 2. 0 (S.D.: 12.7) 4.1–113	27.63 ± 2.255 (S.D.: 10.1) 4.7–44.1	> 0. 05
Protein (mg %)	(in 24 cases 6.721 ± 0.133 (S.D.: 0.6) 6.2–8	(in 17 cases) 6.8 ± 0.271 (S.D.: 1.12) 5.4–8.6	> 0. 05

Discussion

Vitamin-D-deficiency rickets is still seen in some developed countries,[10] but is more prevalent in this part of the world.[5, 11, 12] The rise of serum alkaline phosphatase, accompanied by a decrease in serum phosphorus with low or normal calcium levels, are the characteristic biochemical findings of this disease. Secondary hyperparathyroidism[10] is the factor which usually keeps the calcium level within low normal limits. Since the biochemical changes are not pronounced in malnourished children,[13] diagnosis of the study group was verified by x-ray examinations.

In general our chemical findings are compatible with the diagnoses. The magnesium level is not found to be changed in patients with rickets. However, when the hypocalcemic rachitic patients' Mg++ was compared with that of the non-hypocalcemic rachitic patients, the Mg++ level of the former group was found to be significantly decreased ($P < 0.001$).

Mg++ metabolism closely resembles that of calcium, but in contrast to calcium the highest concentration is found within the cells. Although our knowledge of the interrelationship between magnesium and vitamin D is far from complete, vitamin D appears to enhance gastrointestinal absorption in experimental studies.[14–16] In human studies performed on patients with vitamin D resistant rickets, the effect of vitamin D on magnesium metabolism produces conflicting results.[17, 18] In a pseudo-vidamin D resistant rickets case, Mg absorption was not altered, inspite of decreased calcium absorpiton.[19]

There are several reports which indicate the parathormone effects serum magnesium levels, although they too, are conflicting.[20–23] It should be stressed tha being intracellular cation serum magnesium level does not necessarily reflect total body magnesium, but it alters the production of 1.25 dihydroxycholecalciferol in the kidney.[24]

Since the protein level did not differ between the hypocalcemic and non-hypocalcemic groups of rachitic children, the difference between the magnesium levels could not be explained by the protein levels, which bind one-third to one-fourth of serum magnesium. Although the phosphorus level did not show significant changes, we choose to explain the low magnesium level of the hypocalcemic group by the relative failure parathyroid response to hypocalcemia, which is to be expected as a result of decreased absorption of calcium due to vitamin D deficiency. Of course this unresponsiveness could also beexplained by low serum Mg++ level.[24]

There have been numerous studies of magnesium deficiency in malnutrition,[25, 26] diarrhea,[25, 27] and malabsorption.[22, 28-30] In our study, only 25 per cent of the children with hypocalcemic rickets, and 22 per cent of the non-hypocalcemic group were mildly malnourished. Diarrhea was observed only in one of the former group. Malabsorption syndrome was not diagnosed in any of the patients. Thus these three conditions are improbable explanations for hypomagnesemia in the children observed.

Convulsions were observed in six of the children in the hypocalcemic and hypomagnesemic group. These were all easily treted with calcium infusions, and thus it is unlikely that primary hypomagnesemia with secondary hypocalcemia syndome was present in these patients.[22, 30, 31]

There appeared to be no difference between the response to vitamin D-treatment of the children with hypocalcemia and the non-hypocalcemic group from the standpoint of biochemical findings. Including serum magnesium levels, in four and six patients respectively on whom these determinations could be repeated within a month.

In conclusion, hypomagnesemia should be considered in rachitic children who have hypocalcemia. We consider it to be due primarily to relative failure of parathyroid response to hypocalcemia due to vitamin D deficiency, although we can not give any supporting evidence.

Summary

Serum magnesium levels of 60 children with vitamin-D-deficiency rickets, confirmed by X-ray examination of the wrists, were compared with those of 15 age-matched control children who had no evidence of rickests on radiologic examination. The mean values were 2.095 $\pm$ 0.05 mg and 2.153 $\pm$ 082 mg/dl in the patients and controls, respectively. The difference between these values was not significant ($P > 0.05$).

However, when the magnesium values of 20 hypocalcemic rachitic children were compared with those of 40 normocalcemic patients, they were found to be significantly decreased in the former group ($P < 0.001$).

REFERENCES

1. Wacker, W. E., and Vallee, B. L.: Magnesium metabolism. New. Eng. J. Med. 259: 431, 475, 1958.
2. Ozsoylu, S.: Leukocyte alkaline phosphatase activity in rickets due to vitamin D deficiency. New Eng. J. Med. 280: 1221, 1969.
3. Ozsoylu, S., and Turhan, O.: Duodenal juice alkaline phosphatase activity in rickets due to vitamin D deficiency. Acta. Paediat. Scand. 60: 338, 1971.

4. Ozsoylu, S., and Kanra, G.: Tissue alkaline phosphatase activity in rickets due to vitamin-D deficiency. Turk. J. Pediatric. 16: 53, 1974.
5. Avcin, M.: The role of magnesium in the pathogenesis of rachitogenic tetany, Helv. Paediatrica Acta, 14: 529, 1959.
6. Henry, R. J.: Inorganic ions, Clinical Chemistry. Principles and technics, Harper and Row, New York, 1964, p. 381.
7. Ferro, P. V., and Ham, A. B.: Calcium. Am. J. Clin Path. 28: 208, 1957.
8. Fister, H. J.: Protein. Total manual of standardized procedures for spectrophotometric chemistry 1950, p. 50, a.
9. Frankel, S., and Reitman, S.: Alkaline, phosphatase-Bodansky modified Gradwohl's Clinical Labor, Methodsand Diagnosis, 1: 121, 1963.
10. Fraser, D., Kooh, S. W., anp Scriver, C. R.: Hyperparathyroidism as the cause of hyperaminoaciduria and phosphaturia in human vitamin D deficiency, Ped. Res. 1: 425, 1967.
11. Doxiadis, S. A., and Lapatsanis, P.: Infantile rickets persists in Greece, Lancet. 1: 1149, 1968.
12. Ozsoylu, S., and Berkel, I.: Study on rickets: Presented at the Nutrition Seminar, Ankara, 1968.
13. Reddy, V., and Strikantia, S. G.: Serum alkaline phosphatase in malonurished children with rickets, J. Pediatrics, 71: 595, 1967.
14. Meintzer, R. B., and Steenbock, H. S.: Vitamin D and magnesium absorption, J. Nutrition, 56: 285, 1955.
15. Hanna, S.: Influence of large doses of vitamin D on magnesium metabolism in rats, Metabolism, 10: 735, 1961.
16. Miller, E. R., Ulrey, D. E., Zutant, C. L., Hoefer, S. A., and Lencke, R. W.: Mineral balance studies with baby pig: Effects of dietary vitamin D2 level upon calcium, phosphorus and magnesium balance, J. Nutrition, 85: 255, 1965.
17. Gunther, L., Cohn, E. T., Chon, W. E., and Greenberg, D. M.: Metabolism of bone salts in resistant rickets, Am. J. Dis. Children. 66: 517, 1943.
18. Anast, C-S.: Magnesium stadies in relation to vitamin-Dresistant rickets, Pediatrics 40: 425, 1967.
19. Hamilton, R., Harrison, J., Fraser, D., Radde, I., Morecki, R., and Puanier, L.: The small intestine in vitamin D dependent rickets. Pediatrics. 45: 364, 1970.
20. Harmon, M.: Parathyroid adenoma in a child, Am. J. Dis. Children. 21: 313, 1956.
21. Jones, K. H., and Fourman, P.: Effects of infusions of magnesium and of calcium in parathyroid insufficiency, Clin. Sci. 30: 139, 1966.
22. Muldowney, F. P., McKenna. T. J., Kyle, L. H., Freaney, R., and Swan, M.: Parathormone-like effect of magnesium replenishment in steathorrhea, New. Eng. J. Med. 281: 61, 1970.
23. Niklasson, E.: Familial early hypoparathyroidism associated with hypomagnesemia, Acta. Paed. Scand. 59: 715, 1970.
24. Ozsoylu, S.,: D vitamin metabolizması. Çocuk Sağ. ve Hast. Derg. 20: 1, 1977.
25. Back, E. H., Montgomery, R. D., and Ward, E. D.: Neurological manifestations of magnesium deficiency in infantile gastroenteritis and malnutrition. Arch. of Dis. Childhood. 37: 106, 1962.

26. Caddell, J. L.: Magnesium in the therapy of protein calorie malnutrition, J. Pediatrics. 66: 392, 1965.
27. Savage, D. C. L., McAdam., W. A. F.: Convulsions due to hypomagnesaemai in an infant recovering from Diarrhea, Lancet, 2: 234, 1967.
28. Booth, C. C., Babouris, N., Hanna, S, and Mac Intyre, I.: The incidence of hypomagnesemia in intestinal malabosrption. Brit. Med. J., 2: 141, 1963.
29. Goldman, A. S., Van Fossan, D. D., and Baird, E. F.: Magnesium deficiency in celiac disease, Pediatrics. 29: 948, 1962.
30. Heaton, F. W., and Fourman, P.: Magnesium deficiency and hypocalcemia in intestinal malabosrpiton, Lancet. 2: 50, 1965.
31. Friedman, M., Hatcher, G., and Watson, L.: Primary hypomagnesemia with secondary hypocalcemia in an infant, Lancet, 1: 703, 1967.