Effect of Thyroid Hormone on Gastric Mucus Secretion Around Indomethacin Induced Gastric Ulcers in Rats

F.S. Oluwole and M.T. Saka

The effect of thyroxine on adherent gastric mucus content around indomethacin-induced gastric ulceration was studied in rats. Three groups of animals were used. The first group, which served as control was fed with normal rat’s cubes and water given ad-libitum. The second group was treated with thyroxine (6.8 µg/100 g body weight/day) for 35 days while the third group had misoprostol at a dose of 0.875 µg/100 g body weight for 35 days. Thyroxine and misoprostol significantly reduced the degree of ulceration and increased adherent gastric mucus content when compared to control group (p<0.05). This result indicates that the gastro-protective property of thyroxine was associated with higher values of adherent gastric mucus content, which explains the ability of the hormone to cause rapid production of gastric mucus. These results suggest that gastric mucus involvement in gastro protection could be linked to mucus glycoproteins.

Key words: Thyroxine, misoprostol, adherent gastric mucus, ulceration
INTRODUCTION

The epithelium of the stomach is intrinsically resistant to the damaging effects of gastric acid and other insults. The gastric epithelium is covered by a continuous layer of secreted mucus and bicarbonate which have been widely implicated as an important pre-epithelial protective factor against autodigestion of the gastric mucosa by acid and pepsin (Copeman et al., 1994). The adherent mucus is considered to be the main factor protecting the gastric mucosa (Azzumi et al., 1993). It has been reported that a decrease in gastric mucus render the mucosa more susceptible to injury induced by various aggressive factors (Leonard et al., 1994).

Takezono et al. (2004) suggested that when gastric surface mucus cells are exposed to acid, gastric epithelial permeability decrease rapidly to inhibit acid back-diffusion. Prostaglandins play an important role in this protective response to acid exposure (Hawkey, 1996). Misoprostol was reported to be a potent inhibitor of gastric acid and also increase mucus secretion in man (Wilson et al., 1986).

Misoprostol is a novel synthetic analog of prostaglandin E1 (Dajani, 1987) and has been found to be effective against NSAID-induced gastric and duodenal ulcers (Simon, 1999). It was suggested that thyroxine-ameliorating effect on indomethacin-induced gastric ulceration may be due to increased biosynthesis of gastric mucus (Adeniyi and Oluwole, 1990). In this study, we examined the effect of thyroxine on gastric mucus secretion around indomethacin-induced gastric ulceration.

MATERIALS AND METHODS

Animals: Adult male wistar strain rats (180-260 g) obtained from Preclinical Animal House, College of Medicine, University of Ibadan was used for this study. These rats were randomly divided into two experimental study groups; indomethacin-induced gastric ulceration and adherent gastric mucus content.

Each study group has twenty-four male rats divided into three treatment groups of 8 rats per group. Control animals were not given any drug but were fed normally and given water ad libitum, thyroxine-treated were given thyroxine (6-8 μg/100 g body weight per day) for 35 days and misoprostol-treated were given misoprostol orally at a dose of 0.86 μg/100 g body weight per day for 35 days.

Indomethacin-induced gastric ulceration: Gastric ulceration was induced in the animals using the technique earlier described by Adeniyi and Oluwole (1990). Forty mg kg⁻¹ body weight of indomethacin suspension was administered by oral route using oral dosing needle. All animals were deprived of food, but not of water 24 h before the experiments. Indomethacin produced gastric ulceration in intact male rats in 4 h, a finding similar to that earlier reported by Adeniyi and Oluwole (1990). The rats were later killed by a blow to the head and their stomachs examined macroscopically for the scoring of gastric ulceration as described by Alphin and Wards (1967).

Scoring system

<table>
<thead>
<tr>
<th>Ulcer score</th>
<th>Criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>Normal stomach</td>
</tr>
<tr>
<td>0.5</td>
<td>Pin-point ulcers</td>
</tr>
<tr>
<td>1</td>
<td>Two or more small haemorrhagic ulcers</td>
</tr>
<tr>
<td>2</td>
<td>Ulcers greater than 3 mm in diameter</td>
</tr>
</tbody>
</table>

Determination of adherent gastric mucus content: Adherent gastric mucus was determined by the method of Corne et al. (1974). The stomach of each animal was removed, opened along the great curvature and rinsed in cold saline. The glandular part of the stomach was excised, weighed and immersed for 2 h in 10 mL of 0.1% w/v Alcian blue (sigma) in 0.16 M sucrose solution. The excess dye was removed by rinsing twice in 0.25 M sucrose solution (15 min each). The mucous-bound dye was extracted by immersing the gastric tissue in 0.5 M MgCl₂ solution, which was intermittently shaken for 1 min at 30 min intervals during a 2 h period. The blue extract was shaken with diethyl ether. The emulsion was then centrifuged at 3600 rpm for 10 min and the optical absorbance of the aqueous phase was measured at 605 μm using spectrophotometer. The absorbance of each solution was used to calculate the concentration of dye and the weight of dye expressed in mg was deduced. The results are expressed as weight of dye per gram of tissue (mg/g tissue).

RESULTS

The results obtained in Table 1 shows that rats in control group with a Mean Ulcer Score (MUS) of 20.80±0.78 had significant increase than the rats treated with thyroxine, 3.38±0.80 and Misoprostol-treated rats with mean ulcer score of 0.50±0.27 (p<0.05).

Rats treated with thyroxine have mean adherent gastric mucus content of 0.204±0.061 while those treated with misoprostol have a mean gastric mucus content of 0.452±0.048. From the result, both thyroxine and misoprostol significantly increased adherent gastric mucus content in this study (p<0.05) (Table 2).
Table 1: The mean ulcer scores in rats given different treatments

<table>
<thead>
<tr>
<th>Treatments</th>
<th>No. of animals</th>
<th>Mean ulcer score</th>
<th>p&lt;0.05</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>8</td>
<td>20.8±0.78</td>
<td></td>
</tr>
<tr>
<td>Thyroxine-treated rats (35 days)</td>
<td>8</td>
<td>3.3±0.80*</td>
<td></td>
</tr>
<tr>
<td>Misoprostol-treated rats (35 days)</td>
<td>8</td>
<td>0.50±0.27*</td>
<td></td>
</tr>
</tbody>
</table>

Values are Mean±SEM. *p<0.05 compared with control, S = Significant.

Table 2: The mean adherent gastric mucus content in rats given different treatments

<table>
<thead>
<tr>
<th>Treatments</th>
<th>No. of animals</th>
<th>Mean adherent mucus content (mg g⁻¹)</th>
<th>p&lt;0.05</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>8</td>
<td>0.07±0.006</td>
<td></td>
</tr>
<tr>
<td>Thyroxine-treated rats (35 days)</td>
<td>8</td>
<td>0.20±0.061*</td>
<td></td>
</tr>
<tr>
<td>Misoprostol-treated rats (35 days)</td>
<td>8</td>
<td>0.45±0.048*</td>
<td></td>
</tr>
</tbody>
</table>

Values are Mean±SEM. *p<0.05 compared with control, S = Significant.

DISCUSSION

The role of thyroxine in the possible protection of gastric mucosa has been controversial due to the previously reported effect of thyroxine that it enhances basal and secretagogue induced gastric acid secretion (Adeniyi and Olowokorun, 1989) and also chronic administration of thyroxine increased gastric acid secretion and reduced total ulcer scores induced by indomethacin (Adeniyi and Oluwole, 1990).

Present findings in this study showed that both thyroxine and misoprostol significantly reduced the degree of ulceration with respect to control (Table 1) (p<0.05). In another study (Table 2), a significant increase of adherent mucus content was found in thyroxine and misoprostol pretreated groups with adherent gastric mucus content values at 0.20±0.06 and 0.45±0.05 respectively, as compared with 0.07±0.01 in the control rats (p<0.05).

The results of this research strongly confirmed that thyroxine significantly stimulate an increase in gastric mucus. This supports the concept of Hodin et al. (1996) that thyroid hormone is an important regulator of gut mucosal growth, differentiation and barrier function. Takezono et al. (2004) recently reported that increased level of exposed gastric surface mucus to acid is related to reduction in gastric epithelial permeability which is said to in-turn inhibit acid back-diffusion.

Though indomethacin is known to trigger oxygen free radicals as a means of causing gastric injury. To cope with this situation, gastric mucus was reported to possess antioxidant properties because of its rich glycoprotein content (Cross et al., 1984) which was put at 50 mg mL⁻¹ (Allen, 1981). The mucus glycoproteins and the lipids bound to gastric mucus have been found to protect the mucus against oxygen attack (Gong et al., 1986).

The mechanism of action of thyroxine appears similar to known drugs like misoprostol now used in the treatment of peptic ulcer which by virtue of the fact that it stimulates mucus secretion (mucogenic effect) also has its anti ulcer efficacy in man (Wilson et al., 1986).

REFERENCES


