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Clinical comparison of methylprednisolone aceponate and prednicarbate in chronic eczema

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Abstract

Methylprednisolone aceponate (MPA) is a new topical corticosteroid developed specifically for the treatment of eczematous disorders. A multicentre, controlled, randomized open trial to assess the efficacy and tolerability of a once daily application of MPA in comparison to a twice-daily application of Prednicarbate (PC) was conducted in 566 patients suffering from allergic contact eczema (51.2%), toxic degenerative eczema (46.8%) as well as a combination of allergic contact eczema and toxic degenerative eczema (1.9%). Both treatment groups were approximately the same size, 280 patients being treated with MPA, 286 with PC.

Treatment was carried out for a maximum of 28 days. The median duration of treatment was 22 days with MPA and 21 days with PC. Clinical efficacy was not different between MPA ointment (0.1%) used once daily with 45.5% complete healing and 39.8% marked improvement as compared to PC ointment (0.25%) used twice daily with 48.3% complete healing and 40.2% marked improvement. Both treatments were well tolerated. 4.6% of the patients reported adverse events on MPA-treatment and 3.8% on PC-treatment. No serious events were experienced. From this study it can be concluded that in various eczematous disorders efficacy and tolerability of MPA ointment used once daily are essentially the same as for PC ointment used twice daily.

Key words: Methylprednisolone aceponate; New topical glucocorticosteroid; Eczema, treatment of; Once-daily application

Introduction

Topical corticosteroids are amongst the most important drugs in the current treatment of dermatoses. They are the primary local treatment for eczemas. A wealth of chemical variants have been developed since Sulzberger and Witten introduced topical glucocorticoid therapy to dermatology in 1952 [1]. There is also a range of therapeutic strategies for topical glucocorticosteroids: once or twice-daily application either continuously, discontinuously, or graduated therapy up to on/off-therapy [2,3]. So far there exists no binding therapeutic regimen for

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eczema, one of the most frequent diagnoses in dermatological practise.

Methylprednisolone aceponate (MPA) is a new and potent dermato-corticosteroid (potency class 2 according to Miller and Munro [4]). It was developed specifically for the topical treatment of eczematous disorders. MPA is a non-halogenated di-ester.

Pharmacological studies have revealed a pronounced anti-inflammatory potency with distinctly reduced systemic activity [5–7]. The clinical use of MPA led to excellent therapeutic results in controlled clinical studies in more than 3000 patients [8,9]. A once-daily application of MPA together with the MPA-free ointment base did not show any loss of efficacy compared to twice-daily application of reference corticoids such as betamethasone-17-valerate, prednicarbate and hydrocortisone-17-butyrate [8,9].

It is generally known that the application of an ointment base without an active ingredient possesses a therapeutic value of its own in the case of eczema patients [10]. Therefore it was the aim of this trial to compare the efficacy of MPA based on a purely once-daily application to a twice-daily application of a reference corticosteroid in order to be able to recommend the most user-friendly regimen.

Patients and methods

This trial was conducted as a multicentre, controlled, randomised, open group comparison between a once-daily application of 0.1% MPA ointment (Schering AG, Berlin) and a twice-daily application of 0.25% PC ointment (Cassela-Riedel, Frankfurt).

Patients

566 patients (361 women, 204 men; one patient no sex stated; mean age 40 years) were recruited in 31 centres in Germany. 280 patients were treated with MPA and 286 with PC. They were included in the study when they met the following criteria:

- 18 years or older;
- the presence of chronic eczema (allergic contact eczema and/or toxic degenerative eczema) with lesions on the trunk, legs and/or arms;
- no other medications such as systemic or topical corticosteroids had been administered at least 4 weeks prior to the treatment with the trial medication;
- patients were not affected by diseases in which corticosteroids are contraindicated;
- patients were neither pregnant nor nursing;
- written informed consent had been obtained.

Clinical assessment

Treatment was continued for a maximum period of 28 days. Topical therapy was applied once daily in the evening (MPA ointment) or twice daily, in the morning and in the evening (PC ointment). The patients were assessed on entry into the study. During the treatment period five readings were performed on day 3–5, 6–8, 9–14, 15–21 and 22–28. At these readings the objective symptoms (erythema, scaling, papules, papulovesicles, lichenification, scratch effects and cracks) and the subjective complaints (pruritus, burning and pain) were evaluated according to an arbitrary severity scale. The extension of the lesions was estimated. In addition, the status of the skin was rated according to a 4-point-scale (symptom-free, improved, unchanged and deteriorated). Furthermore, the overall eczematous status compared with the baseline was assessed as follows: complete remission, evident improvement, moderate improvement, unchanged

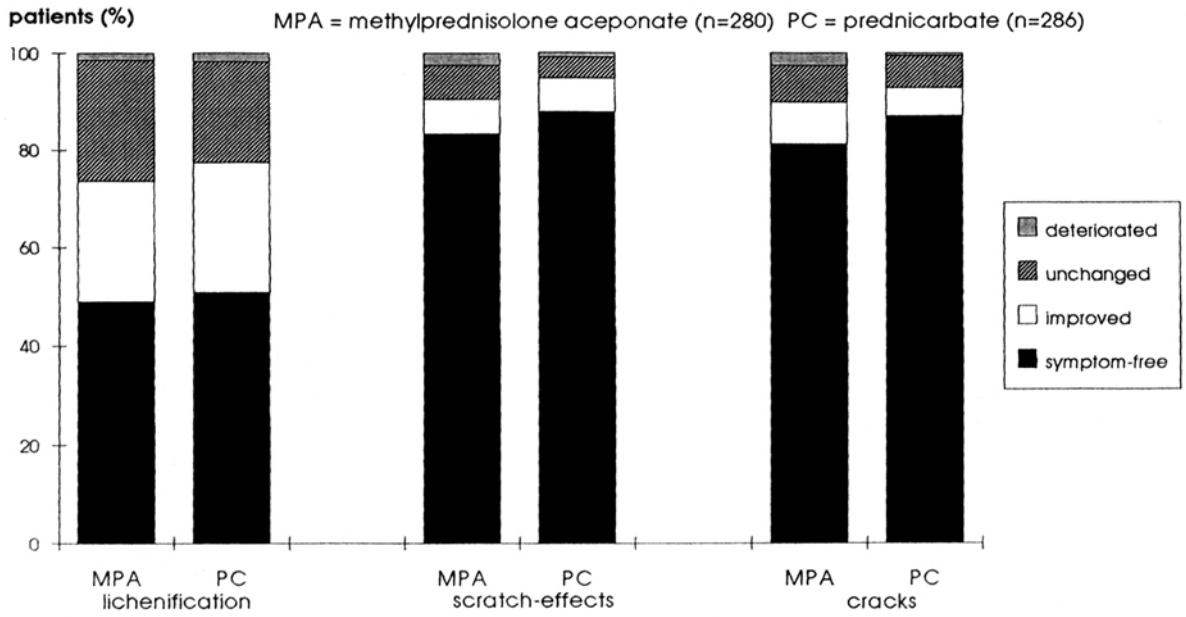

Fig. 1. Clinical symptoms in patients with chronic eczema after therapy with MPA ointment applied once daily and PC ointment given twice daily.

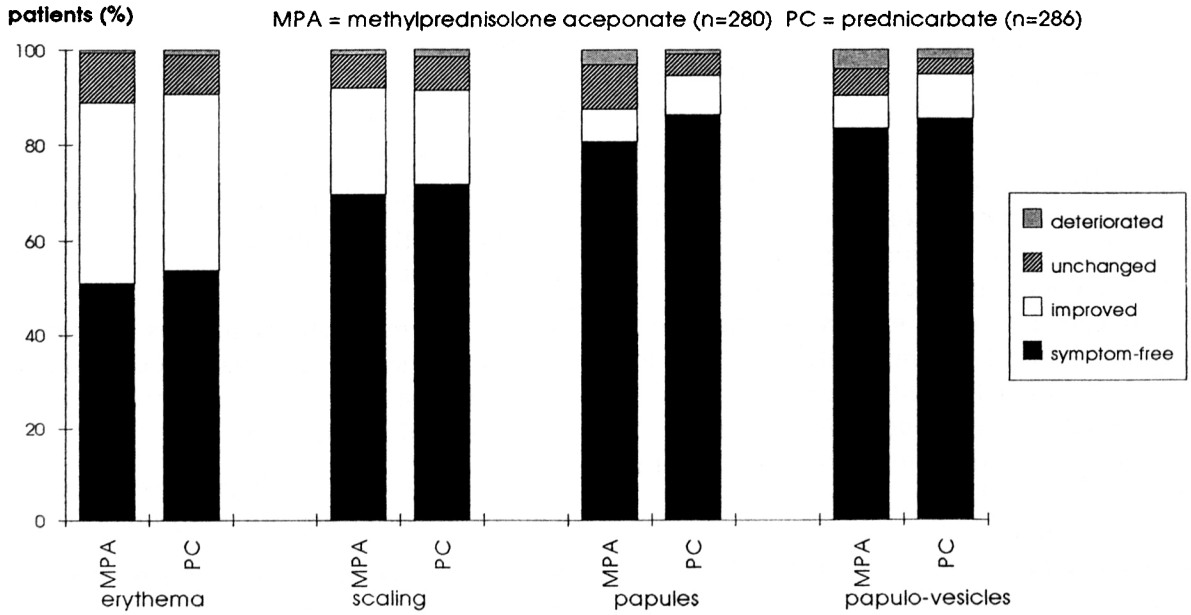

Fig. 2. Clinical symptoms in patients with chronic eczema after therapy with MPA ointment applied once daily and PC ointment given twice daily.

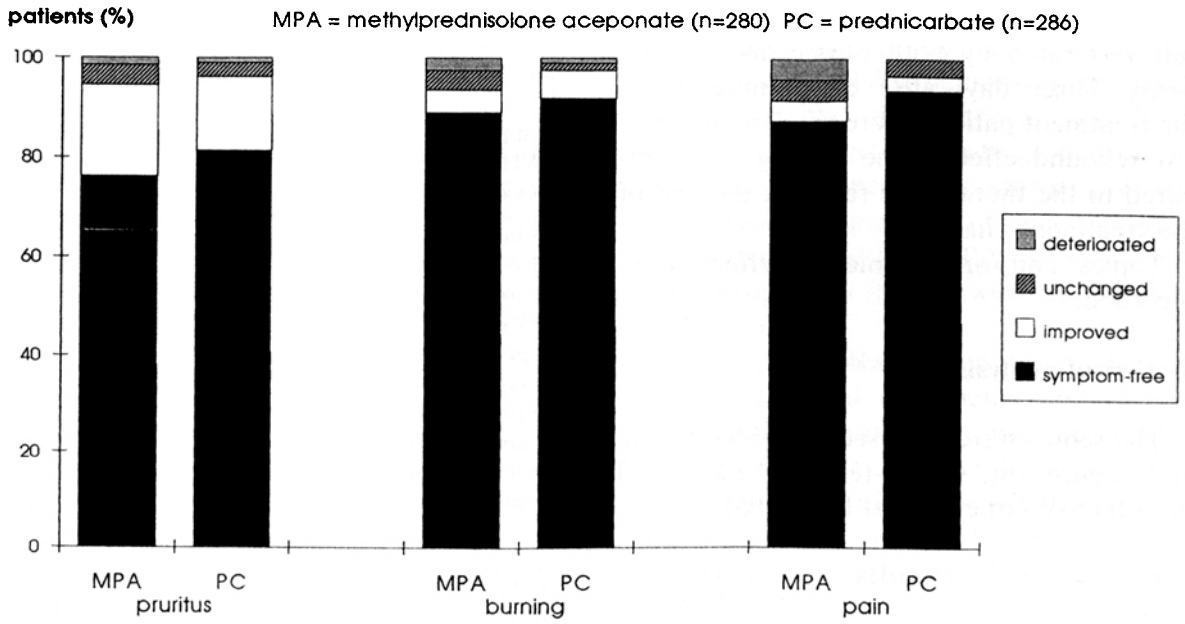

Fig. 3. Clinical symptoms in patients with chronic eczema after therapy with MPA ointment applied once daily and PC ointment given twice daily.

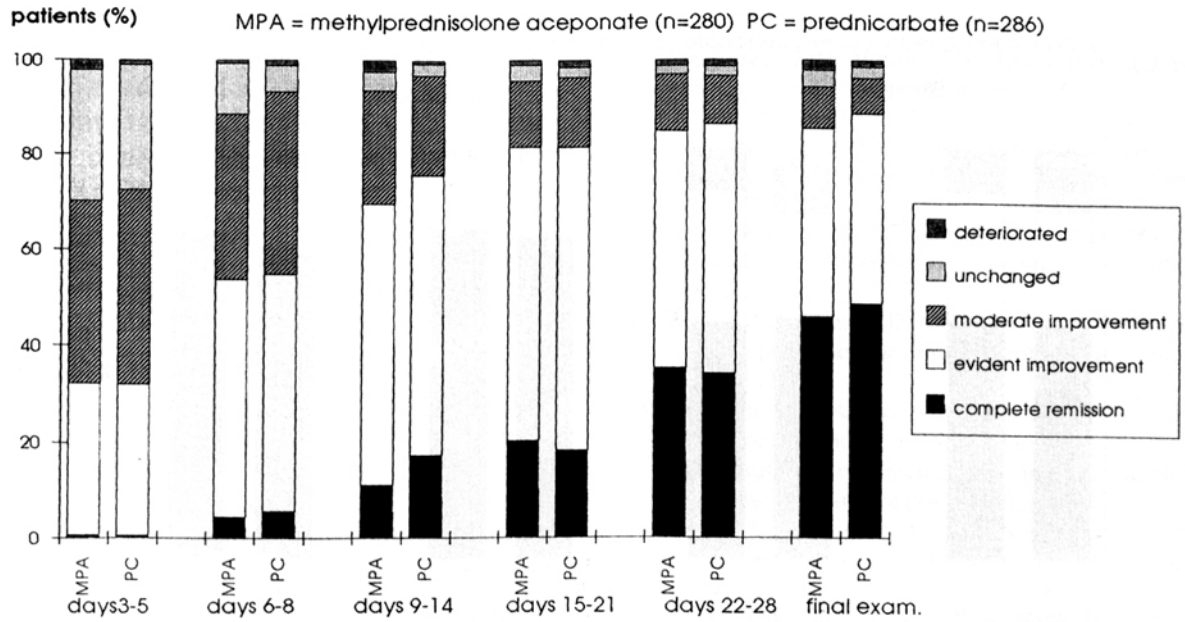

Fig. 4. Development of eczematous state in patients with chronic eczema during treatment with MPA ointment applied once daily and PC ointment given twice daily.

and deteriorated. The final therapeutic result was rated by both physicians and patients. Three days after discontinuation of the treatment patients were assessed to cover any rebound effects. The finding was compared to the therapeutic result at the end of the treatment phase.

Topical and/or systemic side effects were recorded.

Statistical analysis

The scores were analysed one-sided by the equivalence-test, the λ^2-test, the t-test and the Mann-Whitney U-test ($\alpha = 0.05$).

Results

566 patients with allergic contact eczema, toxic degenerative eczema and a combination of both types were enrolled in this trial. The diagnoses had the following distribution: allergic contact eczema accounted for 51.2%, toxic degenerative eczema for 46.8%, and allergic contact eczema combined with toxic degenerative eczema for 1.9%. The average length of treatment was 22 days with MPA ointment and 21 days with PC ointment. Treatment was discontinued in 24 of the 566 patients (MPA ointment, 14; PC ointment, 10 patients). The main reasons for these discontinuations were lack of efficacy in 12 of 280 patients treated with MPA ointment and seven of 286 treated with PC ointment.

Table 1
Reported adverse events during treatment with MPA and PC ointment in patients with chronic eczema

Symptoms (WHO-System Organ Class)	MPA ($n = 280$)	PC ($n = 286$)
Total adverse events	$n = 13$ (4.6%)	$n = 11$ (3.8%)
0100 Skin and appendages disorders	12	8
0410 Central and peripheral nervous system disorders	–	1
1810 Body as a whole/ general disorders	–	2
1820 Application site disorders	2	–

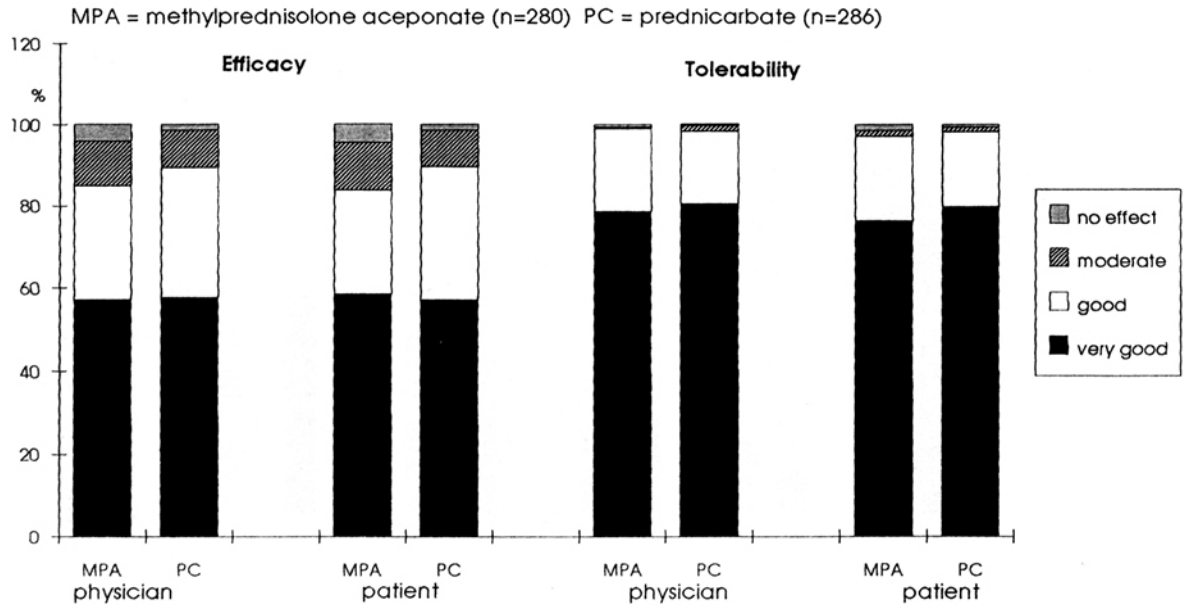

Fig. 5. Global assessment of efficacy and tolerability of MPA ointment applied once daily and PC ointment given twice daily.

The most common cutaneous baseline symptoms were erythema, scaling, lichenification and the effects of scratching occurring in 73–99% of all patients. Pruritus occurred in 95.4% and burning in 72% of the patients, pain was less frequent (46%). The objective and the subjective symptoms regressed to an equal extent with both treatment regimens (Figs. 1–3). No significant differences were seen at the end of the treatment phase for either objective or subjective symptoms. The overall eczematous status (Fig. 4) improved equally under MPA- and PC-treatment. At the end of the treatment 85.3% of the patients treated with MPA ointment once daily showed complete remission (45.5%) or marked improvement (39.8%), whereas 48.3% of the patients treated with PC ointment twice daily were completely free of symptoms and in 40.2% baseline symptoms were markedly improved. The overall ratings of patients and physicians were nearly identical (Fig. 5). Therapeutic effects in the two groups were not different 3 days after the treatment was finished.

Systemic and local tolerability was good in both groups. A total number of 4.6% (MPA ointment) and 3.6% (PC ointment) reported adverse events. Most of them were local complaints (MPA: 12; PC: 8), e.g., burning, itching, erythema and dryness of the skin (Table 1). No serious adverse events were experienced.

Discussion and conclusion

In previous clinical trials it has been shown that a once-daily application of MPA ointment, a new topical corticosteroid, combined with a once-daily application of MPA-free ointment base is as effective and as safe as a twice-daily application of betamethasone valerate ointment, prednicarbate ointment and MPA [9].

A once-daily application of a topical preparation is beyond doubt the most user-friendly type of treatment. Up to the time this clinical trial has been conducted there were no data available demonstrating clearly that a purely once-daily application of MPA ointment is as effective as a twice-daily application of a reference corticosteroid preparation. Therefore the clinical efficacy and safety of once-daily applied MPA ointment has been compared to that of twice-daily applied PC ointment.

From the data obtained in this study it can be concluded that in patients with chronic eczema, MPA ointment requires an application only once a day to reach the same therapeutic effect as PC ointment given twice daily. Both drugs seem to be well tolerated. With regard to the patients' compliance a once-daily application seems to be the optimal mode of therapy. It is simple and efficient, and it may help to reduce 'cortisone fear' in patients suffering from various types of chronic eczema who need topical glucocorticosteroid therapy for a long period of their life.

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