Comparison of Dermal and Systemic Application of Glucocorticoids on the RM 3/1⁺ Macrophage in Human Blood

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Abstract

Dermal administration of either hydrocortisone or fluprednidene to healthy skin causes only a weak and short-lasting increase of the proportion of the anti-inflammatory macrophage RM 3/1 in the blood compared to the effect of the systemic application of glucocorticoids on this cell subtype. On the other hand, a rather permanent increase of these macrophages could be observed in untreated patients suffering from certain skin diseases, e.g. urticaria, atopic dermatitis, psoriasis.

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Glucocorticoids cause profound changes in different cell types of the immune system. Macrophages which play an important role in the regulation of the immune response are also affected in many functions [1]. In a previous work we could demonstrate in vitro that glucocorticoids induce the RM 3/1⁺ macrophage subtype which is found to be associated in inflammatory processes with the down-regulatory phase of the immune response [2]. Recently we have shown that a single intravenous injection of the glucocorticoid prednylidene leads to a long-lasting appearance of the RM 3/1⁺ subtype in the blood of man [3]. Its proportion among blood monocytes increases from a basic level of 3% to about 80% positive cells within 24 h. The present study was designed to investigate the influence of dermal application of glucocorticoids to healthy skin on the RM 3/1⁺ subtype in the blood.

Healthy probands treated a 200 cm² area of forearm skin with either fat of the alp-marmot containing about 35 mg/kg of a mixture of 8 different corticosteroids [4] or an ointment containing 1% hydrocortisone (Pfizer, Karlsruhe, FRG) or a cream containing 0.1% fluprednidene (E. Merck, Darmstadt, FRG) for periods of up to 11 days. The daily doses amounted to 1 mg for the fat of the alp-marmot, 60 mg for hydro-cortisone and 6 mg for fluprednidene. Before and at

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different times during the treatment period blood was taken, the mononuclear cells were isolated using Ficoll-Paque density centrifugation and cytopsin preparations were made. The cells were stained in an indirect immunoperoxidase technique [5] with the monoclonal antibody RM 3/1 and an isotype control antibody. The percentage of RM 3/1⁺ cells was determined by counting at least 400 monocytes. Statistical analysis was carried out using the Student's t test ($p < 0.05$).

Administration of the fat of the alp-marmot ($n = 3$) showed no effect. Treatment with hydrocortisone (fig. 1) or fluprednidene (fig. 2) ointments revealed an increase in the proportion of RM 3/1⁺ cells up to day 4. This increase, however, was only weak compared to the effect of intravenous application of a glucocorticoid (30 vs. 80%) [3]. After day 4 the proportion of

positive monocytes decreased to normal values even if the drug application was continued. The reason for this decrease is not yet clear. On the other hand, a rather permanent increase of the RM 3/1+ subtype was observed in patients suffering from certain skin diseases although they had not been treated with any drug (table 1).

These results show that topical in contrast to systemic application of glucocorticoids causes only a weak and short-lasting increase of the macrophage subtype RM 3/1+ in the blood. They further indicate that administration of glucocorticoids to even small skin areas have some systemic effects although these seem to be too limited to be of therapeutic relevance.

Effect of Dermal and Systemic Glucocorticoids on the RM 3/1+ Macrophage

279

2 4
Days of treatment

Fig. 1. Effect of dermal application of 1% hydrocortisone on the RM 3/1+ in the blood. Mean ± SEM; n = 3. * p < 0.05 versus day 0.

1 2 4
Days of treatment

Fig. 2. Effect of dermal application of 0.1% fluprednidene on the RM 3/1+ macrophage in the blood. Mean ± SEM; n = 4. * p < 0.05 versus day 0.

Table 1. RM 3/1+ monocytes in the blood of healthy probands and patients with skin diseases

Probands1

Percent RM 3/1+ monocytes

Healthy Urticaria

Atopic dermatitis Psoriasis

0–19.5 (range)

71.3

31.7

61.4

40.2

No drug treatment.

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