Itch: Role of Prostaglandins

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Summary

Prostaglandin E, lowers the threshold of human skin to histamine-evoked itching. Though histamine and other mediators may produce itching by a direct action, itching in inflamed skin can also be explained by a pharmacological synergism in which low concentrations of prostaglandins, which do not themselves cause itching, potentiate itching due to histamine and possibly other agents. Alteration of threshold responses of components of inflammation to other mediators may be an important general role of prostaglandins.

Introduction

Itch is the predominant symptom of skin disease but its pharmacological mechanism has up to now been obscure and its treatment empirical. We now present evidence that prostaglandins, known to be present in increased amounts in inflamed skin (Angård et al., 1970; Greaves and Søndergaard, 1970; Greaves et al., 1971; Arturson et al., 1973), contribute to itching indirectly by lowering the itch threshold of skin.

Patients and Methods

The 26 patients studied were of both sexes (age range 12-79 years) suffering from localized non-inflammatory skin conditions and were not taking antipuritic or anti-inflammatory drugs at the time of the study. Their informed consent was obtained in every instance.

Prostaglandin E, was obtained from Upjohn Ltd. and bradykinin from Sandoz Ltd. Histamine acid phosphate concentrations were expressed as histamine base. Phosphate-buffered saline (pH 7.6) was used as a diluent.

Histamine causes pain when injected intradermally, but itching when applied intraepidermally (Keele and Armstrong, 1964). The interaction between histamine itching and prostaglandin E, was investigated in the following manner. The skin of the flexor surfaces of both forearms was prepared by washing with ether. Three 1 cm² areas were lightly scarified on each arm with a No. 12 needle. Great care was taken to avoid any bleeding. A 1 cm³ piece of gauze soaked in prostaglandin E, or phosphate-buffered saline was placed on each scarified area, and left for 30 minutes. Five minutes after removal of the gauze 0.1 ml of histamine 10 μg/ml was placed on the scarified skin and left for two minutes followed, at 2-minute intervals after drying, by increasing concentrations of histamine up to 1,000 μg/ml until itching occurred, whichever was first. A control, in which buffered saline was applied, preceded histamine at each site. The itch threshold was the lowest concentration of histamine which produced itching. In all experiments the concentration of prostaglandin E, used was 1 μg/ml, since higher concentrations sometimes caused oedema which modified itching. Prostaglandin E, did not cause itching by itself either in this or in higher concentrations. In each patient three paired comparisons of saline-treated and prostaglandin-treated sites were made using symmetrical sites, and the allocation of prostaglandin or saline to the six sites on the two arms was random. The itch threshold for the prostaglandin-treated and saline-treated sites was calculated as the mean of the three determinations.

Results

The effect of prostaglandin E, on itch threshold was studied in 23 subjects. In the concentration used, prostaglandin E, did not by itself cause itching after application to scarified skin. Prostaglandin E, increased sensitivity to itching evoked by histamine in 20 of the 23 subjects. In one the sensitivity was lowered and in the remaining two it was unchanged. The mean itch threshold on the prostaglandin-treated site was 115 μg/ml ± 18 S.E. of mean histamine compared with 264 μg/ml ± 41 S.E. of mean on the saline-treated site (see fig.). This difference is highly significant (P < 0.0005).

Slight erythema occurred at the site of application of prostaglandin E, in a minority of patients. The possibility that in these patients the lowering of itch threshold might have been a non-specific effect of vasodilatation was therefore explored. In three patients the skin was scarified in six sites. Buffered saline was applied to three and bradykinin 3 μg/ml to the remaining three sites. This concentration of bradykinin caused erythema about equal in magnitude to the most intense erythema caused by prostaglandin E, 1 μg/ml has been applied. Control = skin on which buffered saline has been applied.

![Prostaglandin E1 on itch threshold. Each result represents the mean S.E. of mean of 69 observations in 23 subjects and shows lowest concentration of histamine causing itching. PG = skin on which prostaglandin E1 1 μg/ml has been applied. Control = skin on which buffered saline has been applied.](image-url)

Discussion

The present results clearly show that prostaglandin E, lowers the threshold of human skin to histamine-evoked itching. We
New Jejunostomy Feed

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Summary
Three patients with duodenal fistulae were fed solely with an easily prepared, inexpensive jejunalostomy feed for 14, 21, and 23 days respectively. Sodium, potassium, and nitrogen balances became positive, diarrhoea did not develop, and body weight increased. The feed was life-saving: the patients' superficial veins were thrombosed, and percutal feeding was considered undesirable.

Introduction
The intravenous and intragastric routes are the usual alternatives for feeding patients with prolonged intestinal dysfunction or alimentary fistulae who cannot be fed by mouth. However, the former requires continuous supervision and engenders a risk of thrombophlebitis—and caval catheterization to avoid that risk introduces others (Wilmore and Dudrick, 1969; Jones and McIntosh, 1973)—and the intragastric route is not suitable for patients with external fistulae of the duodenum. For these latter patients the intrajejunl route is suitable, but, probably because of the usually associated diarrhoea, has been rather neglected.

The ideal jejunostomy feed should provide an adequate intake of energy, nitrogen, electrolytes, water, vitamins, and essential amino-acids, in a moderate volume of fluid, and should contain the correct proportion of calories derived from carbohydrate, fat, and protein. It should be absorbable without gastric digestion and should not cause diarrhoea. Few previously described formulae fulfill these criteria, and some are also expensive and not easily prepared from materials readily available in a ward kitchen. Therefore, we tried to devise a satisfactory formula with none of these drawbacks.

Methods
The feed consists mostly of milk, with glucose and arachis oil (Prosparol) to provide additional carbohydrate and fat (table 1). Each aliquot is homogenized for five minutes in a blender immediately before administration.

The feed was infused intraduodenally through a gastrostomy catheter (Kay, 1964) or a cholecystectomy T-tube at about