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Low-Calcium Water Diet and Hypertensive Plasma Activity of WKY Rats

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Disturbances in calcium metabolism [4], as well as changes in the transport of Ca^{2+} and other cations across the membranes of a variety of cells, in particular erythrocyte membranes [3], have been found to play an important role in the pathogenesis of essential hypertension. These changes are most expressed under conditions of a Ca^{2+}-deficient diet [1]. An inversely proportional dependence between the Ca^{2+} content in the diet, notably in the drinking water, and both the frequency and degree of arterial pressure (AP) increase has been shown in epidemiological studies [4,5].

A search of the humoral factors responsible for the development of arterial hypertension (AH) under conditions of a Ca^{2+}-deficient diet has resulted in the discovery of a plasmatic factor in spontaneously hypertensive rats [6-8], in addition to the well-known erythrocytic factor [9,10].

The present study is based upon data concerning the broad prevalence of cardiovascular diseases under conditions of a diet deficient in Ca^{2+} and Mg^{2+}, especially in the regions with soft drinking water (Saint-Petersburg, Finland, Sweden, Norway, which rank first in incidence of AH), as well as upon data on the universal role of Ca^{2+} ions in the regulation of all cell functions. Additionally, it should be noted that there is a lack of physiological studies concerning the mechanism of the exogenous influence of Ca^{2+} on the formation of vascular tone as well as cardiac output.

The purpose of the present work was to study the influence of low and normal Ca^{2+} concentrations in drinking water on both the AP level and plasma hypertensive activity in WKY rats.

MATERIALS AND METHODS

Rats of the Wistar-Kyoto line (males) weighting 250-280 g at the age 12-16 weeks were used in the experiments. From the moment of the transition to the definitive nourishment the animals were kept on a standard ration with 0.6% Ca^{2+} content. The rats were given water ad libitum. The first (control) group starting from 4-week age was given drinking water with a

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normal Ca^{2+} and Mg^{2+} content (80.0 and 30.0 mg/liter, respectively) [2]. The second group (calcium-deficient) was given drinking water with a low Ca^{2+} and Mg^{2+}content (8.0 and 3.0 mg/liter, respectively) - the Saint-Petersburg water supply.

During the observation period the systolic arterial pressure (SAP) was measured in the caudal artery using the cuff technique.

Animals narcotized with nembutal (40 mg/kg intraperitoneally) were injected with plasma in the acute experiments, and hypertensive activity was studied. Heparinized plasma (500 IU/ml) was injected intraperitoneally at a dose of 5 ml/kg. The mean AP was monitored continuously through the catheter in the carotid artery for 60 min after plasma injection.

Five runs of experiments were carried out (n=7 in each run). In the 1st run control animals were injected with plasma from animals of the Ca^{2+}-deficient group. In the 2nd run control animals were injected with the plasma from animals of the same group. In the 3rd run rats having received Ca^{2+} -poor water were injected with plasma from the same group. In the 4th run, in order to rule out possible reflex as well as hemodynamic effects due to the intraperitoneal liquid injection, the animals were injected with the same volume of polyglucin instead of plasma (5 ml/kg). In the 5th run control animals were injected with plasma from animals of the Ca^{2+}-deficient group after its dialysis across the membrane with the cut-off point 1 kD in order to separate catecholamines, vasopressin, as well as angiotensin.

The results were processed statistically using the Students *t*-test and nonparametric Mann-Whitney test.

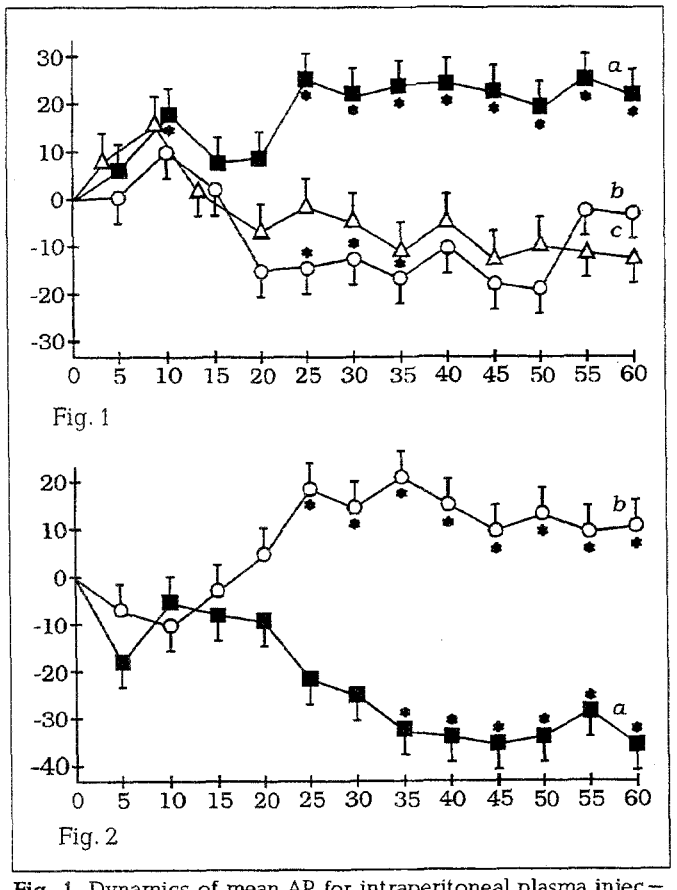

Fig. 1

Fig. 2

Fig. 1. Dynamics of mean AP for intraperitoneal plasma injection: *a*) from Ca^{2+} – deficient group to normal group; *b*) from normal group to the same group; *c*) from Ca^{2+} – deficient group to the same group. Abscissa: time after plasma injection (min); ordinate: mean AP decline value (mm Hg); asterisk: differences are reliable ($p<0.001$) between present and initial AP values.

Fig. 2. Dynamics of mean AP for intraperitoneal plasma injection: *a*) dialyzed plasma from Ca^{2+} – deficient group to control group; *b*) polyglucin to control group. Notation as for Fig. 1.

RESULTS

At the end of the chronic experiment the systolic blood pressure (SBP) in animals of the normal group (n=30) was estimated to be 116±2 mm Hg; in animals of the Ca^{2+}-deficient group (n=30) it was 150±7 mm Hg; and in 11 animals of this group SBP was found to exceed 160 mm Hg and to be 187±10 mm Hg on average.

The results of the first three runs of experiments are presented in Fig. 1. As shown in Fig. 1, *a*, the injection of plasma from the Ca^{2+}-deficient group to the control animals resulted in a 2-stage pressure response. The first AP rise was observed between the 5th and 15th min after plasma injection and the second, more vigorous, rise by 40% of the initial level on average) started at the 25th min and lasted to the 60th min.

The curves of the AP increment due to the intraperitoneal plasma injection in the 2nd and 3rd runs were shown to differ from the one obtained in the 1st run (Fig. 1, *b, c*). Additionally, the injection of plasma from the same group resulted in a significant AP increase only during the first 5-15 min (the initial peak) followed by its normalization and then a drop to a level lower than the initial one. No second peak of the pressure response was observed in these runs in contrast to the first one.

Intraperitoneal polyglucin injection (Fig. 2, *a*) caused an AP decrease (15% on an average) at the 5th min, followed by a return to the initial level at the 10th min. The AP then fell slowly, reaching 50% of the initial level at the 45th min and remained on this level to the end of the experiment. Thus, the pressure response to plasma injection cannot be associated with the effect of intraperitoneal injection of appropriate volumes of osmotically active liquid.

No initial AP rise induced by the injection of dialyzed plasma from Ca^{2+}-deficient animals to the control animals was observed in any cases (Fig. 2, *b*). The initial AP rise in the first three runs of ex-

periments is assumed to be due to the effect of such vasopressors as catecholamines, angiotensin, and vasopressin. This is confirmed by the short latent period of the reaction, as well as the disappearance of the initial peak of the pressor response after plasma dialysis. Apparently, the second AP peak cannot be explained by the effect of known vasopressors.

Thus, the results obtained attest to plasma hypertensive activity in WKY rats under conditions of $Ca^{2+}$and Mg^{2+} deficiency in drinking water. The correction of the Ca^{2+} and Mg^{2+} content in the water may prevent AH development, as well as the appearance of plasma hypertensive activity. A pressure response to plasma injection from the Ca^{2+}-deficient group resembles in its development the effect of the parathyroid hypertensive factor (PHF), which was found by Pang [7,8] in plasma of spontaneously hypertensive rats. This study provided evidence that the exogenous Ca^{2+} effect may be realized through the changes in the state of the ion-transport system playing an important role in AH pathogenesis [1]. This effect is probably mediated by the expression of a Ca^{2+}-dependent hypertensive factor similar to PHF.

The findings clarify some aspects of the pathogenesis of essential hypertension and open up new prospects for its nondrug initial prevention in regions with a low Ca^{2+} and Mg^{2+} content in drinking water.

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The Trophic Influence of the Salivary Glands on the Oral Mucosa

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The neurotrophic maintenance of the oral mucosa (OM) can be provided by neurotransmitters either of the blood or of the saliva, because the mucous membrane has no efferent but only afferent innervation [5]. Catecholamine (CA) content in the saliva depends upon the state of the sympathetic innervation in the salivary glands [1]. Since the participation of specific receptors is necessary for the utilization of the transmitters in tissue, we aimed to elucidate whether there is a correlation between the CA

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