Healing Process of Acetic Acid-Induced Gastric Ulcer and Gastric Mucosal Prostaglandin E Generation Level in Rats

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Abstract—The prostaglandin E (PGE) generation level (PGE level) in the gastric mucosa was investigated in relation to the healing and relapse of acetic acid-induced gastric ulcers in the rat. The PGE level around ulcers showed higher levels after ulcer induction and decreased during the ulcer diminishing period. Thereafter, the PGE levels showed an inclination to increase during the ulcer exacerbation period. In reulcerated rats, PGE levels were significantly higher. In conclusion, a high level of PGE may indicate an ulcer exacerbation state.

Prostaglandin has been widely accepted to play an important role in gastric protection. Recently, the present authors reported a correlation between the PG12 level around ulcers and the healing or exacerbation of acetic acid ulcers (1).

This communication describes the healing process of acetic acid-induced gastric ulcers observed with an endoscope for 203 days and the results of examining the correlation between the gastric mucosal PGE generation levels (PGE levels) around ulcers and the healing process of acetic acid-induced gastric ulcers.

The animals used were Sprague-Dawley strain (Slc:SD) male rats weighing from 220 to 240 g (7 weeks). Acetic acid-induced ulcers were prepared according to the method of Takagi et al. (2) (20%, 0.05 ml). The observation of ulcers and the determination of ulcer-size [Ulcer index (UI) = length (mm) × width (mm)] were performed according to the method of Fukawa et al. (3) at 3, 10, 20, 35, 50, 70, 91, 112, 133, 154, 175 and 203 days after ulcer induction. Cumulative healing and relapse rates (1) were calculated according to the method of Kaplan and Meier (4), because the rats were sacrificed at appropriate intervals for measuring the PGE levels. Determinations of the generation of mucosal PGE were performed on days 3, 20, 50, 91, 154 and 203 according to the methods of Whittle (5). Rats were classified into four groups as follows: 1) Normal rats, 2) Non-healed rats: Ulcer has not been healed, 3) Healed rats: Healing of ulcer has been confirmed by endoscopy, and 4) Reulcerated rats: Healed ulcer reulcerated on Day 154 or 203 (Table 1). To determine the PGE level, a [3H]-Prostaglandin E Radioimmunoassay Kit (Clinical Assays, Division of Travenol Laboratories, Inc.) was used. The results were represented as means±S.E. Statistical analysis was performed by Student’s t-test.

The UI value was 45.6 on Day 3, and it decreased with time. The first healed case appeared on Day 20 and cumulative healing rate was 46.7% on Day 203. The first relapsed case appeared on Day 50, and the cumulative relapse rate was 46.7% on Day 203. The evolutionary phase of acetic acid-induced gastric ulcers was divided into the following periods as reported previously (6): 1) Ulcer diminishing period (Days 3 to 50 after ulcer induction), 2) healing period (Days 35 to 150 after ulcer induction), and 3) ulcer exacerbation period (Days 50 to 203 after ulcer induction).

The time course of the PGE level is shown in Fig. 1. In the present study, on Day 3, the PGE level in the ulcer-induced rats was lower
Table 1. Number of sacrificed rats on each day

| Days after ulcer induction | 3   | 20  | 50  | 91  | 154 | 203 |
|---------------------------|-----|-----|-----|-----|-----|-----|
| Normal rats               | 10  | 10  | 10  | 10  | 9   | 5   |
| Ulcer-induced rats        |     |     |     |     |     |     |
| Non-healed rats           | 11  | 6   | 19  | 16  | 14  | 12  |
| Healed rats               | 3   | 10  | 9   | 7   | 7   | 7   |
| Reulcerated rats          |     |     |     |     |     |     |

Fig. 1. Time course of PGE level in gastric mucosa around the ulcer. Bars represent the mean±S.E. **: Significant difference from normal rats (P<0.05, 0.01). †: Significant difference from non-healed rats on Day 20 (P<0.05). ‡: Significant difference from healed rats on Day 203 (P<0.05).

In conclusion, it was suggested that PGE levels around ulcers change with the ulcer healing or exacerbation and that a high level of PGE may indicate an ulcer exacerbation state.

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