RAPID COMMUNICATION

Preventive Effect of Salmon Calcitonin on Restraint-Induced Gastric Ulcer in Rats

Synopsis Salmon calcitonin was effective in preventing restraint-induced gastric ulcer production in rats. Moreover, calcitonin was also effective in preventing progress of ulcer formation even when calcitonin was administered 2 hr after initiation of restraint.

It was proposed that porcine calcitonin (CT) was effective in inhibiting human gastric acid secretion which was evoked by gastrin administration (Hesch *et al.*, 1971). Recently porcine CT was shown to prevent the ulcer production in Shay rat (Orimo *et al.*, 1972) and the ulcer production by reserpine, gastrin or serotonin (Matsumoto *et al.*, 1972).

In this report, we tested the effect of salmon CT (SCT) on gastric ulcer which was formed by immersing rats in cold water. Male Wistar rats weighing 260–290 g. were divided into three groups, each group consisting of ten animals:

- Group A: SCT was injected subcutaneously at a dose of 16 MRCU/kg body weight 1 hr before the initiation of restraint.
- Group B: SCT was injected subcutaneously at a dose of 16 MRCU/kg body weight 2 hr after initiation of restraint.
- Group C: Vehicle solution was injected subcutaneously 1 hour before initiation of restraint.
1% Na acetate solution adjusted to pH 4 and containing 1% bovine serum albumin was used as vehicle.

Animals were given stock diet and water *ad libitum* until the initiation of the experiment. Each animal was restrained in a metal cage of body size and immersed in water of 25°C up to the height of the xyphoid process for 5 hr. Animals were killed and stomach was opened from the side of the greater curvature. Ulcer index was determined according to the number and extent of ulcer which was measured macroscopically. The experiment of the same design was repeated.

As was shown in Table 1, it might be concluded that SCT was effective in preventing the production of the stomach ulcer which was formed by immersing rats in water for 5 hr. Only one animal in first experiment showed ulcer index 4 (Table 1). SCT was also effective in preventing ulcer production in animals in which CT was administered even 2 hr after initiation of restraint.

As to the pathogenesis of restraint-induced ulcer production, an increase in the free acid concentration was observed under restraint, accompanied by a diminution of secretory volume (Bonfils *et al.*, 1963) and Ader (1960) also proposed that there was an increase in blood pepsinogen in ulcer-bearing rats. Vascular, splanchnic and neuro-endocrine factors also contribute to the production of restraint-induced ulcer in rat (Bonfils *et al.*, 1963). According to the experiment of Charbon (1971), CT inhibited the parathyroid extract-induced augmentation of celiac flow and SCT diminished pepsin output after stimulation of pentagastrin. While CT was reported to decrease the acidity and volume of gastric juice in man (Hesch *et al.*, 1971), CT may inhibit the action or secretion of gastrin. Perhaps CT may prevent

Table 1. Effect of SCT in restraint-induced gastric ulcer

Dose of CT (MRCU/kg) Time of CT administration	Group A 16		Group B 16		Group C vehicle	
	1 hr before restraint		2 hr after restraint		1 hr before restraint	
	Exp. 1	Exp. 2	Exp. 1	Exp. 2	Exp. 1	Exp. 2
No. 1	—	—	++	—	+++	++
2	++++	++	++	—	++	+++
3	—	—	++	—	++	—
4	++	—	—	—	++++	++
Score	5	—	—	++	++++	++
6	+	—	—	++	+++	++
7	—	—	—	—	+	died
8	—	+	+	—	++	+
9	—	—	—	—	+++	+
10	—	—	+	—	+++	++++
Mean of Index	0.7	0.3	0.8	0.4	2.7	1.9

Score and Index are as follows:

—, 0: neither bleeding nor hyperemia observed, $\pm$, 0.5: no bleeding but hyperemia present, + & 1, ++ & 2, +++ & 3, ++++ & 4 represent number of bleeding spots <2, 3–7, 8–13, and <14 and diameter of bleeding area < 3 mm, 3–5 mm, 5 mm or 1/3 of total area of stomach and $\geq$ 1/3 of total area of stomach respectively.

the restraint-induced ulcer production by influencing hemodynamics of the stomach or gastrin secretion.

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