Impact of Dietary Intervention in Patients with Cardiac Arrhythmias on HOMA-IR and Echocardiographic Parameters. A Randomized Double Blind, Placebo-Controlled Pilot Study

Parsi E1*, Bitterlich N2, Winkelmann A1, Rösler D1 and Metzner C1
1Department of Cardiology, Bonn Education Association for Dietetics, Germany
2Department of Biostatistics, Medicine and Service Ltd, Germany
3Department of Dietetics, Bonn Education Association for Dietetics, Germany
4Department of Internal Medicine, Uniklinik RWTH Aachen, Germany

Abstract

Causes of cardiac arrhythmias are often components of the metabolic syndrome and/or electrolyte disturbances. In the latter case, magnesium and potassium are of high importance. In our pilot study we randomized 60 patients with cardiac arrhythmias and cardiovascular comorbidities. The patients of the verum group were a dietary intervention with specific micronutrients over a treatment period of six weeks. We found in the verum group a significant reduction in elevated fasting insulin (p=0.053) as well as in HOMA-IR (p=0.053). In this group also significant improved the echo parameters, like EF in range 54 – 65% (p=0.020), and LVMI (p<0.003) as well as the tendency LVEDD (p=0.050), IVS (p=0.053) and E/A ratio (p=0.051). However, there is no significant group difference in these parameters. These results seem to indicate that the specific micronutrient combination in patients with cardiac arrhythmias reduces insulin resistance and improves left ventricular cardiac function.

Introduction

Causes of Cardiac Arrhythmias (CA) can be components of the metabolic syndrome or micronutrient deficiency. Insulin Resistance (IR) is a risk factor for LV diastolic dysfunction. One exploratory outcome of the present pilot study was to assess the impact of a dietary intervention with specific micronutrients on the IR, Beta-cell (B) Function and fasting (f) insulin levels in patients with CA with the goal to improve the Left Ventricular (LV) function.

Methods

This was a post hoc analysis of the randomized double blind, placebo-controlled pilot study in patients with CA and co morbidities like arterial hypertension, Diabetes 2, coronary artery disease and metabolic syndrome which were recruited using data from patients who were 18 -75 years of age in an outpatient practice of Cardiology. All participants received placebo administration during a one-week run-in period. After evaluation of the Holter ECG at baseline, LV function by standard echocardiography and check of the inclusion criteria at baseline (V3). 60 patients were randomly assigned to the verum or placebo group. Glucose metabolism was evaluated on the basis of the f-glucose level, the f-insulin level and the Homeostasis Model Assessment (HOMA) of Insulin Resistance (HOMA-IR) and Beta-cell function (HOMA-B). Magnesium and potassium were analysed in serum and 24-h urine collection at baseline and at study end (after 6 weeks of dietary supplementation).

Over this period participants were required to take 2 tablets 2 times a day of verum (magnesium, potassium, B vitamins, and coenzyme Q10) or placebo. The pre-existing therapy was continued. Most common drugs were beta blocking agents, ACE-/ARB inhibitors and statins.

Statistical analyses were made by using the Mann Whitney-U test or t test (independent groups) and Wilcoxon test (dependent groups) as well as the Spearman correlation and Cohen´s effect size.

Results and Discussion

6 of 60 patients were excluded by protocol violation: 54 patients were evaluated per protocol,
In the verum group the dietary intervention led to a significant improvement of f-insulin in the range of ≥88 pmol/l (p < 0.02), HOMA-IR (p < 0.05), and ejection fraction in the range 54-65% (p = 0.02). HOMA-B significantly reduced only in male of the verum group (p=0.048). The LVEDD (p ≤ 0.041), E/A (p ≤ 0.051) showed likewise only in the verum group in tendency an improvement. The LVMi in the intervention group is significantly reduced (p < 0.003). Between both groups we found no significant differences notes under (Table 1). The reduction of LVMi was unexpected. Insulin sensitivity increased with dietary intervention and beta-cell function decreased (HOMA-IR and HOMA-B decreased). The decreasing of LVMi after a 3 month intervention of glucose metabolism was described recently (HOMA-IR and HOMA-B decreased). The decreasing of LVMI after 3 months in the verum group was 0.73 (Table 1). This results showed in the verum group, that the smaller the quotient supply/excretion the greater the reduction of VPBs(r = -0.125; p = 0.495).

For magnesium a quotient of unfavorable supply is identified according to our results as ≤3.5, as favorable > 3.5. In the verum group could be found a weak positive correlation of reduction of VPBs, in particular with a quotient of ≤ 3.5 (r = 0.136; p = 0.629). In the placebo group this correlation coefficient is negative (r = -0.137; p = 0.565).

The supplementation of potassium and magnesium does not lead to an elevated serum concentration.

Conclusions

In the post-hoc analysis of this pilot study, dietary intervention with specific micronutrient combination as add-on to concomitant cardiovascular drug treatment reduces the IR and leads to an improvement of LV parameters (LVEDD, E/A, LVMi) in patients with cardiac arrhythmias. These results only were found in the verum group but without statistical difference between the groups. The reducing of VPBs depends significantly from the potassium quotient supply/excretion-the smaller the quotient the greater the reduction. This significant correlation could not be shown for magnesium quotient. Our results should be verified in a study with a larger population.

### Table 2: Comparison of VPBs in all patients depending on the quotient of potassium (supply/excretion).

<table>
<thead>
<tr>
<th>All patients</th>
<th>Group</th>
<th>N</th>
<th>MV</th>
<th>SD</th>
<th>Min</th>
<th>Q25</th>
<th>Median</th>
<th>Q75</th>
<th>Max</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>VPBs V3</td>
<td>Q ≤ 1.4</td>
<td>30</td>
<td>1446</td>
<td>1944</td>
<td>0</td>
<td>10</td>
<td>597.5</td>
<td>1744</td>
<td>7604</td>
<td>0.923</td>
</tr>
<tr>
<td></td>
<td>Q &gt; 1.4</td>
<td>21</td>
<td>1498</td>
<td>1778</td>
<td>0</td>
<td>276</td>
<td>932</td>
<td>2328</td>
<td>5573</td>
<td>0.041</td>
</tr>
<tr>
<td>VPBs V5</td>
<td>Q ≤ 1.4</td>
<td>30</td>
<td>812.9</td>
<td>1144</td>
<td>0</td>
<td>28</td>
<td>161.5</td>
<td>1245</td>
<td>3556</td>
<td>0.014</td>
</tr>
<tr>
<td></td>
<td>Q &gt; 1.4</td>
<td>21</td>
<td>2287</td>
<td>3604</td>
<td>0</td>
<td>7</td>
<td>400</td>
<td>2234</td>
<td>11264</td>
<td>0.014</td>
</tr>
<tr>
<td>VPBs V - V3</td>
<td>Q ≤ 1.4</td>
<td>30</td>
<td>-633.6</td>
<td>1419</td>
<td>-6260</td>
<td>-738</td>
<td>-49.5</td>
<td>8</td>
<td>1155</td>
<td>0.041</td>
</tr>
<tr>
<td></td>
<td>Q &gt; 1.4</td>
<td>21</td>
<td>789.7</td>
<td>2548</td>
<td>-1120</td>
<td>-539</td>
<td>-95</td>
<td>358</td>
<td>9208</td>
<td>0.014</td>
</tr>
</tbody>
</table>

VPBs=ventricular premature beats, MV=mean value, p=p-value, sign. < 0.05

29 in the verum, and 25 in the placebo group. 1 patient in the verum group and 4 patients in the placebo group were excluded caused by incomplete intake of study supplementation and in the placebo group 1 caused by artificial hyperkalaemia.

In the verum group the dietary intervention led to a significant improvement of f-insulin in the range of ≥88 pmol/l (p < 0.02), HOMA-IR (p < 0.05), and ejection fraction in the range 54-65% (p < 0.02). HOMA-B significantly reduced only in male of the verum group (p=0.048). The LVEDD (p = 0.050) and E/A (p = 0.051) showed likewise only in the verum group in tendency an improvement. The LVMi in the intervention group is significantly reduced (p < 0.003). Between both groups we found no significant differences notes under (Table 1). The reduction of LVMi was unexpected. Insulin sensitivity increased with dietary intervention and beta-cell function decreased (HOMA-IR and HOMA-B decreased). The decreasing of LVMi after a 3 month intervention of glucose metabolism was described recently by Verma et al.[1]. The mechanisms of action are until now not fully understood. In these mechanisms magnesium, B-vitamins, and coenzyme Q10 seems to have a great importance [1-5].

In CA the administration of magnesium and potassium is an established add-on treatment [6-8]. Butin our investigation Ventricular Premature Beats (VPBs) were unchanged under verum. A closer look into the samples suggests differences influencing VPBs. The reason for this seems to be the different supply status. The availability of potassium and magnesium is described by the quotient of their supply (inclusive supplementation) and urinary excretion.

An unfavorable quotient for potassium is identified by ≤ 1.4, a favorable > 1.4. At baseline the subgroups Q ≤ 1.4 and Q > 1.4 are not significant different referred to VPBs. At study end this difference is significant with an effect size=0.73 (Table 2). This results showed in the verum group, that the smaller the quotient supply/excretion the greater the reduction of VPBs(r = -0.125; p = 0.495).

For magnesium a quotient of unfavorable supply is identified according to our results as ≤3.5, as favorable > 3.5. In the verum group could be found a weak positive correlation of reduction of VPBs, in particular with a quotient of ≤ 3.5 (r = 0.136; p = 0.629). In the placebo group this correlation coefficient is negative (r = -0.137; p = 0.565).

The supplementation of potassium and magnesium does not lead to an elevated serum concentration.
**Strength and Limitation**

The strength of our monocentric study is that all included patients with different cardiovascular comorbidities like coronary artery disease, arterial hypertension, and premature beats were treated in one Outpatient Practice of Cardiology. This means that all procedures were conducted and repeated under identical conditions described per protocol. Limiting for the significance of this study could be the number of patients and the post-hoc analysis.

**Study Registration**

The study was approved by the Freiburg Ethics Commission International and retrospectively registered with the U.S. National Institutes of Health Clinical Trials Gov ID NCT 02652338 on 16 December 2015.

**References**


