Effects of Magnesium on Myocardial Energy Metabolism: Assessment in Dahl Salt- Sensitive Rats by 31P NMR

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Introduction

Magnesium (Mg) is an essential cofactor in producing ATP and utilizing enzymatic processes. Furthermore, Mg closely relates to pathogenesis of ischemic heart disease, hypertension and cardiac and vascular hypertrophy.

In this study, the effects of Mg on myocardial energy metabolism during myocardial ischemia and during the cardiac cycle were studied in Dahl salt-sensitive rats using 31P NMR.

Methods

The rats (male Dahl/Iwai) were fed a low-salt (0.3% NaCl) diet or a high-salt (8% NaCl) diet with or without Mg in the drinking water (aspartic acid Mg, 15.4 g/L) for 4 weeks. Systolic blood pressure, heart weight and the level of blood ionized Mg (Mg2+) were measured. The isolated hearts were perfused with Krebs-Henseleit buffer by Langendorff method. The levels of myocardial ATP and phosphocreatine (PCr) were measured by 31P NMR. The concentration of intracellular Mg2+ was also determined by the chemical shift difference between α- and β-ATP (1). 31P NMR spectra were obtained on a GX-270 spectrometer with an 89mm-bore vertical magnet of 6.3T. In the first experiment, ischemia of the heart was induced by stopping the perfusion for 15 min followed by reperfusion for 15 min. The concentrations of phosphate metabolites were measured before, during and after ischemia. RF pulses were used with a repetition time of 0.5 s. Each spectrum was a collection of 600 scans in 5 min. In the next experiment, cyclical changes in the concentration of phosphate metabolites during a cardiac cycle were measured using the pacing-gated 31P NMR technique (2). Each pacing-gated phosphorus spectrum at eight different times in the cycle was acquired with the accumulation of 480 FID signals in 3.4 min.

Results

Significant elevation of systolic blood pressure and the increase in heart weight were observed in the high-salt diet rats. On the other hand, the long-term oral Mg treatment significantly prevented these changes, accompanying with the increase in blood Mg2+ level. In all groups, ATP levels significantly decreased during ischemia and then returned to the initial levels during reperfusion as shown in Fig. 1. Intracellular Mg2+ level also significantly increased during ischemia and then returned to the initial level during reperfusion.

These changes during ischemia were significantly bigger in high-salt diet group than that in low-salt diet group. In high-salt diet group, both long-term Mg treatment and acute Mg treatment with perfusate containing high concentration of Mg improved these changes during ischemia. Fig. 2 shows cyclical changes in the relative concentrations of phosphate metabolites obtained at eight positions during the cardiac cycle. In each group, the levels of ATP and PCr decreased at the peak of systole and then returned to the initial levels at the end of diastole. The magnitude of fluctuation of ATP level during the cardiac cycle significantly increased in the high-salt diet group than that in the low-salt diet group. Both the long-term oral Mg treatment and the acute Mg treatment significantly decreased the magnitude of fluctuation of ATP level in high-salt diet group. In each group, the levels of the intracellular Mg2+ were not changed during the cardiac cycle. The concentration of intracellular Mg2+ showed the highest level by the acute Mg treatment in high-salt diet group.

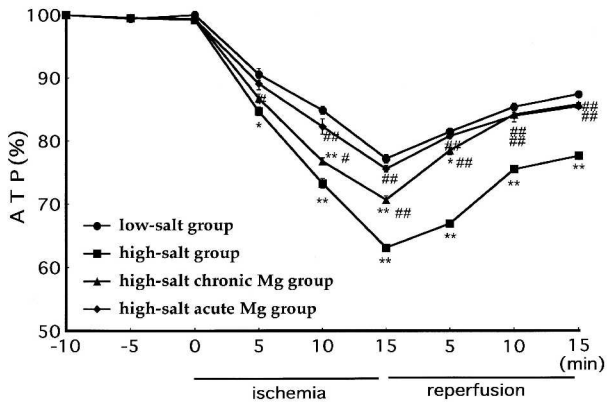

Fig.1 Changes in ATP levels before, during and after ischemia.

Discussion

In the long-term oral Mg treatment group, the decreases in systolic blood pressure and the heart weight, and the improvement of energy phosphate levels during reperfusion and during cardiac cycle were observed accompanying with the increase in blood Mg2+ level. Furthermore, the energy phosphate metabolite levels during reperfusion and during cardiac cycle were improved in the acute Mg treatment group, accompanying with the increase in intracellular Mg2+ level. These results suggest that Mg administration improves the myocardial energy metabolism in Dahl salt-sensitive rats.

References

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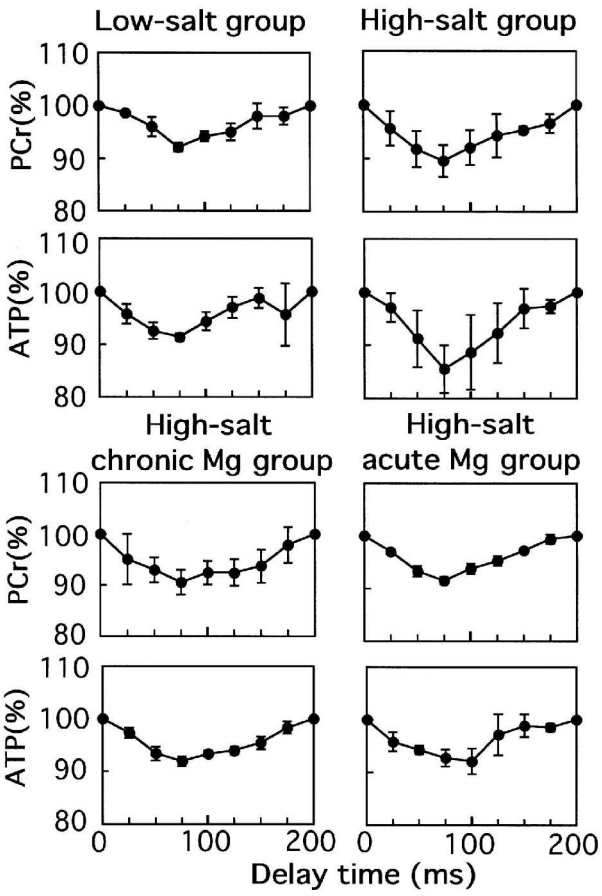

Fig.2 Cyclical changes in the relative concentration of ATP and PCr during a cardiac cycle.