

Increased Suction Blister Concentrations of Prostaglandin E and $F_{2\alpha}$ in Dermatitis Herpetiformis

L. Förström, T. Reunala, H. Vapaatalo¹
and I.-B. Lindén²

Department of Dermatology, University Central Hospital, Helsinki, ¹Department of Biomedical Sciences, University of Tampere and ²Research Laboratories of Medica Ltd, Helsinki, Finland

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Abstract. Prostaglandin (PG) E and $F_{2\alpha}$ concentrations in the fluid of suction blisters were measured by radioimmunoassay in 10 patients with dermatitis herpetiformis (DH). The suction blisters were produced on both inflamed and clinically uninvolved skin on the abdomen. The inflammation was produced by 50% potassium iodide (KI) applied locally. The blister fluid obtained from KI test areas contained on average 12.9 ng/ml of PGE and 26.9 ng/ml of $PGF_{2\alpha}$. The corresponding concentrations in clinically uninvolved skin were significantly ($P < 0.01$) lower, i.e. 3.5 ng/ml of PGE and 12.0 ng/ml of $PGF_{2\alpha}$. Suction blisters were also produced in six controls. The mean concentration of PGE and $PGF_{2\alpha}$ in the KI test area and that of $PGF_{2\alpha}$ in normal skin were significantly ($P < 0.01$) lower than those found in patients with DH. Moreover, none of the controls had measurable amounts of PGE in blister fluid from normal skin. PG concentrations in the fluid of spontaneous blisters were examined in one patient with DH. The values were 4.9 ng/ml and 30.3 ng/ml for PGE and 10.2 ng/ml and 14.0 ng/ml for $PGF_{2\alpha}$. The increased concentrations of PGE and $PGF_{2\alpha}$ in suction blister fluid from clinically uninvolved skin of patients with DH suggest that DH also affects skin devoid of visible lesions. Locally applied KI results in increased blister fluid PG concentrations both in patients with DH and in controls. These findings are compatible with the role PGs seem to play in skin inflammation and blister formation.

Key words: Dermatitis herpetiformis; Prostaglandins; Suction blisters; Potassium iodide

Dermatitis herpetiformis (DH) is a chronic blistering skin disease accompanied by intense itching. The mechanism of itch and blister formation is unknown. IgA and C_3 deposits are common in papillary dermis, and recent studies suggest that complement activation may play an important part in the production of skin lesions in DH (12, 13, 20). In addition to immunological factors, other mechanisms may also be involved. Iodide and other anions are known to cause abnormal cutaneous reactions in patients with DH. Potassium iodide (KI) in particular, used either locally or systemical-

ly, is able to provoke skin lesions which are clinically and histologically similar to the spontaneous lesions of DH (1).

Prostaglandins (PG) have been found to participate in skin inflammation of both toxic and allergic origin (5, 11, 22). Moreover, there is evidence that PGs may act as chemical mediators in the blister formation of burns and of various bullous skin diseases including pemphigoid (2, 4, 21). In the present investigation we have analysed the PGE and $PGF_{2\alpha}$ contents of blister fluid collected by suction from skin inflamed by KI and from clinically uninvolved skin of patients with DH.

METHODS

Patients

Ten patients with DH were examined. The diagnosis of DH was based on a typical clinical picture and histology of the rash and on the demonstration of IgA in the uninvolved skin. All patients were taking dapsone, which was stopped at least 4 days before the examination. None of the patients was on a gluten-free diet. The six control individuals comprised 2 patients with psoriasis, one with atopic eczema and 3 healthy volunteers.

Suction blisters

Epicutaneous tests with 50% KI in petrolatum were performed using the chamber method (16). Six chambers with KI were fixed on the abdomen of each DH patient and control. At this time none of them had skin lesions on the abdomen. The chambers were removed after 24 hours. At that time slight erythema and small papules were seen in the KI test areas of 8 DH patients but not in the controls.

Suction blisters were produced exactly on the KI test areas (inflamed skin) and on the opposite side of the abdomen (uninvolved skin) using a method described by Kiistala (14). This method has proved satisfactory for PG examinations allowing blister formation under controlled conditions (7). In this study the blisters were produced at 20–21°C and the suction pressure was kept between 480 and 540 mmHg.

Radioimmunoassay of PGE and $PGF_{2\alpha}$

Fluid was drawn into a plastic syringe from fully developed blisters. The mean volume obtained from suction blisters was 0.53 ± 0.1 ml in the patients with DH and 0.56 ± 0.2 ml in the controls. The fluid volume was small in spontaneous blisters of patients with DH. A sufficient amount of fluid for PG determinations was obtained from only one patient. The first sample originated from spontaneous blisters less than 24 h old and the second from blisters about 2 h old.

All blister fluid samples were mixed with 0.5 ml ice-cold alcohol, immediately transferred to -20°C and stored until analysed. Before radioimmunoassay the samples were washed with petroleum ether, the pH was adjusted to 3.0 with 1 M HCl and PG extracted with chloroform. Radioimmunoassay kits (Clinical Assays Inc., Cambridge, Mas-

Table 1. Concentrations of prostaglandins E and $F_{2\alpha}$ in suction blister fluid from patients with dermatitis herpetiformis (DH) and from controls

Blister fluid	Patients with DH (n = 10)	Controls (n = 6)	P-value (Student's t-test)
Normal (uninvolved) skin			
PGE	3.5 ± 3 ^a	<1.0	n.s. ^b
PGF _{2α}	12.0 ± 7	3.1 ± 2.5	<0.01
Potassium iodide test area			
PGE	12.9 ± 7	4.8 ± 4	<0.01
PGF _{2α}	29.6 ± 14	10.5 ± 6	<0.01

^a ng/ml, mean ± S.D.

^b Control values approximated to be 1.0 ng/ml.

sachusetts) were used for the determination of PGE and PGF_{2α}. Because of the small sample volume the lower limit for detection of PGE and PGF_{2α} was 1.0 ng/ml.

RESULTS

Mean blistering time

Suction blisters developed somewhat more rapidly in control individuals than in patients with DH (mean 101 ± 19 min vs. 117 ± 10 min) but the difference was not significant. On the other hand, no difference was found in the mean blistering time between the KI test area and clinically uninvolved skin.

PGE and PGF_{2α} concentrations in blister fluid

The results are shown in Table 1. The concentrations of PGE and PGF_{2α} in blister fluid obtained by suction were clearly higher in patients with DH than in controls. Nine of the 10 patients with DH had measurable amounts of PGE in uninvolved skin, whereas none of the blister fluid samples from control individuals showed measurable PGE activity. PGF_{2α} was detected in blister fluid from every patient with DH and in 4 of 6 controls. However, the figures were significantly higher ($P < 0.01$) in patients with DH than in controls.

Blister fluid from the KI test area (inflamed skin) showed markedly higher PG concentrations than blister fluid from uninvolved skin (Table 1). The difference was significant for both PGE and PGF_{2α} in the patients with DH ($P < 0.01$) but only for PGF_{2α} in the controls ($P < 0.05$).

The fluid obtained from spontaneous blisters of one patient with DH contained measurable PG activity; PGE was 4.9 ng/ml in the blister less than 24 h old and 30.3 ng/ml in the blister 2 hours old. The corresponding values for PGF_{2α} were 10.2 and 14.0 ng/ml.

DISCUSSION

This study shows the presence of PGE in the fluid of blisters obtained both by suction and spontaneously from patients with DH. This finding is in agreement with earlier reports demonstrating PGE in spontaneous blisters of other bullous skin diseases such as pemphigoid, pemphigus and erythema multiforme (4, 21). In one previous study the patients with DH were also found to have significantly increased PG activity in blister fluid obtained by suction from uninvolved skin (21). The present results confirm this finding and show that in addition to PGE the concentration of PGF_{2α} is also increased in DH. PGF_{2α} activity has previously been demonstrated in spontaneous blisters of some patients with pemphigoid (6, 21) and elevated concentrations have been found in blister fluid obtained by suction from healthy skin after UVB exposure (3).

In DH the areas susceptible to the rash are the elbows, knees, buttocks and shoulders (1). In this study, suction blisters were produced on the clinically uninvolved skin of the abdomen, i.e. on an area where spontaneous DH lesions are rare. Nonetheless, the PG concentrations were clearly higher than those in the controls. It is interesting that IgA and C₃ deposits are also frequent in the clinically uninvolved skin of patients with DH (13, 19). Thus both chemical and immunological findings indicate that DH also affects skin devoid of visible lesions.

Patients with DH demonstrate abnormal cutaneous reactions to various chemicals including KI and tetrahydrofurfuryl nicotinate (Trafuril). These reactions are most pronounced after 12 to 24 hours, and are clinically and histologically similar to the spontaneous lesions of DH (1, 10, 15, 18). In the present study suction blisters were also produced on skin inflamed by KI of the patients with DH. The concentrations of PGE and PGF_{2α} in blister fluid were found to be significantly higher than those obtained from clinically uninvolved, unpretreated skin. However, an increase in PG concentrations was also found in the controls, although they did not show any visible skin changes after exposure to KI. A

previous study had shown that Trafuril also elicits a skin response in healthy individuals resulting in increased PG concentrations (17). The skin reaction caused by KI or Trafuril in DH therefore seems to be unspecific although it may be mediated by PGs.

In DH a severe burning itch usually precedes the rash (1). Under experimental conditions PGs can potentiate itch by lowering the threshold tolerance of human skin to histamine (8, 9). Although the PG concentrations are high in blister fluid it seems unlikely that PGs are of primary importance in producing itch and skin lesions in DH. Acetylsalicylic acid and other anti-inflammatory agents inhibiting PG synthetase are neither clinically effective nor do they control experimental skin lesions in DH (1, 15). However, the demonstration of increased concentrations of PGE and PGF_{2α} in suction blister fluid from patients with DH is compatible with the role PGs seem to play as chemical mediators in skin inflammation and blister formation.

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Quantitation of Skin Bacteria: Lethality of the Wash Solution Used to Remove Bacteria

Ernest Bloom, Raza Aly and Howard I. Maibach

Department of Dermatology, University of California,
San Francisco, CA 94143, USA

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Abstract. A widely used technique for the quantitative removal of bacteria from the skin uses a detergent, Triton X-100 (*p*, *t*-octylphenoxynonaethoxyethanol), to remove and suspend the bacteria. We determined the half-life for the survival of five common skin bacteria suspended in the solution. The shortest-lived was *Streptococcus pyogenes*