Acid-base conditions regulate calcium and magnesium homeostasis

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Abstract. Background. Previous experimental studies demonstrate that the acid-base balance influences mineral homeostasis by regulating the absorption of calcium and magnesium in the kidneys. No intervention studies are available on population samples. Aims. To study the urinary excretion of calcium and magnesium before and after an intervention with the aim of decreasing the acid load. Methods. Healthy subjects aged 50-75 years were recruited by advertising. Urinary calcium, magnesium and urea as well as blood pressure were measured before and after the intervention. This comprised taking tablets containing potassium hydrogen carbonate or potassium chloride (placebo) during 7-10 days. Results. There were significant relationships between the urinary excretion of urea and magnesium and calcium before the intervention. Comparing before and after intervention, the change in urinary excretion of urea was related to a change in urinary excretion of calcium and magnesium. There was a significant decrease in systolic as well as diastolic blood pressure both after administration of potassium hydrogen carbonate and citrate. Conclusion. The results confirm previous studies showing a relation between acid conditions in the body and the excretion of calcium and add new data on magnesium. A blood pressure decrease after potassium has been found in previous studies. This suggests an alternative for the treatment of moderately increased levels of blood pressure that should be further explored.

Key words: acid-base, magnesium, calcium, urea, potassium

The acid-base balance in the body is of importance for mineral homeostasis. The reabsorption of calcium and magnesium in the renal tubuli is influenced by the acidity or the urine. This has been demonstrated for calcium in an intervention study under carefully controlled conditions regarding intake of different nutrients [1]. Urinary calcium was measured in test persons before and during a controlled supply of protein, a major inducer of acid conditions due to its sulphurous metabolites [2]. When the protein intake was doubled, the urinary excretion of calcium increased and when sodium hydrogen carbonate (70 mEq) was given, the excretion decreased, even at a continued high level of protein intake. The urinary excretion of magnesium is also related to acid-base conditions [3] but no intervention studies have been reported.

A commonly used marker of acid load is the net acid excretion (NAE) in the urine [2]. The analysis of NAE is quite complicated and time consuming.

Many of the studies on acid-base balance reported previously have been performed under laboratory conditions with control of dietary intake of minerals and food items that may influence the acid-base balance. Although important mechanistic information can be obtained through these means, the applicability is uncertain for a public health scenario where dietary intakes are not controlled for.

The present study was undertaken among healthy subjects in their normal environment without restrictions on dietary intakes to evaluate 1) if intervention with tablets with a base-promoting content would increase the basic load, and 2) if the intervention would affect the urinary excretion of calcium and magnesium.
Material and methods

A renewed analysis was carried out using data from a population study that had not previously been analysed [3]. The aim was to evaluate the possibility of using urea as a proxy for acid conditions in terms of net acid excretion (NAE).

For the intervention study healthy subjects were recruited through advertising. Inclusion criteria were age 50-65 and without any serious disease. Exclusion criteria were medication for heart disease or blood pressure. The subjects gave informed consent and the study was approved by the Ethical Committee in West Sweden. There were considerable problems recruiting subjects to the study, probably because of the absence of monetary compensation for the rather tedious collection of urine.

The tablets contained potassium hydrogen carbonate (KHCO₃) and chloride (KCl) as a placebo. They were randomly given to the subjects. The composition was not known to the subjects or the investigators. The subjects took 2 tablets 3 times daily for 7-10 days which corresponded to a daily potassium dose of 30 mEq. The characteristics of the subjects taking the different categories of tablets are shown in Table 1.

The proportion of females was slightly higher in the group receiving KHCO₃. The average age in the groups was very similar.

Before and after the intervention 24 h urine samples were collected. The amount of calcium was analysed using an ion detection instrument (Beckman Coulter UniCel DxC 800 synchron Clinical System, Sweden). Magnesium concentrations were determined using a time related endpoint method reading the absorbance and urea using an enzyme time reaction method. All analyses were performed in a hospital accredited laboratory (Borås, Sweden). Blood pressure was recorded before and after the intervention in 19 of the 31 subjects. Two persons considered the tablets too large and discontinued the study.

Differences between the groups were evaluated using the Mann-Whitney test or the chi² test. Relationships between parameters were tested using the Spearman test. A p-value of 0.05 was considered statistically significant.

Table 1. Gender and age characteristics of the study group.

<table>
<thead>
<tr>
<th>Tablet</th>
<th>n</th>
<th>% females</th>
<th>Age years (mean)</th>
</tr>
</thead>
<tbody>
<tr>
<td>KHCO₃</td>
<td>17</td>
<td>78</td>
<td>62</td>
</tr>
<tr>
<td>KCl</td>
<td>14</td>
<td>57</td>
<td>61</td>
</tr>
</tbody>
</table>

Results

The results from the new analysis of the material from the population study on the relation between the urinary excretion of NAE and urea is illustrated in Figure 1. There was a close relationship \( r^2 = 0.718, p = 0.0001 \). Urea was thus used as a proxy for acid conditions in the intervention study.

Before the intervention there was a significant relation between the excretion of urea and the excretion of calcium \( (r^2 = 0.478, p = 0.008) \) and magnesium \( (r^2 = 0.367, p = 0.046) \) when the two groups receiving KHCO₃ and KCl were amalgamated. There was also a significant relation between the excretion of magnesium and calcium \( (r^2 = 0.606, p < 0.001) \).

Table 2 shows the changes in urinary excretion of urea, calcium and magnesium in relation to the different tablets given in the intervention.

In the group receiving the active tablet, there was a significant decrease in the average excretion of urea \( (p = 0.037) \) and 13 out of 18 subjects decreased their urea secretion. In the placebo group the corresponding numbers were 4 out of 13 \( (p = 0.033, \text{chi}² \text{test}) \). This illustrates that the KHCO₃ tablet had an acid reduction effect but for some people, their normal nutritional habits overcame this effect.

Figure 2 illustrates the relation between the changes in urea and calcium and magnesium levels in the group receiving KHCO₃.
There was a significant relationship for calcium \((p = 0.016)\) but not for magnesium \((p = 0.126)\). Similar relations were found for the group receiving KCl \((p = 0.079 \text{ and } 0.024)\). If the groups were amalgamated, the relationships were \(p = 0.008\) for calcium and \(p = 0.046\) for magnesium.

**Table 3.** Urinary excretion of urea, calcium and magnesium (mmol/24 h) before and after administration of tablets containing potassium hydrocarbonate or chloride.

<table>
<thead>
<tr>
<th>Tablet</th>
<th>Urea Before</th>
<th>Urea After</th>
<th>Calcium Before</th>
<th>Calcium After</th>
<th>Magnesium Before</th>
<th>Magnesium After</th>
</tr>
</thead>
<tbody>
<tr>
<td>KHCO₃</td>
<td>360 (89)</td>
<td>326 (99)*</td>
<td>3.4 (1.2)</td>
<td>3.4 (1.5)</td>
<td>3.9 (1.8)</td>
<td>4.4 (2.1)</td>
</tr>
<tr>
<td>KCl</td>
<td>396 (102)</td>
<td>439 (102)</td>
<td>4.9 (2.2)</td>
<td>4.7 (1.3)</td>
<td>4.0 (1.5)</td>
<td>4.2 (1.6)</td>
</tr>
</tbody>
</table>

Mean and (SD); * \(p = 0.037\).

**Figure 2.** Relation between changes in urea and calcium and magnesium intervention with K-hydrogen carbonate.

There was a significant relationship for calcium \((p = 0.016)\) but not for magnesium \((p = 0.126)\). Similar relations were found for the group receiving KCl \((p = 0.079 \text{ and } 0.024)\). If the groups were amalgamated, the relationships were \(p = 0.008\) for calcium and \(p = 0.046\) for magnesium.

**Table 3** shows the difference in systolic and diastolic blood pressure after the intervention.

There was a decrease in systolic and diastolic blood pressure after the intervention. There was no difference between the groups taking potassium hydrogen carbonate or chloride.

**Discussion**

The major results from the study were:
- a decrease in the excretion of urea related to decreases in the secretion of calcium and magnesium irrespectively of the intervention;
- a decrease in systolic as well as diastolic blood pressure after administration of the tablets.

There are certain shortcomings in the study. The number of subjects is fairly small due to the recruitment problems. In spite of this, significant differences which support previous results were found. The subjects studied are not representative of the popula-

**Table 3.** Systolic and diastolic blood pressure (BP) before and after treatment with tablets containing potassium hydrocarbonate or chloride.

<table>
<thead>
<tr>
<th>n</th>
<th>Systolic BP (mmHg) Before</th>
<th>Systolic BP (mmHg) After</th>
<th>Diastolic BP (mmHg) Before</th>
<th>Diastolic BP (mmHg) After</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>19</td>
<td>132.1 (17.5)</td>
<td>122.9 (20.0)</td>
<td>79.1 (9.2)</td>
<td>74.6 (7.5)</td>
<td>0.003</td>
</tr>
</tbody>
</table>

Mean and (SD).
tion in general – none of the subjects was a smoker. This reflects the selection process in studies of this kind, where voluntary recruitment favours the inclusion of health conscious persons. The parameters studied are, however, related to basic physiological functions and the results should thus be applicable to the population in general. An advantage in the study is the use of an elderly population sample as renal function which regulates uptake of minerals is reduced with age [8]. Urea is not an exact mirror of acid conditions – if meat is consumed the excretion of urea increases but if vegetables are consumed at the same time, there is no effect on the acid-base balance. NAE is a better indicator of acid conditions but such measurements could not be performed due to technical limitations.

In some subjects the excretion of urea increased in spite of the administration of the base-promoting tablet. There was no difference in mean values of excreted calcium and magnesium between the two groups, although there was a significant relationship between the urea excretions. The reason for this is probably due to variations in the diet - there were no dietary restrictions for the participants and the effect induced by the tablet was thus masked by normal variations in the daily nutritional intake, in some cases leading to a urea reduction also in the placebo group.

Overall the results show a relation between the changes in urinary excretion of urea and calcium and magnesium. This confirms the results from a previous laboratory study on calcium [4] and supports the hypothesis that the acid-base balance is important for mineral homeostasis among subjects consuming their regular daily diet without laboratory induced restrictions. Regulation of acid conditions could thus be a tool for treatment of mineral deficiency.

The decrease in blood pressure after administration of tablets containing potassium supports earlier findings using potassium chloride and citrate [5-7] and also demonstrated an effect of K hydrocarbonate. As no control tablet was included it cannot be excluded that part of the decrease was due to habituation of the subjects to the blood pressure recording procedure. On the other hand, the measurements were made on persons most of whom were familiar with the procedure and an appropriate resting period was applied. It is thus unlikely that all of the effect is due to habituation. In a previous intervention study a mineral water with a high level of potassium also caused a decrease in blood pressure [8]. Should the beneficiary effect of this dose of potassium be proven in future studies, this opens an interesting possibility for medication in subjects with only slightly elevated blood pressure.

In conclusion, the results support a relation between acid conditions in the body and an increased urinary secretion of magnesium and calcium. Regulation of acid-base conditions are thus an alternative for reducing calcium and magnesium deficiency. Intervention with potassium caused a decrease in systolic and diastolic blood pressure. This finding should be further explored with the possibility of providing an alternative for treatment of moderately increased blood pressure.

**Disclosure**

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**References**