EFFECT OF WATER-IMMERSION STRESS ON PROSTAGLANDIN E₂ IN RAT GASTRIC MUCOSA

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Summary

We investigated the effect of stress on the prostaglandin E₂ levels in rat gastric mucosa. In untreated controls, prostaglandin E₂ levels were higher in the antral than the fundic mucosa. Stress experiments showed that 30-min stress induced no gastric lesions but effected a significant (p<0.05) increase in antral prostaglandin E₂; after 7-hr stress exposure, hemorrhagic lesions and prostaglandin E₂ levels significantly (p<0.05) below normal control values were noted. The formation of HCl-induced gastric mucosal lesions was markedly inhibited if 30-min stress preceded HCl-administration. The infusion of 5 μg/kg 16, 16-dimethyl prostaglandin E₂ prior to 7-hr stress exposure inhibited ulcer formation markedly. Our results suggested that stress-induced decrease in intramucosal prostaglandin E₂ plays an important role in the pathogenesis of stress ulcer formation.

Key Words: prostaglandin E₂, intramucosal prostaglandin E₂, stress, gastric mucosal lesion, cytoprotection.

Introduction

Clinical experience suggests that stress plays a role in the induction of gastric mucosal lesions. Regarding the pathogenesis of stress ulcer, a reduction in the gastric mucosal blood flow¹,²) and an acceleration of gastric secretion³, ⁴) have been mentioned. However, to our knowledge, the endogenous prostaglandin (PG) levels in the gastric mucosa have not been investigated under stress conditions.

The gastric mucosa is protected against many ulcerogens by various PG compounds and their synthetic analogues⁵⁻¹³) and it has become clear that they represent an important part of the gastric mucosal barrier. However, only few studies on intramucosal PG have been reported, probably because of the difficulties encountered in the extraction and purification of these PG¹⁴⁻¹⁶). In our earlier investigation¹⁷) we noted that the previously reported procedures of PG extraction were relatively crude and unreliable, and established a new assay method to determine the PG level in the rat gastric mucosa.

The present study was undertaken to examine the pathogenesis of stress ulcer by investigating the effect of stress on PGE₂ levels in the rat gastric mucosa.

Materials and Methods

Male Wistar rats weighing 180–250 g were
fasted overnight before use. To induce stress, the animals were restrained and immersed in 23°C water for 30 min, 2 or 7 hrs. Control rats were untreated.

1. Separation of Mucosal Tissue Layer and PGE₂ Determination

The animals were sacrificed by decapitation. The stomach was excised, opened along the greater curvature and washed with tap water. Tissue from the fundus and the pyloric antrum was cut into 1 x 1 cm pieces, mounted mucosal side down on a glass slide and covered with another glass slide. Each preparation was immersed in hexane in a dry ice-acetone bath, so that the frozen tissue adhered tightly to the slides. The mucosal tissue layer was obtained by pulling the two slides apart rapidly (Fig. 1).

The mucosal tissue was weighed and homogenized in 5 ml methanol, using 1,000 cpm ³H-PGE₂ (The Radiochemical Centre, Amersham) as recovery markers. The homogenizer was washed out with 10 ml chloroform and the resultant solution was mixed vigorously with the homogenate, which was allowed to stand for 30 min. Lipids except PGs were removed with carbon tetrachloride, PGs in residue were subjected to thin-layer chromatography to separate PGE. Radioimmunoassay (RIA) was employed for PGE₂ determination, using PGE₂-antiserum (Ono Pharmaceutical Co., Ltd., Osaka, Japan) with a cross-rativity of 67.7% with PGE₁, 10.8% with PGB₁, 17.6% with PGB₂ and of <0.65% with PGF₁α and PGF₂α (Fig. 2).

2. Effect of 30-min Stress on HCl-Induced Gastric Mucosal Lesions

The rats were stressed for 30 min and then 2 ml of 0.6N HCl infused intragastrically 30 min prior to decapitation. Control rats were not stressed but otherwise treated identically.