Protective Effect of Taurine against Ammonia-Induced Gastric Mucosal Lesions in Rats

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Abstract—We examined the role of gastric ammonia in the development of gastric lesions in rats. Exposure of the gastric mucosa to ammonia (30 mM) produced microscopic injury, but no macroscopic lesion was observed. However, exposure of the stomach to ammonia in rats subjected to ischemia resulted in macroscopic gastric lesions. The macroscopic lesions were markedly inhibited by pretreatment with taurine, a scavenger of hypochlorous acid (HOCl) and monochloramine (NH₂Cl). These results indicate that ammonia is deleterious to gastric mucosa, and monochloramine may be involved in the pathogenesis of ammonia-induced mucosal lesions.

Recent evidence suggests that reactive oxygen metabolites (O₂⁻, H₂O₂) are mediators of the tissue injury associated with ischemia (1, 2). In the ischemic stomach of the rat, xanthine oxidase and neutrophilic myeloperoxidase (MPO) are activated (3). Superoxide anion (O₂⁻) is reduced spontaneously or by superoxide dismutase to H₂O₂. H₂O₂ oxidizes Cl⁻ in the presence of MPO to yield hypochlorous acid (HOCl), which reacts with NH₃ to yield monochloramine (NH₂Cl) (4, 5).

Recent evidence has demonstrated that the stomach with *Campylobacter pylori* (CP) infection contains a high concentration of toxic ammonia and that CP infection is associated with active chronic gastritis (6, 7). However, the pathophysiological role of elevated ammonia in the stomach is unknown. We recently demonstrated that exposure of the stomach of rats to ammonia or urea with urease resulted in gastric mucosal lesions (8–10). High concentrations of ammonia (0.5–1.0%) caused macroscopic lesions, but low concentrations (0.025–0.1%) produced only microscopic injury (7). We hypothesized that ammonia damages the gastric mucosa via conversion to NH₂Cl, a potent

toxic oxidant. In this study, we have examined whether or not taurine (H₂NCH₂-CH₂SO₃H), a scavenger of HOCl and NH₂Cl, protects gastric mucosa against the deleterious effect of ammonia.

Male Sprague Dawley rats (220–250 g) were deprived of food, but allowed free access to water for 24 hr prior to the experiments. Rats were anesthetized with urethane, and an ex vivo gastric chamber was prepared (11). The chamber was filled with 2 ml of saline, and transmucosal potential difference (PD) was continuously recorded as an index of mucosal integrity. Rats were subjected to ischemia (reduction of blood pressure to 30 mmHg by withdrawal of blood from femoral vein) with or without exposure of the gastric mucosa to 30 mM ammonia (ca. 0.05%). Ammonia was diluted in saline. Pretreatment with taurine was given 30 min before administration of ammonia. The animals were killed after 1 hr exposure to ammonia, and the stomach was examined for macroscopic lesions under a dissecting microscope. The area of each lesion was measured, and the summation of areas was used as the total lesion area (mm²). Statistical analysis was performed using Student's *t*-test.

Fig. 1. Effect of ischemia, ischemia plus 30 mM NH₃, and 30 mM NH₃ on gastric mucosa. Ischemia or NH₃ alone did not produce macroscopic lesions. Exposure of the gastric mucosa to ammonia in rats subjected to ischemia produced macroscopic hemorrhagic erosions. Pretreatment with taurine significantly inhibited ammonia plus ischemia induced lesions.

Withdrawal of blood (3–3.5 ml) from the femoral vein resulted in a reduction of systemic blood pressure to about 30 mmHg. In rats subjected to ischemia alone, transmucosal PD level was decreased for only a short period, and no macroscopic lesion was observed. In contrast, when rats were subjected to ischemia before the gastric mucosa was exposed to 30 mM ammonia, significant macroscopic gastric lesions and a marked decrease in transmucosal PD were observed after exposure to ammonia. Pretreatment with taurine (instillation of 2 ml of 250 mM taurine into the gastric chamber for 30 min) significantly inhibited both the development of ammonia-induced macroscopic lesions and the decrease in transmucosal PD. Exposure of the gastric mucosa to 30 mM ammonia without ischemia resulted in a slight decrease of transmucosal PD and histological gastric mucosal injury, but no macroscopic lesion was observed (Figs. 1 and 2).

Recent evidence has indicated that the ammonia in the stomach is produced from hydrolysis of urea by the urease of CP (6). Our study demonstrated that 30 mM ammonia induced macroscopic mucosal lesions in the pathological state of ischemia. In the ischemic state, superoxide anion, H₂O₂, and HOCl increase due to activation of neutrophilic oxidase or conversion of xanthine

Fig. 2. Effect of ischemia and ischemia plus 30 mM NH₃ on gastric transmucosal potential difference (PD). Normal stomach generated a stable PD of -35~-40 mV (mucosa negative) under the present condition before instillation of ammonia and/or ischemia. The change in PD was calculated by expressing the PD as a percentage of PD before exposure of the stomach to ammonia and/or ischemia. Ischemia plus ammonia produced a marked decrease in PD (○-----○). Pretreatment with taurine inhibited the fall of PD in rats subjected to ammonia plus ischemia (○—○).

dehydrogenase to oxidase. HOCl is unstable and reacts with endogenous nitrogen compounds such as ammonia and taurine to yield derivatives containing a nitrogen-chlorine (N-Cl) bond (5, 12). The reaction of HOCl with NH_3 yields NH_2Cl . NH_2Cl is a powerful oxidizing agent that reacts rapidly with target cell components. In contrast, the reaction of HOCl with taurine yields taurine-chloramine (TauNHCl). TauNHCl is hydrophilic and has little toxicity as an oxidant (12). Taurine acts as a scavenger of HOCl and NH_2Cl , protecting cells against oxidative attack of NH_2Cl by competing with NH_3 for reaction with HOCl.

Thus the protective effect of taurine against the deleterious effect of ammonia plus ischemia suggests that ammonia damages gastric mucosa by its conversion to NH_2Cl .

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