Potassium and Magnesium Content in the Peripheral Blood Lymphocytes in Patients with Essential Hypertension

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Zusammenfassung

Bei 48 Kranken mit essentieller Hypertonie EH und bei 64 Gesunden wurde der Kalium (K)- und Magnesium (Mg)-Gehalt in Lymphozyten (L) des Blutes mit Hilfe der Elektronen-Röntgen-Mikroanalyse untersucht. Der K-Gehalt in L bei EH-Kranken war niedriger ($p < 0.002$). Bei Kranken in der 1. Phase der Hypertonie (nach WHO) war er vermindert ($p < 0.05$) und in der 2. Phase wurde er weiter herabgesetzt ($p < 0.005$). Die Mg-Gehalte in L der Kranken und der Gesunden zeigten statistisch keinen Unterschied. Bei Kranken wurde signifikante Korrelation zwischen Lymphozyten-K und -Mg und dem arteriellen Druck festgestellt. Die Korrelation zwischen Mg- und K-Gehalt in L war auch signifikant.

Summary

In 48 patients with essential hypertension and in 64 healthy subjects potassium (K) and magnesium (Mg) content was measured in blood lymphocytes by electron probe X-ray microanalysis. K content was lower in the hypertensives ($p < 0.002$). In class I hypertensives (WHO) K content was lowered ($p < 0.05$), decreasing further in class II ($p < 0.005$). Mg did not differ between both groups. The hypertensives showed a significant correlation between lymphocyte K and Mg and blood pressure values. There was also a significant correlation between Mg and K content.

Résumé

Chez 48 malades avec l'hypertension artérielle primaire et chez 64 personnes de référence les concentrations lymphocytaires du potassium (K-L) et du magnesium (Mg-L) dans sang ont été analysées par une microsonde électronique à rayons X. K-L chez les malades a diminuée ($p < 0.002$). Chez les malades hypertendue du grade I (d'après l'OMS) K-L a diminuée ($p < 0.05$) et diminuait progressivement chez ceux-ci du grade II ($p < 0.005$). Mg-L entre les malades et les personnes de référence ne differaient pas. Chez les malades il y a été une correlation signicative entre K et Mg et la pression artérielle. La correlation entre les concentrations du Mg et K a été aussi significative.

Introduction

Changes in electrolyte homeostasis of the body are one of the factors contributing to the development of essential hypertension (EH). The role of elevated intracellular sodium and calcium levels in the pathogenesis of EH has been well documented [3, 15] whereas the role of potassium (K) and magnesium (Mg) in the course of the disease is still controversial. The fact that defects in the cellular membrane permeability are present concomitantly in the vascular smooth muscle cells and other cells permits us to study much easier available biological material i.e. erythrocytes, leukocytes, platelets [8, 15]. It has been emphasized that leukocytes and particularly lymphocytes (L) are more useful in this type of studies [4, 17].

The purpose of the present study was to measure K and Mg content in the peripheral blood L in patients with EH and in healthy controls.

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Materials and Methods

The studies included 48 patients with EH admitted to the Outpatient Hypertensive Department. The patients selected for entry had not been treated with hypotensive drugs before. The studied group of patients consisted of 16 women and 32 men ranging in age from 16 to 55 years ($\bar{x} = 33,0$). The patients were classified by severity according to the WHO criteria as class I-28 patients and class II-20 patients. Of the whole group 32 patients gave a positive family history of essential hypertension.

The control group consisted of 64 healthy subjects i.e. 36 men and 28 women aged from 16 to 45 years ($\bar{x} = 28,5$). They were blood donors or patients referred to our Division with a suspicion of cardiovascular disease excluded in the course of hospitalization. Both the patients and normal subjects were the inhabitants of Kraków. Their diets were not restricted with respect to sodium, potassium, calcium and magnesium. In both groups ion concentrations of these elements in serum, glucose and cholesterol levels as well as renal indices were normal.

K and Mg content was determined in blood L isolated by a modified *Boyum's* method [5]. Blood samples were drawn at 8.00 a.m. after 20–30 min rest. Stable conditions of sample preparation, time to analysis and instrument parameters were maintained throughout the studies. Lymphocyte K and Mg content was determined by an Electron Probe X-ray Microanalyser ARL combined with a scanning microscope. An electron beam accelerated to 20 keV was

bombarding the sample producing emission of X-rays characteristic for a given element. Quantitative analysis was based on the intensity of X-ray radiation (a number of photons per time unit). By comparing the intensity of X-ray radiation from a sample of unknown content of the element with the intensity of radiation emitted from a model of known content of this element, K and Mg concentrations were determined and the results expressed as weight per cent. In all patients 30 single lymphocytes of the same size were selected by scanning microscopy to measure K and Mg in each. Concentrations of a given element in each L were calculated from a modified *Castaing*'s formula [14]. From these results mean K and Mg content in L was calculated in each patient. The results were exact to 0.001 % due to a low content of these elements. Statistical differences between mean K and Mg content in L were determined by using Student's t-test taking into consideration sex, severity of the disease and family history of essential hypertension. A linear correlation coefficient between lymphocyte K and Mg and arterial blood pressure values was determined. A correlation coefficient between the patients' age and lymphocyte K and Mg content as well as between K and Mg content was also found. Statistical significance was taken as $p < 0.05$.

Results

In the 48 hypertensives total K content in the peripheral blood L was $\bar{x} = 0.1129 \pm 0.041$ % and was significantly lower than in the 64 healthy subjects: $\bar{x} = 0.156 \pm 0.042$ % ($p < 0.002$ (Tab. 1). A decreased K content at $p < 0.05$ was found irrespective of patients' sex. A difference in mean K content between women and men of both groups was not significant. K content in class I hypertensives ($n = 28$) was lowered at $p < 0.05$ and in class II hypertensives ($n = 20$) at $p < 0.005$ as compared with normal subjects (Tab. 2). A difference in mean K content between class I and class II hypertensives was not significant. A difference in mean K content between patients with a positive and negative family history of essential hypertension ($\bar{x} = 0.131 \pm 0.044$ % vs. $\bar{x} = 0.126 \pm 0.038$ %) was not significant, either. A significant low negative correlation between K content and systolic blood pressure was found in the hypertensives ($r = -0.321$, $p < 0.05$). No correlation between K content and diastolic blood pressure ($r = -0.178$) and between the patients' age and K content ($r = -0.219$) was detected. Total magnesium content did not differ statistically between the hypertensives and normal subjects (Tab. 3). These differences were not significant, either while taking into account the patients' sex and severity of the disease. A significant low negative correlation ($r = -0.298$, $p < 0.05$) was found between Mg content and diastolic blood pressure, whereas Mg content did not correlate with systolic blood pressure ($r = -0.071$) and the patients' age ($r = -0.175$). A significant low positive correlation between Mg and K contents was found in the hypertensives ($r = 0.337$, $p < 0.05$) and in normal subjects ($r = 0.292$, $p < 0.05$).

Tab. 1.: Potassium content in blood lymphocytes in patients with essential hypertension as compared to controls.

Sex	Hypertensives		Controls		p
	n	K [%]	n	K [%]	
Men	32	0.129 ± 0.040*	36	0.151 ± 0.038	$p < 0.050$
Women	16	0.130 ± 0.046	28	0.162 ± 0.048	$p < 0.050$
Total	48	0.129 ± 0.041	64	0.156 ± 0.042	$p < 0.002$

* – mean value and standard deviation

Tab. 2.: Potassium content in blood lymphocytes in patients with essential hypertension in reference to severity as compared to controls.

Hypertensives		Controls		p
n	K [%]	n	K [%]	
28	I class (WHO) 0.133 ± 0.049*	64	0.156 ± 0.042	$p < 0.05$
20	II class (WHO) 0.123 ± 0.029	64	0.156 ± 0.042	$p < 0.005$

* – mean value and standard deviation

Tab. 3.: Magnesium content in blood lymphocytes in patients with essential hypertension as compared to controls.

Sex	Hypertensives		Controls		p
	n	Mg [%]	n	Mg [%]	
Men	32	0.053 ± 0.009*	36	0.049 ± 0.024	NS
Women	16	0.053 ± 0.014	28	0.056 ± 0.012	NS
Total	48	0.053 ± 0.011	64	0.052 ± 0.020	NS

* – mean value and standard deviation

Discussion

A relation between changes in intracellular electrolyte content and disturbances of membrane transport in EH is still controversial. The following factors may be contributory: age, race, genetic predisposition, drugs, concomitant diseases such as hyperlipoproteinemia, hyperthyroidism, obesity as well as dietary habits, especially with respect to high salt content in food. Various laboratory techniques of sample preparation also bias the measurements of electrolyte content in the intracellular space. In the present study the choice of electron probe X-ray microanalysis as a unique method permitted a quantitative analysis of the element content in a single cell. This technique was applied for instance by *Hook* et al. (9) and *Aleksandrowicz* et al. [1]. They used different mathematical calculations, therefore their results could not be compared with the results of the present study. Total K and Mg content in the peripheral blood L is not given in absolute values due to the limitations of L preparation technique.The present results therefore reflect changes in K and Mg content in L in the hypertensives versus normal subjects.

This study showed a lowered total K content in blood L in patients with EH in comparison with healthy subjects. *Iwaoka* et al. [10] obtained similar results in leukocytes, *Skrabal* et al. [18] in erythrocytes and *Ambrossioni* et al.. [2] in lymphocytes. K content in the hypertensives was decreased irrespective of the patients' sex. It is probably due to the fact that the patients belonged to an age group of a limited range. Therefore a decrease in intracellular K content with age, especially in women reported in the literature was not found in the present study [7]. While taking into account severity of hypertension classified according to the WHO criteria a decreased total K content was found in class I patients with a further decrease in class II patients, as compared with healthy subjects. According to the literature data a decreased K level in blood L in the hypertensives may suggest an abnormal transmembrane transport of K. An excessive secretion of hypothalamic natriuretic factor leads to an inhibition of active K transport dependent on sodium-potassium pump in the cellular membrane [12, 23]. Dysfunction of this pump increases passive efflux of K from the cell, accompanied by an increase in intracellular sodium and calcium levels resulting in an increased tone of the vascular smooth muscle cells which means an increase in the peripheral vascular resistance [3]. The hypertensives showed a significant negative correlation between K content and systolic blood pressure. *Ambrossioni* et al. [2] obtained similar results in correlation of K content with diastolic blood pressure, and *Iwaoka* et al. [10] in correlation with mean arterial blood pressure . While taking into account the family occurrence of arterial hypertension a difference between mean K concentrations in these patients was not significant. This is in accordance with other reports pointing to a lack of genetic determination of active K transport defect dependent on sodium-potassium pump in the course of EH [2, 18].

Total Mg content in L in the hypertensives did not differ from that in normal subjects. There were no differences with respect to severity of the disease, sex and age of the patients, either. Lack of differences between both groups may be accounted for by the fact that mainly free Mg ions are considered important in biochemical processes. This is supported by the results of *Resnick* et al. [16] who showed that free Mg ion content in blood erythrocytes was lowered in patients with EH. It correlated negatively with systolic and diastolic blood pressure values. In the present study the hypertensives exhibited a significant negative correlation between total Mg content in L and diastolic blood pressure. *Motoyama* et al. [13] and *Dyckner* and *Wester* [6] in their clinical studies also showed a relation between intracellular Mg content and arterial blood pressure values.

In both groups a positive correlation coefficient between total Mg and K content was significant. It has been confirmed in many reports dealing with associations between Mg and K balance [22]. Intracellular Mg deficiency affects intracellular K content activating membrane Na-K ATP-ase. Therefore according to *Motoyama* et al. [13] treatment with Mg preparations increased membrane activity of Na-K ATP-ase decreasing intracellular sodium content.

The present results emphasize the role of K changes in the prevention and management of essential hypertension. Low sodium diet is an accepted mode of treatment [11]. Clinical studies showed that administration of K salts in a dose of 120–175 mmol daily to hypertensives decreased arterial blood pressure by 3–10 % [19]. Mixed diet i.e. with low or high sodium content combined with high K content produced hypotensive effects [21]. The studies on the role of K in the development of EH include clinical trials with K channel activators [20]. The above-mentioned reports point to hypotensive effect caused by an increased Mg supply [6, 13].

In the light of today's knowledge on electrolyte changes in patients with EH it seems important to recommend food containing larger amounts of K and Mg apart from low salt diet. This may permit us to use lower doses of hypotensive drugs and in certain cases of mild arterial hypertension to modify diets without pharmacotherapy.

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