Acetylsalicylic acid-induced biochemical changes in gastric juice: a failure of adaptation?

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Background: Acetylsalicylic acid (ASA) causes gastric mucosal damage which diminishes with continued use due to adaptation. Methods: To determine the net effect of these processes on the gastric juice, we estimated acid, osmolality, bicarbonate concentration in nonparietal gastric juice, calcium, potassium and sodium in 18 patients (9 men; mean age 32 years, range 20-46) with irritable bowel syndrome, before and after 600 mg of ASA taken post-cibum thrice daily for 4 weeks. Osmolality was determined by an osmometer, acidity by titration, and Na⁺, K⁺ and Ca²⁺ using a sodium-potassium-calcium analyzer; bicarbonate was derived from the two-component model of Feldman. Results: Gastric juice K⁺ and Na⁺ increased significantly from mean (SE) 14.6 (0.5) and 197.5 (16.3) to 16.7 (0.4) and 256.8 (18.1) mEq/L, respectively. The other parameters remained unchanged. Conclusion: After four weeks of ASA ingestion there is a dichotomy of gastric mucosal injury and adaptation, with preservation of acid secretion but continuous loss of Na⁺ and K⁺. [Indian J Gastroenterol 1998; 17: 4-6]

Key words: Aspirin, gastric acid secretion, gastric electrolyte loss

Acetylsalicylic acid (ASA)-related gastric mucosal injury is accompanied by increased fluxes of ions across the gastric mucosa due to increased vascular permeability, and changes in acid secretion and emptying. Gastric mucosal adaptation to prolonged aspirin use has been documented and attributed to increased cellular regeneration. Despite improvement in mucosal appearance with adaptation, gastric microbleeding occurs throughout the period of ASA administration. The impact of this process of adaptation on the biochemical profile of gastric juice is not known.

We estimated biochemical parameters in the gastric juice before and after four weeks of ASA intake.

Methods

Patients with irritable bowel syndrome attending the Gastroenterology Clinic of Nehru Hospital were eligible for the study. Work-up included clinical assessment, hemogram, stool examination and upper gastrointestinal endoscopy. Malabsorption work-up was undertaken wherever indicated. Patients taking diuretics, NSAIDs, calcium-channel antagonists, antacids, H₂-receptor antagonists or proton pump inhibitors within 2 weeks of starting the study or during the study period, and those who drank alcohol or smoked, were excluded from the study.

Informed consent was obtained from all subjects. The study was approved by the institute Ethics Committee.

Procedures

After overnight fast, a nasogastric tube was positioned fluoroscopically with its tip in the most dependent part of the gastric antrum, with the patient in the left lateral decubitus position. Overnight gastric juice was aspirated and discarded. For the next one hour gastric juice was aspirated with a syringe at 5-min intervals; the patients were instructed to spit out saliva. None of the gastric juice samples was noted to be bile- or blood-stained. Ten millilitres of heparinized venous blood was drawn at 30 minutes for estimation of plasma osmolality.

The subjects were then prescribed 600 mg of aspirin thrice daily after meals for 4 weeks; they were instructed not to take any other medication. All subjects were asked to report after 2 weeks for stool examination; after a further 2 weeks gastric juice was collected again.

All measurements were done at room temperature. Gastric juice volume was measured to the nearest 0.5 mL. Osmolality of gastric juice and venous plasma samples was measured by freezing-point depression method (3DH Osmometer, Advanced Instruments, Needham Heights, USA) and expressed in milliosmoles/Kg. Hydrogen ion concentration was measured by in vitro titration to pH 7.0 with 0.1 N NaOH, using digital pH meter.

Gastric acidity, bicarbonate concentration and nonparietal volume secretion were calculated using equations derived from the two-component model of gastric secretion. It was assumed that the H⁺ concentration of parietal secretion was 160 mmol/L, that the composition of the nonparietal secretion was similar to that of interstitial fluid with bicarbonate concentration of approximately 25 mmol/L, and that the osmolality of pure parietal secretion was 1.06 times the plasma osmolality.

Na⁺, K⁺ and Ca²⁺ concentrations in gastric juice were measured using an ion-sensitive glass capillary electrode (working range 40-250 mmol/L, resolution 0.1 mmol/L at room temperature), an ion-sensitive liquid-membrane electrode (working range 0.2-20 mmol/L, resolution 0.01 mmol/L at room temperature) and a calcium ion-sensitive liquid-membrane electrode (working range 0.1-6.0 mmol/L, reso-
Aspirin-induced changes in gastric juice

**Discussion**

The study revealed a net loss of Na⁺ and K⁺ into the gastric juice after 4 weeks of ASA ingestion while all other parameters were unchanged. Since these tests were performed in patients after overnight fast and by aspirating gastric juice the increased Na⁺ and K⁺ can be ascribed only to an increase in mucosal permeability. Chloride was not estimated but is expected to change parallel to Na⁺.

Stern et al. demonstrated an increase in Na⁺, decrease in H⁺ and unchanged K⁺ in the gastric juice of humans. Theirs was an acute study in which the titratable acidity and osmolality were controlled. In another acute study in monkeys, Shea Donohue et al. found a decrease in Na⁺ and K⁺ in gastric juice after subcutaneous aspirin.

Gastric acidity did not decrease and the volume of gastric juice and nonparietal volume were unchanged in our study, suggesting that back-diffusion of H⁺ was not occurring. This is supported by the preserved bicarbonate concentration. Though there was a significant increase in Na⁺ and K⁺, the osmolality of gastric juice showed only an insignificant rise. This could be due to a decrease in other ions, like chloride, phosphate, sulfate and nitrite.

It appears that gastric mucosal adaptation is unable to restore Na⁺ and K⁺ leakage into the gastric juice even though acid secretion is normal. Though changes in Na⁺ and K⁺ could result from blood loss into the stomach, it is unlikely that this would occur as an isolated phenomenon sparing gastric acidity and bicarbonate concentration.

In conclusion, ASA-induced altered permeability of gastric mucosa to Na⁺ and K⁺ somehow escapes the adaptive effort of the gastric mucosa.

**References**


**Table: Gastric juice before and after acetylsalicylic acid**

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Before</th>
<th>After</th>
</tr>
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<tbody>
<tr>
<td><strong>Gastric juice</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Volume (millilitres)</td>
<td>121.3</td>
<td>117.8</td>
</tr>
<tr>
<td>Acidity (mmol/L)</td>
<td>37.7</td>
<td>41.6</td>
</tr>
<tr>
<td>Bicarbonate (mmol/L)</td>
<td>59.9</td>
<td>55.5</td>
</tr>
<tr>
<td>Bicarbonate concentration</td>
<td>77.0</td>
<td>77.6</td>
</tr>
<tr>
<td>(nonparietal volume) (mmol/L)</td>
<td>77.0</td>
<td>77.6</td>
</tr>
<tr>
<td>Calcium (mEq/L)</td>
<td>1.3</td>
<td>1.5</td>
</tr>
<tr>
<td>Potassium (mEq/L)</td>
<td>14.5</td>
<td>16.7</td>
</tr>
<tr>
<td>Sodium (mEq/L)</td>
<td>197.5</td>
<td>256.8</td>
</tr>
<tr>
<td>Osmolality (mOsm/Kg)</td>
<td>172.6</td>
<td>185.6</td>
</tr>
<tr>
<td>Plasma osmolality (mOsm/Kg)</td>
<td>283(2)</td>
<td>286(2)</td>
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</table>

* p < 0.001

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