THE EFFECT OF PLASMA LIPIDS ON GASTRIC MUCOSAL PROTECTION IN STRESS ULCER

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SUMMARY : Besides the well known components of the gastric mucosal barrier, the role of gastric phospholipids in other words gastric surfactant is a new concept and yet it remains to be studied more. In this study, hypercholesterolemic rats which were subjected to restraining and cold stress were compared to their controls by means of gastric ulcer scores, mucosal phospholipid, cholesterol, total lipid and mucin contents. Since our results showed that the mucosae of hypercholesterolemic rats are more resistant to stress than those of controls we conclude that gastric mucosal lipids might be an important component of gastric mucosal barrier.

Key Words: Gastric barrier, gastric surfactant, hypercholesterolemia stress ulcer.

INTRODUCTION

It has been shown that the gastric mucosal barrier prevents self digestion by pepsin and acid secretion by several components. These are mucin, bicarbonate secretion, mucosal blood flow and the cytoprotectivity of gastric mucosa (1-6). It is generally accepted that back diffusion of hydrogen ions is prevented by these components.

Recently the phospholipid content of gastric mucosa has been proposed an another component of the barrier (1,5,6). Since there is a close similarity between the composition of lung surfactant and mucosal phospholipids, this component is also named as a gastric surfactant (7,8).

Gastric phospholipids forming a hydrophobic mucosal surface between luminal secretions and the epithelium may repel H^+ ions and keep the surface of the epithelium dry by preventing the contact of luminal acid. Indeed the repelling of H^+ ions from the gastric epithelium is an important hypothesis to explain the protective mechanism of the mucosal phospholipid component of the gastric barrier.

If this hypothesis is true the change in the composition and content of the lipid component would play a significant role in breaking down the barrier, based on the pathophysiology of gastric ulcers.

Observations the differences in the phospholipid patterns of ulcerated and control gastric tissue has supported this idea. Strong support for this hypothesis comes from a study by Duane *et al.* (9) who found a strengthening effect with the addition of cholesterol. Lichtenberger *et al.* (10) also examined the mucosal protective effect of cholesterol in his study, Öner *et al.* (11) showed that there was a significant increase in gastric mucosal phospholipid, mucin and cholesterol content and a decrease in acid output in hypercholesterolemic rats.

Lysolecithin, bile salts and ASA have a weaking effect on the gastric barrier by disturbing the membrane lipids (1,2,6,9,12) which are under the control of their plasma levels (8,13). When taking these studies into consideration it may be assumed that gastric protective capacity may be influenced by the changes in plasma lipid levels which are strongly related to the cholesterol intake. In another words hypercholesterolemia may have a clinical importance for producing a gastric protectivity and resistance to stress ulcer.

This study was designed to investigate the role of plasma lipid levels in the resistance of stressed gastric mucosae in hypercholesterolemic rats.

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MATERIALS AND METHODS

Nine, three and a half months old albino rats were fed with a diet containing 1% cholesterol for six weeks. The rats were subjected to restraining stress at 4©C for six hours. At the end of restraining stress, the nine hypercholesterolemic rats and ten normocholesterolemic rats were anesthetized with light ether and their abdomens were opened by midline incision. The lowermost level of the esophagus was tied preserving the vagal nerves and vessels. A catheter placed through the duodenum into the stomach was used for repeated gastric irrigation with 37©C saline. 2 ml of distilled water (pH 7) were passed into the stomach via this catheter. The water remained for 30 minutes and was then examined for the titration of acidity with 0.01 N NaOH using Toepfer solution as an indicator.

Then the stomachs of the control and hypercholesterolemic rats were opened by lesser curvature and examined with loupes for the number of ulcers and petechial bleedings. For scoring of the ulcers 3 areas of petechial bleedings were accepted as one ulcer. Half of the gastric mucosa was used in the determination of acidic mucopolysaccharides using the method of Corne *et al.* (14). The remaining gastric mucosa was scraped off and stored at -17© C and used for lipid extraction. After extraction of blood and mucosa with Folch's method the remainder was used for cholesterol and phospholipid determinations (15).

RESULTS

The mean weight of the control rats was 204.1 ± 30.2 g and of hypercholesterolemic rats was 196.2 ± 23.9 g.

A diet rich in cholesterol for six weeks caused a significant increase in plasma cholesterol levels. The mean plasma cholesterol was found to be 72.7±10.5 mg/dl in control group and 143.3±28.5 mg/dL in experimental rats (p<0.001, Figure 1).

FIgure 1: Total plasma cholesterol, mucosal cholesterol and phospholipid.

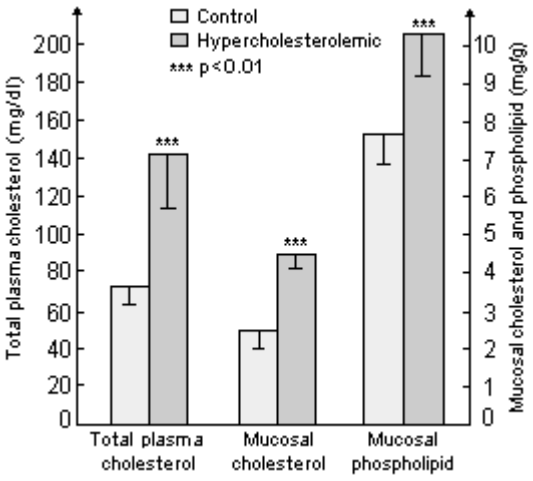
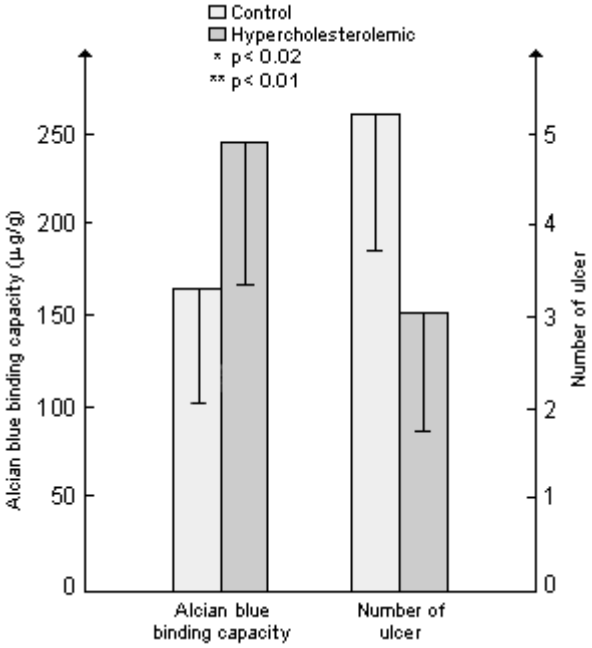


FIgure 2: Alcian blue binding capacity and number of ulcers.



The mean gastric acid output was increased to 8.5±1.2 mEq/hour from 7.8±4.4 mEq/hour. However this increase was not significant.

The mean alcian blue binding capacity of gastric mucosa which is accepted as an indicator of acidic mucopolysaccharide content was 245.2±78.4 µg/g tissue in hypercholesterolemic rats. It was significantly higher than that of control rats (166.2±60 µg/g tissue) (p<0.02, Figure 2).

The cholesterol content of gastric mucosa was elevated from 2.5±0.4 mg/g to 4.5±0.3 mg/g (p<0.001) and the gastric mucosal phospholipid content was found to increase from 7.6±0.8 mg/g to 10.3±1.05 mg/g due to hypercholesterolemia (p<0.001, Figure 1).

The number of gastric ulcers was 5.21±1.5 in the control group and 3.08±1.3 in the hypercholesterolemic animals. This decrease in the mean ulcer count was also statistically significant (p<0.01, Figure 2).

DISCUSSION

Our previous study (11) evaluating the effect of high cholesterol intake on hydrophobic component of gastric mucosa in rats showed that there is a close relationship between nutrition and gastric barrier. In this mentioned study a significant elevation of gastric mucosal cholesterol content due to high blood cholesterol levels was

observed. However the protective importance of this increase in mucosal cholesterol has not been studied properly before.

Therefore our present report showing the protective capacity of increased cholesterol in gastric mucosa of hypercholesterolemic rats subjected to restraining and cold stress might have a clinical importance. Togetherness of high mucosal cholesterol and phospholipid with a low ulcer count as well as elevated gastric mucin in our stressed animals has obviously pointed out gastric mucosal resistance.

Studies indicating a positive correlation between plasma lipids, arachidonic acid and gastric mucin secretion as well as gastric mucin secretion as well as gastric cytoprotectivity of prostaglandins (1-4,16,17) seem to back up the hypothesis which relies on the barrier weaking effect of factors impairing the membrane phospholipids (1,6,9,12).

A strong support for the present study comes from the report of Lichtenberger *et al.* (10) who demonstrated the protective effect of phospholipid addition into gastric lumen of rats subjected to ulcerogenic dose of acid.

In our study we did not find a significant change in gastric acidity. According to Davenport (18) who accepts the low acidity as an indicator of H^+ ion back diffusion this unchanged acidity may also be a positive remark for strengthening of gastric barrier.

As a result this study showed that diet induced hypercholesterolemia helps for maintaining the mucosal integrity against stress. However the clinical of this experimental finding remains to be studied in details.

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