14.* T. Vartio, A. Vaheri, R. Essen, et al., Eur. J. Clin. Invest., 11, 207 (1981).
15. K. M. Yamada, S. S. Yamada, and I. Pastan, Proc. Natl. Acad. Sci. USA, 72, 3158 (1975).

*Reference 13 missing in Russian original – Publisher.

CYCLIC NUCLEOTIDE CONCENTRATION IN THE RENAL CORTEX OF VITAMIN D DEFICIENT RATS

Yu. G. Antipkin, G. V. Valueva, and L. I. Omel'chenko

UDC 616.391:577.161.2-]-008.64-07:616.61-008.93:577.123.3

KEY WORDS: cyclic nucleotides; kidneys; vitamin D; calcium-phosphorus metabolism.

A deficiency of vitamin D, a powerful factor controlling mineral metabolism, leads to considerable changes in biological systems responsible for maintenance of calcium and phosphorus homeostasis in the body [5]. The development of the diverse pathological manifestations of vitamin D deprivation is a problem many aspects of which remain unsolved, and this may to some extent account for the sometimes delayed normalization of biochemical and clinical parameters when the deficient vitamin alone is given therapeutically.

An important role in the regulation of calcium and phosphorus homeostasis in the body is played by the kidneys, which serve as the target for calcium-regulating hormones, synthesize active vitamin D metabolites, and are also the site of intensive formation of cyclic nucleotides, which are directly involved in the mechanism of the biological effect of many hormones and, perhaps, also of active forms of vitamin D [8].

To clarify the causes of disturbances of calcium and phosphorus metabolism in vitamin D deficiency, the concentrations of cyclic nucleotides in the renal cortex were studied and parameters of calcium and phosphorus metabolism in the blood were studied in experiments on rats with vitamin D deficiency.

EXPERIMENTAL METHOD

Experiments were carried out on 35 Wistar albino rats of both sexes, weighing 40-50 g, divided into two groups: control, consisting of 10 animals, and experimental, consisting of 25 rats, in which vitamin D deficiency was created at the level of State Standard 11222-65. Four weeks after the rats had developed signs of rickets, due to vitamin D deficiency, the animals were decapitated and the kidney tissue quickly frozen.

Concentrations of cAMP and cGMP in the renal cortex were studied by radioimmunoassay using standard commercial kits (Amersham International, England). Radioactivity was counted on a Mark III liquid scintillation system (Tracor Europa, USA).

The calcium concentration in the blood serum and erythrocytes was determined by a complexometric method [4]; the phosphorus concentration in the blood serum and erythrocytes and the concentration of 2,3-diphosphoglycerate (2,3-DPG) was determined by the method in [6], and alkaline phosphatase activity as in [7], and expressed in Bodansky units.

EXPERIMENTAL RESULTS

In experimental vitamin D deficiency a marked increase (more than twofold) in the cAMP concentration in the renal cortex of the rats was observed (Fig. 1). This was accompanied by a less marked but significant fall in the cGMP concentration. In animals deficient in vitamin D significant deviations were observed in the parameters of calcium and phosphorus metabolism, as reflected in the data for blood serum and erythrocytes (Table 1). The calcium

Kiev Research Institute of Pediatrics, Obstetrics, and Gynecology, Ministry of Health of the Ukrainian SSR. (Presented by Academician of the Academy of Medical Sciences of the USSR, E. M. Luk'yanova.) Translated from Byulleten' Éksperimental'noi Biologii i Meditsiny, Vol. 105, No. 1, pp. 33-35, January, 1988. Original article submitted June 23, 1986.

 0007-4888/88/0001-0040$12.50

TABLE 1. Calcium and Inorganic Phosphorus (P_i) Concentrations in Serum and Erythrocytes, Alkaline Phosphatase Activity, and 2,3-DPG Level in Erythrocytes in Normal and Vitamin D Deficient Rats (M ± m)

Group of animals	Serum			Erythrocytes		
	Ca, μmoles/ml	P_i, μmoles/ml	alkaline phos., Bodansky units	Ca, μmoles/ml	P_i, μmoles/ml	2,3-DPG, μmoles P_i/ml of eryth. suspension
Control	4,00±0,17	2,32±0,10	11,9±0,8	14,10±0,30	1,91±0,01	16,56±0,19
Experimental	1,85±0,12*	1,64±0,18*	20,0±1,10*	9,10±0,20*	0,55±0,01*	10,49±0,11*

Legend. Asterisks indicate significance of differences compared with control.

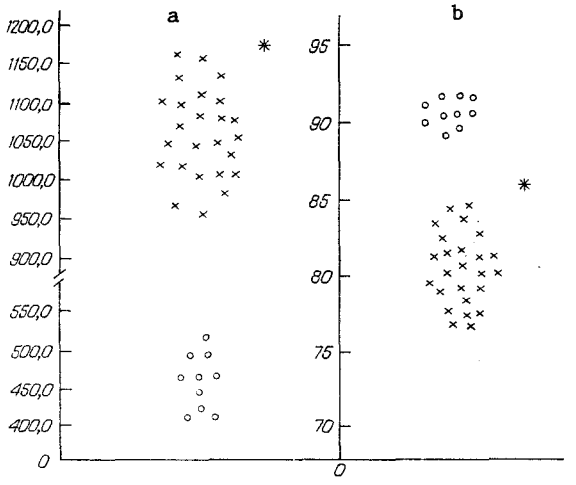

Fig. 1. cAMP (a) and cGMP (b) in renal cortex in nmoles/g tissue in normal rats (circles) and rats with vitamin D deficiency (crosses). Asterisks indicate that changes are significant compared with control.

and phosphorus levels in the serum and erythrocytes and the 2,3-DPG concentration in the erythrocytes were appreciably lower than in the control. The decrease in 2,3-DPG concentration in the erythrocytes we regarded as an indirect indicator of the severity of the vitamin D deficiency of the animal [1]. Increased alkaline phosphatase activity in the blood of rats with vitamin D deficiency confirmed the severity and the diverse character of the pathological process and involvement of the animals' skeletal system in it.

The unequal deviations in the cyclic nucleotide concentrations in the renal cortex in vitamin D deficiency may be one cause of the disturbance of ionic transport of calcium and phosphorus in the renal tubules in this pathology. The increase in the cAMP concentration in kidney tissue may be the result of activation of adenylate cyclase or inhibition of phosphodiesterase, whereas the decrease in the cGMP concentration may be the result of a decrease in guanylate cyclase activity. Disturbances of the lipid composition of the plasma membranes of the renal tubules, discovered by the writers previously in animals with experimental vitamin D deficiency, may point to a possible decrease in the activity of enzyme concerned with cyclic nucleotide formation. In particular, a decrease in the concentration of sterols, mainly cholesterol and its esters, and a twofold increase in the concentrations of phosphatidylethanolamine and phosphatidylcholine was found [2].

The changes discovered may also be the result of the state of functional strain of the endocrine glands producing Ca-regulating hormones, which leads to the development of secondary hyperparathyroidism and to inhibition of function of the thyroid C cells [3].

Vitamin D deficiency in animals was thus accompanied by considerable changes in the cyclic nucleotide concentration in the renal cortex.

LITERATURE CITED

1. L. I. Apukhovskaya, E. M. Luk'yanova, V. P. Vendt, and L. I. Omel'chenko, Abstracts of Proceedings of the Third Ukrainian Biochemical Congress [in Russian], Donetsk (1977), p. 7.
2. L. I. Apukhovskaya, S. P. Ivashkevich, and L. I. Omel'chenko, Vopr. Med. Khim., No. 3, 105 (1982).
3. L. S. Myakisheva and T. V. Kovalenko, Vopr. Okhr. Mat., No. 6, 40 (1985).
4. D. W. Barron and J. K. Bell, Clin. Chim. Acta, 2, 326 (1957).
5. H. F. De Luca, Fed. Proc., 33, 2211 (1974).
6. B. S. Dyce and S. P. Bessman, Environ. Health, 27, 205 (1973).
7. J. Motzok and A. M. Whyne, Biochem. J., 47, 187 (1950).
8. R. A. Nissenson, Mineral Electrol. Metabol., 8, 151 (1982).