Influence of Various Beverages on Urine Acid Output

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ABSTRACT

High dose methotrexate therapy requires a high alkaline urine output. In order to evaluate the effect of various beverages on the urine acid output, healthy volunteers (n = 6) took 1.5-2 liters of a test drink during a 2-h period. On the test day urine pH and urine acid excretion (titratable acid plus ammonia minus bicarbonate) were measured. Controls received water and tea as test drink. Orange juice (pH 3.64) and tube feeding (pH 6.78) both led to alkaline urine pH and significantly decreased urine acid output compared to the control group (n = 4, P < 0.01 and n = 3, P < 0.001, respectively). Yoghurt (pH 4.1), buttermilk (pH 4.58), and Coca-Cola (pH 2.54), on the other hand, all induced a higher acid output than the control group (n = 6) and a urine pH < 7.0 during the whole test day (n = 6, NS; n = 6, P < 0.02; n = 4, P < 0.05, respectively).

If high urine output with an alkaline pH is required, fruit juices or well balanced tube feeding, both with low cation and low sulfur-bound amino acid content, can accomplish this. Drinks with high inorganic acid content (such as Coca-Cola) or high sulfur-bound amino acid content such as yoghurt and buttermilk will result in acidification of the urine.

INTRODUCTION

In a number of clinical conditions alkaline urine may be favorable. An example of a situation in which the urine pH should be more than 7 for only a few days is high dose MTX chemotherapy. MTX is a chemotherapeutic drug that in high dosage is effective in combating a variety of tumors (1). A severe complication of high dose MTX, however, is renal toxicity. The mechanism for the nephrotoxicity can be explained, in part, by the fact that at a urine pH of 7.0 the drug is fully ionized, but when the pH is lowered to 5.7 a dense precipitate in the tubulus is formed. Dehydration adds to the tubular precipitation (2-4).

With this in mind, patients receiving such a therapy are hydrated and given oral or intravenous bicarbonate previous to high dose MTX treatment. Drug administration is only started if urine pH is over 7, and special attention is given to adequate p.o. and/or i.v. fluid intake to get a urine output exceeding 3 liters/day.

Recently Djerassi et al. (5) and Reggev et al. (6) emphasized the necessity of restriction of the intake of all acid-containing food or liquids. They prohibit all fruit juices, fresh fruits, and various sodas such as Coca-Cola and Seven-Up. In their experience, intake of acid-containing liquids during treatment with high dose MTX has caused immediate acidification of the urine with actual precipitation and crystal formation of MTX in the urine.

The influence of food composition has been evaluated in many long term acid-base balance studies (7-9). These data are, however, not easily applicable to the clinical situation in which one needs a rapid elevation of the urine pH. If the avoidance and the intake of certain foods and/or fluids could raise the urine pH and lower the acid output quickly, this would greatly facilitate high dose MTX therapy and could even make this regimen possible on an outpatient basis.

As large fluid intake is also important during MTX therapy, it seems obvious to study the influence of urine pH of beverages that can be taken in substantial amounts. In this study we thus chose to evaluate the influence of beverages on urine acid load in healthy volunteers.

MATERIALS AND METHODS

This study was performed on 25 healthy volunteers (9 males, 16 females), age 22-40 years. An inventory of food intake during the 2 days before the test day was obtained. Calorie, protein, carbohydrate, and fat intake were calculated. On the test day each volunteer received at least 1.5-2 liters of a test drink between 8 and 10 a.m. During the rest of the day the only beverages allowed were water and tea and as solid food only bread, biscuits, rice, and sugar, with a total calorie intake of at least 1800 kcal. This regimen was chosen in order to minimize protein and acid intake on the test day. The control group (n = 6) received as test drink tea and water. Yoghurt (n = 6), buttermilk (n = 6), Coca-Cola (n = 4), and orange juice (n = 4) were the test drinks.

The test beverages were chosen as representatives of groups of drinks that might have a big influence on urine acid output and might be easily used by the patients in high volumes.

After emptying their bladders before 8 a.m. on the test day, the urine was collected from the volunteers in separate portions for 24 h. The urine for bicarbonate determination was collected under oil. The volume of each portion was subsequently measured. The volunteers were asked to urinate, if possible, at least every 2 h during the day.

In a separate group three patients were studied who received only Nutrison nasogastric tube feeding, continuously over 24 h. This feeding consisted of 2 liters/24 h with 80 g protein, 80 g fat, 240 g carbohydrate, and 2000 kcal/day. The same urine sampling was performed as in the volunteer group.

The pH of every separate urine sample was measured immediately. For all of the samples the titratable acid concentration was determined and urine ammonia concentration was directly measured, by measuring absorbance with a Unicam SO spectrophotometer (10). Bicarbonate was determined by back titration with NaOH 0.01 n after acidification with 0.01 n HCl and phenol red as indicator. The net acid excretion was then calculated as the sum of the excretion of titratable acid and ammonia, minus the excretion of bicarbonate.

Of the test beverages, the pH and titratable acid concentration was measured. Of the drinks, the total acidity, defined as the net content of organic anions in excess of organic cations, was also estimated by comparing the sum of the measured inorganic cations (Na+ + K+ + Ca2+ + Mg2+) with the sum of the measured inorganic anions (Cl− + P + SO42−). The amount of phosphorus is calculated according to the method of Lennon et al. (8). Total acidity, according to some authors (8, 11), makes it possible to predict the urine acid output. Information on the ion, acid, and sulfur containing amino acid content of the different liquids was obtained from the different manufacturers and, if necessary, additional measurements were performed.

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1 The abbreviation used is: MTX, methotrexate.
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Table 1
Data on the test drinks

<table>
<thead>
<tr>
<th></th>
<th>pH</th>
<th>Titratable acid (mmol/liter)</th>
<th>Total acidity (mmol/liter)</th>
<th>Inorganic acid content (mmol/liter)</th>
<th>Organic ion content (mmol/liter)</th>
<th>Sulfur containing amino acid content (g/liter)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tap water</td>
<td>7.77</td>
<td>-5.88</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tea</td>
<td>7.77</td>
<td>-12.02</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Coca-Cola</td>
<td>2.54</td>
<td>5.47</td>
<td>+29.74</td>
<td>H₃PO₄, 5.47</td>
<td>Citrate, 44</td>
<td>Oxalate, 1.11</td>
</tr>
<tr>
<td>Orange juice</td>
<td>3.64</td>
<td>48</td>
<td>-45.33</td>
<td></td>
<td>Oxalate, 3</td>
<td></td>
</tr>
<tr>
<td>Yoghurt</td>
<td>4.10</td>
<td>130</td>
<td>-42.76</td>
<td></td>
<td>Lactate, 130</td>
<td>1.10</td>
</tr>
<tr>
<td>Buttermilk</td>
<td>4.58</td>
<td>82.5</td>
<td>-30.36</td>
<td></td>
<td>Lactate, 53</td>
<td>0.99</td>
</tr>
<tr>
<td>Nutrisco Tube</td>
<td>6.78</td>
<td>3.64</td>
<td>+2.44</td>
<td></td>
<td>Citrate, 17.7</td>
<td>1.22</td>
</tr>
</tbody>
</table>

For each test, per subject, the integrated response for titratable acid, ammonia, and total acid secretion in the urine was calculated. For the integrated responses the acid secretion per 2 h was calculated. The different groups were compared with the unpaired t-test.

RESULTS

Table 1 shows some data of the test drinks. All volunteers used a typical Dutch diet consisting of bread, potatoes, vegetables, meat, and milk products. The mean intake during the 2 days preceding the test was 1935 kcal, 75 g protein, 77 g fat, and 236 g carbohydrate.

The fasting urine pH on the test day was below 6 for all subjects. No significant amounts of bicarbonate were found in any of the urine samples. The total urine acid excretion during the 24-h period from the start of the test at 8 a.m. was 56.88 meq for the control group, 28.03 meq for the orange juice, 69.39 meq for the yoghurt, 81.86 meq for the buttermilk, and 104.6 meq for the Coca-Cola group. Normal total acid excretion is 50–60 meq/24 h (12).

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The main influence of the test drink on the urine acid load can be expected during the first part of the test day. The study of the first 14 h also has the advantage that it excludes the urine acid production during fasting at night. For this reason the integrated responses for titratable acid, ammonia, and total acid secretion in the urine was calculated over 2-h periods for the first 14 h (Charts 1 and 2; Table 2).

Table 2 shows that the integrated response for the urine acid excretion was significantly lower in the orange juice and tube feeding group as compared to the control group. The yoghurt, buttermilk, and Coca-Cola groups had a significantly higher acid excretion than did the control group.

There was no relation between the pH of the test drink and the urine pH. The urine pH in the control group and in the Coca-Cola, buttermilk, and yoghurt groups was below 7.0 during the whole test period of 14 h. The four subjects in the orange juice group had a urine pH >7.0 from 11 a.m. to 6 p.m. on the test day. The patients who received tube feeding had a urine pH >7.0 during almost the whole day (Chart 3).

DISCUSSION

This study shows that high volume oral liquid has a rapid and significant influence on renal acid secretion.

Various methods have been postulated to calculate the influence of oral food intake on the renal acid secretion. It is well known that there is no relation between titratable acid content of the drink and urine acid output. In earlier years it had been postulated that the total acidity of dietary ash, calculated as the content of sodium, potassium, calcium, and magnesium minus the content of chloride, phosphorus, and sulfur, could predict the urine acid output. In practice it is difficult to calculate the impact of each element. Phosphate, for example, can appear in organic (phosphoprotein and phospholipid) and inorganic form (mineral phosphate). Coca-Cola contains a large amount of the strong acid H₃PO₄; yoghurt and buttermilk contain H₂PO₄⁻ and HP₀₄²⁻. Free sulphate is usually present in only a low amount. Relman et al. (9), however, showed that another cause for the acid in the urine was the oxidation of sulfur from dietary sulfur-containing amino acids (9).

In this study volunteers who received yoghurt, buttermilk, or Coca-Cola had a statistically significant higher acid excretion compared to the control group, which received tea and water. The subjects who received orange juice and enteral tube feeding excreted a significantly lower amount of acids than did the controls.

For Coca-Cola the high amount of ammonia excretion can be explained by the high H₃PO₄ content (550 mg/liter) of this drink. The pK of phosphoric acid is too low for H₃PO₄ to be excreted in the urine, and therefore the remaining hydrogen ions are excreted as ammonium ions. During acute metabolic acidosis,
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Chart 2. Mean amount of titratable acid (meq) excretion in the urine per 2 h for the various groups from 8 a.m. to 10 p.m., after test drink of 1.5–2 liters from 8–10 a.m.

Table 2
Integrated responses of titratable acid, ammonia, and total acid for the test drinks in relation to controls

<table>
<thead>
<tr>
<th></th>
<th>Titratable acid (meq)</th>
<th>Ammonia (meq)</th>
<th>Total acid (meq)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Controls (n = 6)</td>
<td>15.97 ± 4.79</td>
<td>23.25 ± 5.55</td>
<td>49.5 ± 7.2</td>
</tr>
<tr>
<td>Yoghurt (n = 6)</td>
<td>39.49 ± 7.87</td>
<td>42.57 ± 5.87</td>
<td>82.07 ± 13.7</td>
</tr>
<tr>
<td>Buttermilk (n = 6)</td>
<td>38.8 ± 6.4</td>
<td>42.12 ± 5.51</td>
<td>64.2 ± 8.85</td>
</tr>
<tr>
<td>Coca-Cola (n = 4)</td>
<td>45.2 ± 4.44</td>
<td>60.05 ± 7.22</td>
<td>105.35 ± 5.87</td>
</tr>
<tr>
<td>Orange juice (n = 4)</td>
<td>7.6 ± 1.67</td>
<td>10.82 ± 4.33</td>
<td>23.5 ± 5.4</td>
</tr>
<tr>
<td>Tube feeding (n = 3)</td>
<td>1.44 ± 0.75</td>
<td>10.8 ± 4.67</td>
<td>13.3 ± 5.1</td>
</tr>
</tbody>
</table>

* Mean ± SE.
α P < 0.05.
α Not significant.
α P < 0.02.
α P < 0.01.
α P < 0.001.

renal ammonia excretion increases predominantly due to "trapping" of NH₄⁺ in the acidic tubule fluid (13). This explains the high ammonia excretion after Coca-Cola ingestion. Apart from H₃PO₄, Coca-Cola contains CO₂, no ammonia, and probably no other acids.

The fact that yoghurt and buttermilk have a high anion content but lead to acid urine production can probably be explained by the presence of a high amount of sulfur-bound amino acids, namely 330 and 270 mg/liter, respectively.

The tube feeding used had a low cation content and almost no sulfur-bound amino acids. This explains the alkaline urine during Nutrison tube feeding administered over the whole day.

Orange juice has a high anion content. This, and the fact that the organic acids in fruit juices are oxidized completely to CO₂ during Nutrison tube feeding administered over the whole day.

If one wants to achieve rapid alkalinization of the urine with high volume load this can be achieved with fruit juices like orange juice. This directly contradicts the statement of Djerassi et al. (5), who advise the avoidance of (acid) fruit juices. We think that fruit juices might even facilitate high fluid intake during high dose MTX therapy.

Enteral tube feeding will guarantee a high fluid intake over the day of treatment, as well as resulting in a stable alkaline urine pH and contributing to a positive nutritional balance (14). Its application in these situations might therefore be considered.

When alkaline urine is a necessity one should avoid beverages with high amounts of sulfur-bound amino acids such as yoghurt and buttermilk or high amounts of inorganic acids (for example, H₃PO₄) such as Coca-Cola.

REFERENCES
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