



Effects of alkaline ionized water on gastric mucosal injury induced by aspirin in rats

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Summary

One of the objectives of this study is to determine effects of alkaline ionized water (AIW) on acute gastric mucosal injury induced by aspirin in rats. Oral doses of acidified aspirin (200 mg/kg) resulted in linear hemorrhagic erosion and increase in myeloperoxidase (MPO) activity, an index of neutrophil infiltration, in gastric mucosa. These instances of increase in total erosion and MPO activity were inhibited by administration of AIW (pH 10.5, ORP 450mV) for two weeks. Aspirin administration resulted in early increase in values of tumor necrosis factor (TNF α /cinc2 ~) plasma and tissue levels. The increase in TNF α /cinc2 ~ was also inhibited by administration of ArW. These results indicate that chronic administration of AIW is effective against aspirin induced gastric mucosal injury, and that its cyto protective action is associated with inhibition of neutrophil accumulation on gastric mucosa or with decline of inflammatory cytokine production.

Purpose of tests

Hopeful examples of clinical application of alkaline ionized water to gastrointestinal disorders are as follows;

- 1) Non ulcer dyspepsia (NUD) (at epigastria)
- 2) Irritable bowel syndrome (IBS)
- 3) Constipation caused by constitutional disorders (ex. diabetes, hypothyroid syndrome).
- 4) Peptic ulcer disease
- 5) Habitual users of non steroid anti inflammatory drug (NSAID).

As to 1) and 2) above, clinical tests have already been conducted. We have been studying mechanism of gastric mucosal injury in detail, and reported the meaning of inflammatory reactions and the role of active oxygen and lipid hyperoxidation in its process. Also for this symposium, we have examined effects of alkaline ionized water by testing experimental models of gastric mucosal injury using rats as well as cultured gastric mucosal tissues. As a result, we have found the following;

- 1) Alkaline ionized water does not act directly to offset active oxygen.
- 2) Cyto protective action on gastric mucosa is not recognized in the tests with short term dose of AIW
- 3) According to the tests on rats that were given AIW for 2 weeks, experimental gastric mucosal injury was found to be significantly inhibited.

Gastric mucosal injury models we studied include those induced by ischemia reperfusion, aspirin and stress. Nonsteroid antiinflammatory drug (NSAID) is one of the most commonly used drugs in clinical treatment these days due to its wide range of pharmacological functions. However, its side effect, gastric mucosal injury is becoming a problem. It is believed that the main mechanism

of this injury is caused by the inhibitory action of cyclooxygenase 1 (COX 1). Recently, another inhibitor COX 2 with less inhibitory action than COX 1 has been tested clinically. In fact, it is reported that application of COX 2 inhibitor reduces the frequency of gastric mucosal injury. However, since aspirin is used not only as anti-inflammatory drug, but also for inhibition of platelet aggregation, improvement of microcirculation and growth repression of large intestine tumor, its clinical use is expected to remain popular. Therefore, prevention of gastric mucosal injury caused by aspirin is extremely important. The purpose of our study for the symposium is to examine effects of alkaline ionized water against gastric mucosal injury in rats caused by aspirin.

Test methods

Male Sprague Dawley rats (weighing 160-180g) were used. During 2 weeks of testing, one of the groups was freely given alkaline ionized water (pH 10.5, ORP 450mV) produced by National TK780 electrolyzer. The other group, control group was freely given tap water. Acute gastric mucosal injury was induced by administering aspirin (200mg/kg) and hydrochloric acid (0.15N) in the stomach of rats on a 18 day fast. Hemorrhagic erosions found on gastric glands after periodic doses of aspirin underwent microscopic inspections, and the sum of longer diameter of erosions was measured as the total erosion (mm). Then, homogenate was created from scraped gastric mucosa treated with phosphoric acid buffer to measure the level of inflammatory cytokine production (TNF- α , IL-1 β) as well as myeloperoxidase (MPO) activity as an index of neutrophil infiltration based on given data. Each of these values was adjusted by protein concentration.

Test results

- 1) No significant difference between the 2 groups was found as to weight, physiological blood properties and antioxidant enzyme after raising them for 2 weeks. The number of leukocyte in peripheral vessels has slightly gone up.
- 2) Three hours after administering aspirin, erosive mucosal injury emerged on the rats' stomach glands which was significantly inhibited for the alkaline ionized water group.
- 3) MPO activity has significantly climbed after aspirin administration and was inhibited in alkaline ionized water group.
- 4) Concentration of inflammatory cytokines (TNF- α , IL-1 β) in gastric mucosa has significantly risen after aspirin administration, and was inhibited by administration of alkaline ionized water.

Conclusion

Effect of alkaline ionized water against gastric mucosal injury caused by aspirin, the representative NSAID, was confirmed. As part of its mechanism, a possibility is indicated that inhibitory function of active neutrophil and inflammatory cytokine production of alkaline ionized water is involved. Recently, it was reported that TNF- α plays a major role in triggering gastric mucosal injury caused by aspirin and resulting in apoptosis of gastric mucosa. We would like to further examine DNA fragmentation in vivo after aspirin administration to study other effects of alkaline ionized water.