Effects of topical treatment with budesonide on parameters for epidermal proliferation, keratinization and inflammation in psoriasis

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Abstract

Corticosteroids are important in the treatment of inflammatory dermatoses, such as psoriasis. They have anti-inflammatory, anti-proliferative and immunosuppressive effects. In this study, the effect of budesonide on proliferation, inflammatory cells and cytokines in psoriasis was investigated. In order to elucidate the time course of the different effects of corticosteroid treatment in psoriasis, six patients were treated for 3 weeks with budesonide 0.025% ointment (Preferid®), and biopsies were studied immunohistochemically, before treatment and after 1 and 3 weeks of treatment. Clinical scores together with staining with antibodies indicating proliferation, keratin 16, keratin 10, T-lymphocytes, monocytes, polymorphonuclear leukocytes, Langerhans cells, interleukin-1α, (IL-1α) interleukin-6 (IL-6), interleukin-8 (IL-8), tumor necrosis factor-α (TNF-α), and intercellular adhesion molecule-1 (ICAM-1) were performed. ‘Psoriasis area’ and ‘severity index’ (PASI) scores were significantly reduced after 1 week and 3 weeks of treatment. Epidermal hyperproliferation (Ki-67 binding) and suprabasal keratin 16 (Ks8.12) expression decreased within 1 week, while keratin 10 (RKSE60) expression did not change. Five out of 6 patients showed cytokine levels (IL-1α, IL-6, IL-8, and TNF-α; detected immunohistochemically) in the normal range, while 1 patient had highly increased cytokine levels. In this patient, cytokine levels decreased during treatment. In 4 patients, showing high dermal ICAM-1 expression before treatment, a consistent reduction of ICAM-1 on endothelial cells was observed. The inflammatory infiltrate (T-lymphocytes (T11), monocytes/macrophages (WT14), polymorphonuclear leukocytes (PMN, anti-elastase)) was reduced to some extent after 3 weeks. The number of Langerhans cells (OKT6) did not change. These results indicate that the psoriatic lesions, although clinically comparable, show interindividual differences in cytokine expression. Corticosteroid treatment for 1–3 weeks improves clinical scores and hyperproliferation. Cytokine levels are reduced during steroid treatment in the patient who showed high levels before treatment. To suppress the infiltrate entirely, longer steroid treatment is probably necessary. This may explain the relapse seen after short term corticosteroid therapy.

Keywords: Psoriasis; Corticosteroids; Immunohistochemistry

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1. Introduction

Lesional psoriatic skin is characterized by epidermal hyperproliferation and disturbed keratinization in combination with epidermal leucocyte accumulation. Evidence is accumulating that recruitment of cycling cells from the resting Go population is the mechanism of epidermal hyperproliferation in psoriasis [1,2,3]. The reduced expression of keratin 10 and the suprabasal expression of keratin 6 and 16 in psoriatic skin are indicators of the disturbed differentiation and hyperproliferation [1,2,3].

Various cytokines play an important role in homeostasis of normal skin and in skin pathology. Diverse stimuli trigger a cutaneous inflammatory response by directly inducing epidermal keratinocytes to elaborate specific pro-inflammatory cytokines and adhesion molecules. After that, activation of dermal vascular endothelial cells and selective accumulation of specific mononuclear cells in the dermis and epidermis can be seen [4]. In psoriasis, interleukin-1α (IL-1α), interleukin-6 (IL-6), interleukin-8 (IL-8), tumor necrosis factor-α (TNF-α), and interferon-γ (IFN-γ) are considered to be of relevance to the pathogenesis and regression of a lesion [5–11]. Upon stimulation by cytokines [4], lesional endothelial cells and keratinocytes focally express intercellular adhesion molecule-1 (ICAM-1), the intercellular adhesion molecule which binds leucocyte function-associated antigen-1 (LFA-1) expressing granulocytes and lymphocytes. Primarily T helper cells infiltrate the lesions, and subcorneal accumulation of granulocytes results in microabsesses [12,13].

Transforming growth factor-α (TGF-α) is a potent autocrine growth factor for keratinocytes that can be induced by IFN-γ and TNF-α, and IL-6 and IL-8 are also growth factors for keratinocytes [4]. Epidermal acanthosis and keratinocyte mitosis have been observed in delayed type hypersensitivity reactions and after intradermal injection of IFN-γ [14]. Thus, abnormal hyperproliferation of keratinocytes has been suggested to be linked to cytokines released by the inflamed epidermis [4].

Keratin 16 expression have been reported to normalize after a minimum of 7–9 weeks of dithranol treatment [15]. Oxholm et al. [6] reported that IL-6 intensity and extension were increased in lesional as compared to non-lesional skin. Simultaneously with clinical improvement during PUVA therapy, the IL-6 staining became weaker. Recently, it was reported that ICAM-1 expression on papillary endothelium is reduced after cyclosporin A (CsA) treatment, but not after PUVA or CD4 monoclonal antibody treatment [16]. In contrast, CsA treatment was not associated with any change in density and phenotype of dermal and epidermal leukocytes, in contrast with the marked diminution of the cellular infiltrate induced by PUVA therapy. Horrocks et al. [17] reported that CsA treatment of psoriatic patients, reduced ICAM-1 expression on keratinocytes, but not on endothelial cells.

Corticosteroids have been of much benefit in the treatment of inflammatory dermatoses. They possess anti-proliferative, anti-inflammatory and immunosuppressive properties [18–20]. Corticosteroids directly suppress gene transcription (probably promter regions of specific genes), and the mobilization of mRNA. In addition non-nuclear modes of action have been postulated [21–23]. Recently it has been shown that various corticosteroids block the production of IL-1α, IL-6, IL-8 and TNF-α by keratinocytes in vitro [5–7]. Corticosteroid treatment of psoriatic patients has been shown to restore the increased T4/T8 ratios [23] and to decrease the number and function of Langerhans cells [24,25]. However, it remains to be elucidated whether corticosteroids inhibit epidermal growth and differentiation directly or alternatively whether corticosteroids reduce inflammation and inhibit epidermal growth indirectly. Budesonide 0.025% ointment (Preferid®, Brocades Pharma, Leiderdorp, The Netherlands) is a moderate to potent corticosteroid [26,27], which is at least as effective as betamethasone-17-valerate 0.1% ointment [26], and has little effect on plasma cortisol levels and urinary cortisol excretion [27].

In order to elucidate the time course of different effects of corticosteroid treatment in psoriasis on proliferation and inflammation in vivo, six patients were treated for 3 weeks. The effect of treatment with budesonide 0.025% ointment on parameters for proliferation, keratinization and inflammation was studied, using antibodies
against an epitope on the nucleus of proliferating keratinocytes (Ki-67), against keratin 13/16 (Ks8.12) and keratin 10 (RKSE60). In the same biopsies the presence of IL-1α, IL-6, IL-8, or TNF-α and ICAM-1 expression was assessed using specific antibodies. The inflammatory cells were analyzed using monoclonal antibodies against T-lymphocytes (T11), monocytes/macrophages (WT14), polymorphonuclear leukocytes (PMN; anti-elastase) and Langerhans cells (OKT6). The response of the psoriatic lesions to budesonide was assessed after 1 week and 3 weeks treatment in order to determine how the various aspects of the lesions are modulated by this treatment in vivo.

2. Materials and methods

2.1. Patients

Six patients (one male and five females) with moderate chronic plaque psoriasis participated in the study. Their age varied from 24–67 with an average of 47.5 years. They had used no systemic treatment for at least 2 months, and no topical treatment for at least 2 weeks. Patients applied budesonide ointment 0.025% (Preferid®, Brocades Pharma B.V., Leiderdorp, The Netherlands) twice daily thinly and evenly to the psoriatic lesions for 3 weeks. Clinical scores were recorded before treatment, after 1 week and after 3 weeks of treatment for the lesions on the upper extremities, trunk and lower extremities. Erythema (E), infiltration (I) and scaling (S) of the lesions were assessed using a 5-point scale: 0, no cutaneous involvement; 1, slight; 2, moderate; 3, severe; 4, severest possible involvement. The area (A) of the body surface that was involved was recorded using a 7-point scale: 0, no involvement, 1, < 10%; 2, 10–29%; 3, 30–49%; 4, 50–69%; 5, 70–89%; 6, 90–100% of the body surface involved. The PASI-score was calculated as follows:

\[
\text{upper extremities: } 0.2 \times A(E+I+S) + \\
\text{trunk: } 0.3 \times A(E+I+S) + \\
\text{lower extremities: } 0.4 \times A(E+I+S)
\]

Punch biopsies (φ 4 mm) were taken from a nummular to palmsized lesion before treatment, after 1 week and after 3 weeks of treatment. For staining with anti-IL-α, IL-6, ICAM-1, IL-8, and TNF-α normal skin biopsies from healthy volunteers were used as a control.

This study was approved by the medical ethical committee, and all patients were informed of the nature of the experiment and gave written consent.

2.2. Immunohistochemical stainings

2.2.1. Antibodies. The primary antibodies used are listed in Table 1.

2.2.2. Tissue processing. The biopsies were immediately embedded in Tissue-Tek OCT Compound (Miles Scientific, Elkhart, USA), snap frozen in liquid nitrogen and stored at −80°C until further processing. Normal healthy skin and untreated psoriatic lesional skin from other patients were processed in parallel with the experimental tissues. Seven-μm cryostat sections were placed on 0.1% poly-L-lysine coated slides. After air-drying the sections were fixed for 10 min at room temperature in acetone, acetone/ether 60/40% or in an aqueous 4% paraformaldehyde solution (see Table 1). The sections destined for cytokine staining and for ICAM-1 staining were processed immediately. The others were stored at −80°C until further processing.

Four immunohistochemical techniques were used to visualize the different markers (see Table 1). For the direct and indirect peroxidase technique, the slides were incubated with the primary antibodies in the proper dilutions (see Table 1) for 30 min. After repeated washing, the slides for indirect staining were incubated for 30 min with a 1:50 dilution in phosphate buffered saline (PBS) of peroxidase conjugated rabbit-anti-mouse-immunoglobulin (Dakopatts, Copenhagen, Denmark). After washing and pre-incubation in sodium acetate buffer, pH 4.9 (NaOAc-buffer), the slides were stained with 3-amino-9-ethylcarbazole (AEC, Sigma, St. Louis, USA)/H₂O₂ in NaOAc-buffer for 10 min.

For the peroxidase-anti-peroxidase technique the slides were incubated for 60 min with the monoclonal antibodies. After washing, the slides were incubated with rabbit-anti-mouse immunoglobulin (RAM-Ig, Dakopatts, Copenhagen, Denmark) 1:25 in PBS for 20 min. After washing they
Table 1
List of primary antibodies, specificities, fixation and immunohistochemical procedures

<table>
<thead>
<tr>
<th>Antibody clone</th>
<th>Specificity</th>
<th>Mono/poly</th>
<th>Fixation</th>
<th>Dilution first AB</th>
<th>Immunohistochemical procedure</th>
<th>Source</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ki-67</td>
<td>Human Ki-67-antigen</td>
<td>M</td>
<td>A/E²</td>
<td>1:40</td>
<td>*P-SAb³</td>
<td>Dakopatts, Copenhagen, Denmark</td>
</tr>
<tr>
<td>RKSE60</td>
<td>Keratin 10</td>
<td>M</td>
<td>A³</td>
<td>1:10</td>
<td>*P-SAb</td>
<td>F. Ramaekers, Maastricht, The Netherlands</td>
</tr>
<tr>
<td>Ks8.12</td>
<td>Keratin 13,16</td>
<td>M</td>
<td>A</td>
<td>1:25</td>
<td>*P-SAb</td>
<td>Sigma, St. Louis, USA</td>
</tr>
<tr>
<td>84H10</td>
<td>ICAM-1</td>
<td>M</td>
<td>A</td>
<td>1:50</td>
<td>AB⁶</td>
<td>Immunotech, Marseille, France</td>
</tr>
<tr>
<td>Anti-IL-1α</td>
<td>IL-1α</td>
<td>P¹</td>
<td>A</td>
<td>1:50</td>
<td>AB</td>
<td>Genzyme, Cambridge, USA</td>
</tr>
<tr>
<td>Anti-IL-6</td>
<td>IL-6</td>
<td>P¹</td>
<td>PF⁴</td>
<td>1:1000</td>
<td>AB</td>
<td>Gift from L. May, New Haven, Connecticut, USA</td>
</tr>
<tr>
<td>Anti-IL-8</td>
<td>IL-8</td>
<td>P¹</td>
<td>PF</td>
<td>1:50</td>
<td>AB</td>
<td>AMS, Oxford, UK</td>
</tr>
<tr>
<td>Anti-TNF-α</td>
<td>TNF-α</td>
<td>P¹</td>
<td>PF</td>
<td>1:1000</td>
<td>AB</td>
<td>Genzyme, Cambridge, USA</td>
</tr>
<tr>
<td>T11</td>
<td>CD2</td>
<td>M</td>
<td>A</td>
<td>1:100</td>
<td>PAP⁷</td>
<td>Dakopatts, Copenhagen, Denmark</td>
</tr>
<tr>
<td>WT14</td>
<td>CD14</td>
<td>M</td>
<td>A</td>
<td>1:100</td>
<td>PAP</td>
<td>W. Tax, Nijmegen, The Netherlands</td>
</tr>
<tr>
<td>Anti-elastase</td>
<td>Leukocyte-elastase</td>
<td>P</td>
<td>A</td>
<td>1:100</td>
<td>D⁸</td>
<td>Serotec, Oxford, UK</td>
</tr>
<tr>
<td>OKT6</td>
<td>CD1a</td>
<td>M</td>
<td>A</td>
<td>1:100</td>
<td>PAP</td>
<td>Ortho Diagnostic Systems, Raritan, USA</td>
</tr>
</tbody>
</table>

Notes:
1All polyclonal antibodies were raised in rabbit. ²A/E, acetone/ether 60/40%. ³A, acetone. ⁴PF, 4% aqueous paraformaldehyde. ⁵*P-SAb, peroxidase linked second antibody. ⁶AB, streptavidin-biotin method. ⁷PAP, peroxidase-anti-peroxidase method. ⁸D, direct method.

were incubated with peroxidase-anti-peroxidase-complexes (PAP-complexes, Dakopatts, Copenhagen, Denmark) 1:100 in PBS for 20 min. Incubations with RAM-Ig, and with the PAP-complexes were repeated. The slides were stained in the same solution of AEC/H₂O₂ in NaOAc-buffer, as mentioned above.

For the avidin-biotin method the sections were pre-incubated with a 10% normal goat serum (Dakopatts, Copenhagen, Denmark) solution, and incubated with the primary antibodies for 1 h. After washing, they were incubated for 30 min with biotinylated goat-anti-rabbit immunoglobulin (Dakopatts, Copenhagen, Denmark), diluted 1:200 (after 84H10 for ICAM-1). After washing, the sections were incubated for 30 min with a 1:200 dilution of peroxidase labelled streptavidin-biotin complex (Dakopatts, Copenhagen, Denmark). The colour reaction was performed by incubation with the AEC/H₂O₂ solution. All slides were counterstained with Mayers haematoxylin (Sigma, St. Louis, USA) and mounted in glycerol gelatin (Sigma, St. Louis, USA).

2.3. Scores
Histological changes in the epidermal and dermal compartment were assessed by two separate investigators in a double blind approach, using a semi-quantitative scale [28]: Epidermis: 0, no
staining; 1, sporadic staining; 2, minimal staining; 3, moderate staining; 4, moderate-pronounced staining; 5, pronounced staining. Dermis: 0, no stained cells; 1, sporadic; 2, 1–25% of the infiltrate cells stained; 3, 26–50%; 4, 51–75%; 5, 76–99%; 6, 100% of the infiltrate cells stained. Ki-67-positive nuclei were counted/mm length of epidermis.

2.4. Statistical analysis
The Wilcoxon ranking test for matched pairs was used for the statistical analysis.

3. Results

3.1. Clinical response
The treatment with budesonide was well-tolerated. After 1 week of treatment, the PASI-score had diminished in a statistically significant manner (P < 0.03) from 5.36 ± 0.98 (Mean ± S.E.M.) to 3.63 ± 0.67. After 3 weeks of treatment, the average PASI-score was 2.12 ± 0.58 (P < 0.03 as compared to the situation before treatment).

3.2. Immunohistochemical observations
Assessment of epidermal proliferation and keratinization, before and after 1 and 3 weeks of treatment is summarized in Table 2 and illustrated in Fig. 1. The number of Ki-67 stained nuclei diminished significantly (P < 0.03) after 1 week of treatment. After 3 weeks, their numbers had diminished further (P < 0.03). Suprabasal staining with Ks8.12 (keratin 16) diminished significantly (P < 0.03) after 1 week and continued to decline between 1 and 3 weeks of treatment. In contrast, keratin 10 showed no significant changes during treatment with budesonide.

Although the lesions biopsied, clinically had a comparable appearance, a large interindividual variation was seen with respect to the expression of the cytokines in untreated psoriatic skin. In 5 of the 6 patients the untreated lesions showed low IL-1α expression in the epidermis; this level did not change during treatment. In one patient, IL-1α expression was very high, and declined during 1 and further after 3 weeks treatment (see Table 3). In addition, in 5 out of 6 patients the untreated lesions showed low levels in the epidermis of IL-6, IL-8 and TNF-α, which did not change during treatment (see Table 3). In the same patient, showing a marked IL-1α staining, IL-6, IL-8 and TNF-α staining were also pronounced in the epidermis. Within 1 week of treatment with budesonide these cytokines were reduced markedly in this patient, and they had normalized in 3 weeks. Fig. 1 illustrates the expression of TNF-α.

Epidermal staining of ICAM-1 in untreated psoriatic plaques was high in only one patient. In this patient epidermal ICAM-1 expression was reduced after 1 week treatment, and absent after 3 weeks. TIL stained cells (T-cells) and Langerhans cells in the epidermis did not change during treatment (Table 4). However, epidermal WT14-stained cells (monocytes/macrophages) diminished significantly (P < 0.03) in 3 weeks, and the PMN infiltrate decreased steadily although not significantly.

ICAM-1 staining of the capillaries was high in 4 patients, and diminished markedly within the first week of treatment (P < 0.03). The dermal infiltrate declined between 0 and 3 weeks (P < 0.05). The number of PMNs in the dermis diminished significantly within 1 week (P < 0.05). In contrast the percentage of T-lymphocytes, monocytes/macrophages and Langerhans cells remained unchanged during the observation period.

4. Discussion
In the biopsies of psoriatic patients before budesonide treatment, we found high Ki-67 expression, high suprabasal keratin 16, and decreased
keratin 10 expression. This indicates a clear hyper-proliferative status, as in normal skin, Ks8.12-binding is virtually absent, and the numbers of Ki-67 positive nuclei are low (30-50/mm length of epidermis) [1,2]. In this study we found only one patient with intense staining for IL-1α, IL-6, IL-8 and TNF-α. The other patients showed cytokine levels in the range of normal skin. ICAM-1 expres-
Table 3
Cytokine expression in normal human epidermis, 1 patient ('high') with high cytokine levels, and 5 other patients ('low') with low cytokine levels.

<table>
<thead>
<tr>
<th></th>
<th>IL-1α</th>
<th>IL-6</th>
<th>IL-8</th>
<th>TNF-α</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal human skin</td>
<td>3</td>
<td>1</td>
<td>0</td>
<td>2</td>
</tr>
<tr>
<td>'High' psoriasis patient</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Before</td>
<td>3</td>
<td>3</td>
<td>2</td>
<td>4</td>
</tr>
<tr>
<td>After 1 week</td>
<td>1</td>
<td>2</td>
<td>0</td>
<td>2</td>
</tr>
<tr>
<td>After 3 weeks</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>'Low' psoriasis patients</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Before</td>
<td>1.6 ± 0.4</td>
<td>0.6 ± 0.2</td>
<td>0.5 ± 0.3</td>
<td>1.6 ± 0.2</td>
</tr>
<tr>
<td>After 1 week</td>
<td>1.6 ± 0.4</td>
<td>0.6 ± 0.2</td>
<td>0.4 ± 0.2</td>
<td>1.6 ± 0.2</td>
</tr>
<tr>
<td>After 3 weeks</td>
<td>2</td>
<td>0.7 ± 0.3</td>
<td>0</td>
<td>1.7 ± 0.3</td>
</tr>
</tbody>
</table>

In the study, we found that cytokine expression in keratinocytes was also only high in this one particular patient. ICAM-1 expression on endothelial cells was increased in most patients. We found quite high numbers of PMN and monocytes/macrophages and a substantial amount of T-lymphocytes.

In literature, it is described that IL-1α is present in both normal and psoriatic skin [29,30], and that IL-6, IL-8, or TNF-α is low or absent in normal skin, and is increased in untreated psoriatic lesions [31–35]. ICAM-1-staining in untreated psoriatic lesions is focal in most cases and absent in normal skin [36]. More recently, contradictory reports have been published on immunoreactive cytokine levels in psoriatic lesions [37]. It has been suggested, that technical problems, or different antibodies, cause these variations. However, as can be seen from our study, clinically comparable, untreated psoriatic lesions, from different psoriatic patients show different cytokine patterns, although processed and stained in exactly the same way. This means, that the differences are real, and that either each patient has his own psoriasis, or that the stage of development of the lesion is of crucial importance [32,35,38].

During 3 weeks of treatment with budesonide, a pronounced reduction was observed with respect to epidermal hyperproliferation. Various studies have demonstrated an effect of corticosteroids on mitotic activity of keratinocytes in culture and in situ in the epidermis [8,9]. In a previous investigation on the interference of corticosteroids with the response to sellotape stripping, it was shown that the recruitment of cycling cells from the resting

Table 4
Markers for inflammation during treatment with budesonide (mean ± S.E.M.)

<table>
<thead>
<tr>
<th></th>
<th>Anti-elastase</th>
<th>T11 positive cells</th>
<th>WT14 positive cells</th>
<th>OKT6 positive cells</th>
<th>ICAM-1 positive cells</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Epiderm</td>
<td>Derm</td>
<td>Epiderm</td>
<td>Derm</td>
<td>Epiderm</td>
</tr>
<tr>
<td>Before</td>
<td>1.6 ± 1.2</td>
<td>1.6 ± 0.5</td>
<td>2.3 ± 0.8</td>
<td>3.6 ± 0.8</td>
<td>1.6 ± 0.5</td>
</tr>
<tr>
<td>After 1 week</td>
<td>0.6 ± 1.0</td>
<td>0.8 ± 0.4</td>
<td>*1.8 ± 0.4</td>
<td>3.3 ± 1.0</td>
<td>1.3 ± 0.5</td>
</tr>
<tr>
<td>After 3 weeks</td>
<td>0.2 ± 0.4</td>
<td>0.8 ± 0.4</td>
<td>1.4 ± 0.6</td>
<td>3.8 ± 0.8</td>
<td>1.4 ± 0.8*</td>
</tr>
</tbody>
</table>

*Indicates a statistically significant reduction compared to scores at previous visit.
G₀ population was arrested [39]. During treatment with budesonide, significant inhibition was observed of keratin 16 expression in the suprabasal compartment (Ks8.12 binding), also indicating reduced hyperproliferation [3].

The staining with antibodies against the cytokines revealed highly variable results. Although a consistent reduction of all the cytokines was observed after treatment with budesonide in the patient demonstrating a marked staining in the untreated lesional skin, in all the remaining patients only a mild to moderate staining was observed before treatment, without a significant reduction during budesonide treatment. Further studies on cytokine patterns in the psoriatic lesion in a larger group of patients are needed to elucidate this further. Sticherling et al. [10] showed low immunoreactivity of IL-8 in lesional psoriatic skin. This is in line with the low levels of IL-8 in the pretreatment biopsies of our patients. In vitro studies demonstrated inhibition of the stimulated transcription of IL-1α, IL-6, IL-8, or TNF-α by corticosteroids, including budesonide [5]. The present study shows, that if cytokine levels are high in vivo before treatment, a reduction of cytokine staining can be seen after treatment with budesonide.

This study suggests that there are at least two populations in psoriatic patients in terms of cytokine expression. Corticosteroids have been shown to interfere with inflammation control in various ways. They modulate the accumulation and functioning of PMN [40], T-lymphocytes [24], and Langerhans cells [24,25]. The first significant reduction of PMN accumulation was observed within the first week of treatment and coincided with a substantial reduction of epidermal proliferation. Interestingly, a significant reduction of ICAM-1 expression in the capillaries occurred, whereas no statistically significant reduction of the percentage of T-cells was noticed.

From the present study it can be concluded that epidermal hyperproliferation is reduced during budesonide treatment. This seems not to be the result of a reduction of the inflammatory infiltrate. The change in cytokines and infiltrate composition was less pronounced probably due to relatively low pretreatment values. Epidermal proliferation, therefore, seems an important target in the anti-psoriatic working principle of budesonide. To elucidate whether changes in cytokines precede changes in proliferation and inflammation, the early changes induced by corticosteroid treatment should be investigated. The period between 0 and 7 days seems to be of crucial importance in unravelling this cascade. Following cessation of treatment with corticosteroids a relatively fast relapse occurs [40–43]. It could be of value to determine whether prolonged treatment with corticosteroids, until the point of resolution of inflammation was reached, might lengthen the remission periods.

References


