



## Natriuretic Peptides, Hypertension, Heart Insufficiency and Magnesium

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### Commentary

The role of magnesium substitution in heart insufficiency and in hypertension is of special interest. A positive effect on blood pressure lowering and on N-terminal-pro Brain Natriuretic Peptide (nT-proBNP) values has been described in this context. Brain Natriuretic Peptide (BNP) and nTproBNP are of similar quality, but nTproBNP is more stable under clinical conditions. Measurements of BNP has to be done 4 – 8 hours after blood sampling, nT-proBNP determinations can be performed within 2–3 days under room temperature.

BNP is the most important natriuretic peptide of heart ventricles and its overexpression indicates heart insufficiency [1].

In newer investigations the role of ionized magnesium is an advanced technique in biology and medicine. The Ohasa study described the association between N-terminal pro B-type natriuretic peptide and day-to-day blood pressure and heart rate variability in a general population: the results of this study suggest day-to-day variability in Blood Pressure (BP) and Heart Rate (HR) being associated with target-organ damage leading to elevated NT-proBNP levels [2].

An editorial comment by Parati et al. concerns natriuretic peptides and cardiovascular variability [3].

The authors describe that BNP is a hormone secreted by cardiomyocytes under conditions characterized by various types of cardiac overload and its secretion reflects hemodynamic alterations and left ventricular dysfunction [4]. As a hallmark of heart failure, BNP has become an essential element in diagnosis, management and prognostic stratification of heart failure patients.

The BNP level increases in the presence of left ventricular hypertrophy in patients with hypertension and additionally a role of NT-pro BNP as an independent predictor of cardiovascular events was described [5,6].

In newer studies the blood pressure lowering and cardioprotective effect of a magnesium therapy has often been described. This effect is dose dependent and the supplementation time is of importance. Most studies describe a positive effect of about 300 mg magnesium daily, given 2-3 times orally [7]. The MACH study showed a positive effect of magnesium orotate on heart insufficiency concerning life quality and expectancy [8]. In this monocentric, controlled, double-blind study, 79 patients with severe heart failure (NYHA IV, New York Heart Association, classification of heart insufficiency degree I – IV severest) under optimal medical cardiovascular treatment (e.g. diuretics,  $\beta$ -blockers etc.) were randomised to receive either magnesium orotate (6000 mg for 1 month, 3000 mg for about 11 months, n=40) or placebo (n=39).

In the magnesium orotate group the survival rate was 75.7% compared to 51.6% under placebo ( $p < 0.05$ ). Clinical symptoms improved in 38.5% in patients treated with magnesium orotate [8].

In a recent study of our group with similar design we investigated hypertensives with heart insufficiency NYHA III-IV given additional magnesium therapy (magnesium orotate of about 2610 mg daily 3 times).

The results showed in all magnesium treated hypertensive patients a positive effect on blood pressure, heart rhythm disorders and a lowering positive effect on nT-pro-BNP values as a marker for heart insufficiency [9]. Pre-treatment nT-proBNP values decreased significantly in the magnesium orotate group already within 1 week (4761 +/- 2284 versus 3516 +/- 2114 pg/ml;  $p < 0.01$ , Wilcoxon-Test).

In conclusion the data show that magnesium orotate can be effective in hypertensive heart disease lowering nT-pro-BNP values and in hypertension lowering blood pressure significantly. This can be due to the calcium magnesium antagonism, influencing TRMP 6 or 7, Sodium magnesium antiport or by influencing sodium potassium ATPases [7].

Further information is also needed on the possible relevance of elevated levels of natriuretic peptides in hypertension and cardiovascular disorders. In this context supplementation of magnesium can play an important therapeutic role.

Advanced techniques to determine total and ionized magnesium concentrations in biology and medicine are of special importance in several cardiovascular diseases, e.g. heart insufficiency or hypertension [7,10]. To assess total body magnesium stores correctly is still difficult as plasma or serum magnesium stores constitute only 1-5 % of total body magnesium content in humans. To determine ionized magnesium capillary blood can be measure by Phoxplus M, Nova Medical, Rödermark, Germany and USA. There is a significant correlation to serum or plasma magnesium concentrations with this new method [10]. Furthermore ionized magnesium is the active magnesium.

In each hypertensive patient magnesium status has to be determined and a magnesium deficiency has to be corrected immediately to avoid further organ damage.

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