Positive Effect of Magnesium Orotate Therapy in Hypertensive Heart Disease

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Abstract

According to the results of the MACH study additional magnesium orotate therapy has shown a positive effect on life expectancy and quality of life in patients with severe forms of heart insufficiency. Both magnesium and orotate can be cardio protective. In the presented data here additional magnesium orotate therapy was tested in 11 patients with hypertensive heart disease NYHA III-IV as compared to 10 patients with hypertensive heart disease NYHA II-IV as controls. Additional magnesium orotate therapy was 4500 mg magnesium orotate daily for 1 week. NTproBNP levels decreased significantly in the magnesium orotate group versus controls (\(p<0.01\)). Under therapy quality of life improved significantly as well. Kidney function remained stable in the normal range.

In conclusion an additional therapy with magnesium orotate is safe and can be of additional benefit in hypertensive heart disease with insufficiency.

There is an improvement in quality of life and life expectancy in heart insufficiency under an additional magnesium orotate therapy.

Keywords: Magnesium; Orotate; Heart insufficiency

Introduction

It is well known that magnesium deficiency plays an important role in the pathogenesis of essential hypertension [1-25]. Likewise the efficacy of an oral therapy with magnesium is well documented in hypertension and borderline hypertension. Also in lipid disorders and in the development of atherosclerosis or cancer magnesium deficiency is commonly involved [26-31].

The combination of hypertension and diabetes mellitus is more severe with involvement of magnesium deficiency [9,10,27,32-34].

The MACH study showed a positive effect of an oral therapy with magnesium orotate in patients with heart failure NYHA IV. Patients who were treated had an enhanced life expectancy compared to the controls. In the same way the quality of life improved significantly over the course of one year in the majority of patients [35]. Similar results were obtained by Geiss et al. [36], showing the positive effect of magnesium orotate in patients with coronary heart disease.

Because of these pathophysiological interrelationships and the past studies we conducted the following study.

Patients and Methods

We performed an observational study with 11 patients who were suffering from hypertensive heart disease and heart failure NYHA III-IV. Additionally they were treated with magnesium orotate whereas 10 patients with heart failure served as controls. The clinical data can be seen in Table 1.

Statistically the groups were not significantly different concerning age and gender distribution. All patients had healthy kidneys. Severe side effects under the additive magnesium therapy did not occur.

We measured NTproBNP before the beginning and at the end of the therapy of one week duration. The verum group was treated additionally with 3 x 3 tablets Magneron CLASSIC N (300 mg magnesium/d). Furthermore the patients underwent ECG and long-term ECG (holter) analysis. The serum-creatinine was measured before and after the treatment.

| Gender (m/f) | + Mg-orotate | - Mg-orotate |
|-------------|--------------|--------------|
| 6/5         | 5/5          |

| Age (years) | + Mg-orotate | - Mg-orotate |
|-------------|--------------|--------------|
| 67.2 ± 5.6  | 69.7 ± 7.1   |

| Serum creatinine (mg/dl) | + Mg-orotate | - Mg-orotate |
|--------------------------|--------------|--------------|
| 1.0 ± 5.6                | 1.1 ± 0.2    |

| Side effects | + Mg-orotate | - Mg-orotate |
|--------------|--------------|--------------|
| 2 (soft stools) | 4            |

| Life quality | + Mg-orotate | - Mg-orotate |
|--------------|--------------|--------------|
| (improved)    | 7            | 4            |
| (deteriorated)| 1            | 2            |

Table 1: Clinical data study of 11 patients with heart failure with additional magnesium orotate therapy compared with 10 controls with heart failure (mean+/+ standard deviation).

The statistical analysis was performed with Wilcoxon test. The measured values were mean +/- standard deviation, \(p<0.05\) was determined as statistically significant.

All patients gave their written consent for this observational study.

Results

The 11 patients with hypertensive heart disease NYHA III-IV who received magnesium orotate therapy measured a statistically significant reduction of their NTproBNP blood values. This reduction was considerably higher in comparison to the control group without additive magnesium orotate therapy.

NTproBNP blood values of the magnesium treated group were 4761 +/- 2284 pg/ml pre therapy and 3516 +/- 2114 pg/ml post therapy.
The control group pre therapy measured 43311+/-2688 pg/ml. After the therapy the results were 40911+/-2491 pg/ml. There was also a reduction of NTproBNP in the control group. However the results concerning the reduction of NTproBNP in the magnesium orotate treated group were significantly lower (p<0.01).

The serum creatinine levels did not change significantly in the control group as well as in the magnesium treated group to the pretreated values. All results were within normal range. In the magnesium treated group two patients complained about slight side effects concerning smooth stool. The results of the questionnaire of life quality concluded that 7 of 11 patients in the magnesium treated group stated an improvement of their life quality, whereas 1 patient complained of worsening of his life quality.

In the group, that was treated without magnesium 4 patients stated an improvement and 2 patients a worsening of their life quality.

Discussion

As it is known recently, changes in magnesium balance in hypertension have gathered fair amounts of attention.

Many basic studies have shown that magnesium deficiency might be involved in the development of essential hypertension or borderline hypertension [14-25,37-41]. In intensive care medicine you often see magnesium deficiency in patients which is a corresponding risk factor for their prognosis [42]. In the same way magnesium deficiency may be induced or veiled in the treatment of hypertension, e.g. with diuretics. Reasons of magnesium deficiency are manifold. The most important pathophysiological mode of action is its calcium antagonistic effect. Furthermore there is a sodium-magnesium-antiport. In recent years autonomous magnesium channels were found in the gut, then, 2 years ago they were found in the kidney as well. In the development of hypertension first analyses of mutations of these TRPMs and 7 channels in this regard are available [43]. Table 2 shows the reasons of magnesium deficiency.

Drug interaction often may induce magnesium deficiency as well. This Table 3 shows drugs that can trigger QT-elongation and Torsade-de-pointes tachycardia. whereby a magnesium deficiency may worsen it [41]. Table 4 shows contraindications and side effects of magnesium therapy.

| Antiarrhythmic agents | Quinidine, Sotalol, Amiodarone, Flecaïnide |
|-----------------------|------------------------------------------|
| Antibiotics           | Erythromycin, Clarithromycin, Levofloxacin, Moxifloxin, Pentamidine |
| Antihistamines        | Diphenhydramine, Clemastine |
| Antidepressants       | Amitriptyline, Imipramine, Desipramine, Maprotiline, Fluoxetine, Sertraline, Citriprom |
| Neuroleptics          | Haloperidol, Pimozide, Thoridazine |
| Anti-malarial tablets | Quinine, Chloroquine |
| Analgesics            | Leveomethadone |
| Cytostatic drugs      | Arsenic trioxide |
| Antiemetic drugs      | Domperidone |

Table 3: Drugs that trigger QT-elongation and Torsade-de-points tachycardia.

| Contraindications |
|-------------------|
| Oral administration | advanced renal insufficiency (dosage adaptation should be considered in case of impaired kidney function) |
| Parenteral administration | AV block or other cardiac conduction disorders |

Adverse reactions

| Oral administration | even at higher dosages no severe side effects: soft stools (often just temporary) are possible |
| Parenteral administration | cardiac conduction disorders of sinus- and AV nodes |
| Parenteral administration | peripheral vasodilatation (flush) |
| Parenteral administration | sweating |
| Parenteral administration | nausea and vomiting |

Table 4: Contraindications and adverse reactions of magnesium therapy.

In cardiology an intact magnesium balance is of particular interest. The MACH study could show the beneficial use of magnesium orotate as adjuvant therapy in patients on optimal treatment for severe congestive heart failure in a follow-up study of 1 year [35]. It is also well known, that magnesium has a significant value in the treatment of cardiac arrhythmia. Torsade-de-points tachycardia responds especially well to the intravenous administration of magnesium sulfate [26,41,44-50]. There is however scant data for the treatment of heart failure with an additional magnesium therapy. The MACH study, cited above, which showed a positive effect in severe cases of heart failure, served for this study as status [35].

In this already short observation period of 1 week with additional daily treatment with 300 mg magnesium orotate, values of NTproBNP decreased markedly and statistically significant which is known as a marker to assess heart failure (Figure 1). Furthermore most of the treated patients stated a distinct clinical improvement of their complaints.

As magnesium orotate is used in the presented study, we closely monitored kidney function because of the orotate component.

None of the magnesium orotate treated patients showed in the course a change of serum creatinine compared to the pretreated values. Already during the 1990s a positive effect of orotate in heart failure could be shown in investigations with animal model. Here, stabilization of cardiac cell functions was described. It could additionally be demonstrated that orotic acid could distinctly improve the metabolism of myocardial cells. In this way the metabolism of glycogen in the hypertrophic heart could be markedly improved by administration of orotate [35,45].
In summary, here the conducted study shows that a therapy with magnesium orotate can be considered as a safe mode of treatment for patients with hypertensive heart disease and heart failure NYHA III-IV. The patients showed markedly improved NT-proBNP values already after one week of treatment [51]. This was, from a statistical standpoint, significantly better than the group without treatment. Furthermore, a reduction in clinical complaints was seen. The kidney function was stable at all times. Severe cardiac arrhythmia did not occur in the course of this observational study. Table 5 shows the symptoms of magnesium deficiency.

To summarize, the presented study shows that the treatment with magnesium orotate has significant value in the treatment of patients with heart failure regarding life expectancy, life quality as well as incidence of cardiac arrhythmia [52]. In either case magnesium deficiency should be taken into consideration for high-risk patients.

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