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Activity of Different Desoximetasone Preparations Compared to Other Topical Corticosteroids in the Vasoconstriction Assay

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Key Words
Desoximetasone · Corticosteroids · Chromametric measurement · Bioavailability

Abstract
Introduction: We report on a double-blind, vehicle-controlled, single-center confirmatory study with random assignment. The purpose of the study was to investigate the topical bioavailability of different topical corticosteroid formulations in healthy human beings focussing on desoximetasone (DM). ***Materials and Methods:*** Two DM 0.25% formulations [ointment (DM-o) and fatty ointment (DM-fo, water-free); class III corticosteroids], the corresponding active ingredient-free vehicles and three comparators of different strength [clobetasol propionate 0.05% (CP 0.05%), fatty ointment, class IV; hydrocortisone (HC) 1%, fatty ointment, class I, and betamethasone (BM) 0.05%, fatty ointment, class III] were tested using the vasoconstriction assay. The degree of vasoconstriction (blanching) in the treatment field was compared to the one found in untreated control fields using chromametric measurements and clinical assessment. ***Results/Conclusion:*** DM-o 0.25%, DM-fo 0.25% and BM 0.05% showed similar vasoconstrictive potential, i.e., clear blanching. In fact, both DM preparations were proven to be noninferior to BM 0.05%, while CP 0.05% was found a little less active. HC 1.0% and the DM vehicles showed no clear-cut vasoconstrictive effect. No adverse events related to the study medications were observed. Good topical bioavailability of both DM formulations was detected by chromametric measurement and clinical assessment.

Introduction

Topical corticosteroids represent the treatment of choice for numerous different inflammatory skin diseases, in particular atopic eczema. The great variety of topical corticosteroid formulations currently available does not always allow dermatologists and general practitioners to easily select the best suitable corticosteroid in a given context. The desired anti-inflammatory effects of corticosteroids with conventional formulations unfortunately correlate strictly with the undesired effects, e.g. skin atrophy [1]. The potency of the corticosteroids has been classified by Niedner [2]. Accordingly, class I comprises mild corticosteroids, class II medium potent ones, class III potent ones and class IV the strongest congeners. The classification reflects their relative efficacy. The vasoconstriction assay (blanching test), first described by McKenzie and Stoughton [3] in 1962, is a test known to be suitable to determine the activity of topically applied corticosteroids [3–5]. Vasoconstriction is a pharmacolog-

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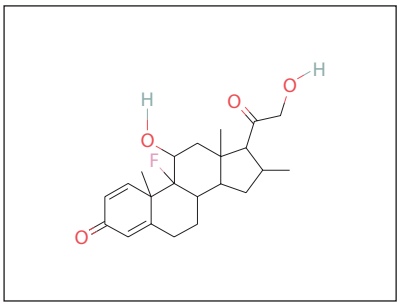

Fig. 1. Structure of DM.

ical activity, which correlates well with clinical efficacy. The intensity of skin blanching after a single topical application under occlusion as a sign of pharmacological activity corresponds generally to the clinical efficacy after repeated application without occlusion. The test describes the time- and dose-dependent blanching of the skin after the single application of a corticosteroid with respect to the anti-inflammatory activity and thus indirectly allows to assess topical bioavailability [6].

Desoximetasone (DM), introduced into clinical therapy more than 25 years ago [7], has been known to be an effective topical therapeutic option for the treatment of atopic dermatitis [8] and other types of eczema [9, 10]. Yet there is still a need for experimental data allowing a comparison of different DM formulations and other topical corticosteroid formulations of different potency. In the present study, different corticosteroid formulations and their vehicles were tested using the vasoconstriction assay in particular to obtain information about the topical bioavailability of the active pharmaceutical ingredients.

Materials and Methods

Study Design

This clinical trial was conducted conforming to EC-GCP (European Community Good Clinical Practice) standards as a single-center, vehicle-controlled, double-blind study with random assignment. The final study protocol was approved by the relevant Ethics Committee before the start of the study. Male and female eligible volunteers, older than 18 years with healthy skin demonstrating vasoconstriction to topical corticosteroids, i.e. 'responders', were included after having given their informed consent.

Two DM 0.25% test preparations [Topisolon® ointment (DM-o) and Topisolon® fatty ointment (DM-fo, water-free), each class III corticosteroids], the corresponding active ingredient-free vehicles and three comparators of different strength [Karison® (clobetasol-17-propionate 0.05% [CP 0.05%], class IV), Sanatison® Mono 1% (hydrocortisone 1.0% [HC 1.0%], class I) and Diprosis® (betamethasone dipropionate 0.064% = betamethasone 0.05% [BM 0.05%], water-free, class III)] were tested in a nonocclusive manner. The chemical name of DM is pregna-1,4-diene-3,20-dione-9-fluoro-11,21-dihydroxy-16-methyl-(11β, 16α). Its structure is depicted in figure 1.

The test fields were compared intraindividually. Altogether 9 test fields were evaluated. Four test fields were located on one volar forearm and 5 on the other. Two untreated test fields, 1 on each arm, served as internal controls. A single application under occlusion of each formulation was performed for 6 h. Chromametric measurements and clinical assessments were performed at baseline (prior to application) and 1, 2, 4, 6 and 18 h after application. One single nonocclusive application of each formulation over 6 h ± 15 min was performed. A self-adhesive electrocardiogram (ECG) ring (inside diameter 16 mm) was centered and attached to each of the test fields (allowing at least 2 cm between test fields). A Teflon ring (inside diameter 16 mm, height approximately 3 mm) was attached to the inner opening of the electrocardiogram ring. Approximately 50 μl formulation were applied to each test field. The test fields were covered with a single layer of gauze being fixed on the edges with an adhesive bandage to prevent contamination. The individual test fields were treated using a 1-ml syringe in accordance with the permutation in the randomization list. A total dose of approximately 50 μl of DM-o and 50 μl of DM-fo correspond together to 0.125 mg DM each; 50 μl of CP 0.05% correspond to 0.025 mg CP; 50 μl of HC 1.0% correspond to 0.5 mg HC, and 50 μl of BM 0.05% correspond to 0.025 mg BM dipropionate. All subjects received the same treatments. There was no interindividual subdivision into treatment groups. The test fields with the active formulations and the corresponding vehicles were arranged contralaterally. The three comparators were randomly assigned to 1 of the 3 remaining test fields. The investigational products were blinded in neutral tubes.

Relevant previous treatments applied within 12 weeks before the study were documented. The following concomitant treatments were not permitted during this study: any vasoactive (constrictor or dilator) medication that modulates blood flow including nitroglycerin, antihypertensives, antihistamines, nonsteroidal anti-inflammatory drugs, aspirin and cough/cold products containing antihistamines and/or either phenylpropanolamine or phentolamine and glucocorticoids.

Study Population

Thirty healthy subjects were enrolled in the study, randomized and treated with the study medications. All subjects finished the study as planned. All included volunteers received one application of each formulation over 6 h ± 15 min and one additional application with BM 0.05% during the screening examination over 6 h ± 15 min in order to determine whether they were blanching responders. Ten male and 20 female subjects formed the study population. Their age ranged from 18 to 69 years (mean = 35.8, SD = 13.0). Four subjects were using concomitant medication for contraception. Two other volunteers once took paracetamol for the treatment of headache during the study.

Chromametry

Skin color measurements were made according to the method of Queille-Roussel et al. [11] with a Chromameter CR 300 (Minolta, Ahrensburg, Germany). Values were measured in accordance with the L*a*b* system. The a* value (redness value) is a

Table 1. Scores to measure the degree of vasoconstriction of a treatment field compared to the untreated control field

0	No vasoconstriction
1	Mild vasoconstriction
2	Moderate vasoconstriction
3	Intense vasoconstriction

well-accepted parameter in the context of vasoconstrictor assays. Measurements were performed by placing the detector without additional pressure on the test fields. Three measurements were taken at each field at a given time point.

Clinical Assessment

The degree of vasoconstriction was clinically assessed at the treatment field compared to the untreated control field on the same forearm (table 1). This clinical assessment of the test fields was performed by an independent observer. Bathing, showering, sauna, natural sun bathing or solarium was not allowed during the study. Extensive exercising especially with the arms had to be avoided during the study. The use of skin care products (e.g. creams, emollients) on both forearms 24 h prior to and throughout the study was prohibited, as was any caffeine intake during the study.

Data Handling

Double data entry was performed. The first and second data entry was carried out by two different persons (data entry operators). Vasoconstriction properties were determined by evaluation of the degree of blanching in the test fields. The primary efficacy variable was the a* value (redness value) measured by chromametry. Clinical assessment scores for the degree of vasoconstriction were recorded as a secondary variable.

Statistical Analysis

The statistical evaluation in this confirmatory trial was performed using the software program SAS. The study aim was to prove the efficacy of the active study preparations (DM-o and DM-fo) compared to the corresponding vehicles and to compare them to other corticosteroids. Vasoconstriction (blanching), expressed as a* values, was used as a measure for efficacy. The a* values for the assessment point 1 h after treatment were used. Since two active study preparations (DM-o and DM-fo) were tested versus the corresponding vehicles, an alpha adjustment according to Bonferroni was performed [12]. The following hierarchical approach was performed for both active study preparations (DM-o and DM-fo) and the corresponding active ingredient-free vehicles.

(1) Comparison of blanching induced by the active study preparations (DM-o and DM-fo) with blanching due to the corresponding vehicles. The difference between the treatments was estimated with a 2-sided 97.5% confidence interval and compared to 0.

(2) Comparison of blanching induced by the active study preparations (DM-o and DM-fo) with a comparator of lower strength. The difference between the treatments (comparator minus active study preparation) was estimated with a 2-sided 95% confidence interval corresponding to an upper 1-sided 97.5% confidence interval. The upper 97.5% confidence interval was discussed with reference to 25% of the mean of the data related to the comparator.

(3/4) Comparisons with comparators of similar and higher strength, respectively, as outlined in 2. Step 2 was only to be performed if the comparison of the active study preparation and the vehicle in step 1 revealed superiority of the active study preparation. In analogy, steps 3 and 4 were performed if steps 2 and 3 revealed noninferiority of the active study preparation. This ordered test procedure kept the overall significance level of 5%.

Sums of clinical assessment scores were evaluated descriptively.

Results

Analyses of the Primary Activity Parameter – Blanching

The efficacy analysis was primarily performed based on chromametric data measured 1 h after the 6-hour application period. The baseline-corrected, untreated control site-corrected a* values reflect the degree of blanching. Clear blanching was observed in the fields treated with DM-o, DM-fo and the active comparators BM 0.05% and CP 0.05%. The mean degree of blanching was similar for DM-o, DM-fo, BM 0.05% and CP 0.05%. Since the lower 97.5% confidence limits of DM-o and DM-fo were greater than 0, it can be concluded that both preparations were active with respect to blanching. The lower 97.5% confidence limits of BM 0.05% and CP 0.05% were also greater than 0. In the fields treated with the comparator HC 1.0% only slight blanching was observed. The lower 97.5% confidence limit for HC 1.0% was –0.07. Therefore, it could not be verified that HC 1.0% is significantly active with respect to blanching.

For the DM-o and DM-fo vehicles, a slight blanching was observed. The mean degree of blanching was comparable for the DM-o vehicle and the DM-fo vehicle. The lower 97.5% confidence limits were 0.21 and 0.06 for the DM-o and DM-fo vehicles, respectively. The comparison of DM-o with its vehicle showed no overlap between the corresponding 97.5% confidence intervals. Since the lower 97.5% confidence limit of 1.62 was greater than 0, it can be concluded that DM-o was more effective than its vehicle.

In order to judge whether DM-o was noninferior to HC 1.0%, the difference of mean blanching after treatment with HC 1.0% minus mean blanching after treatment with DM-o was calculated. It could be confirmed that DM-o was noninferior to HC 1.0% when considering a 25% margin. In order to judge whether DM-o was non-

Table 2. Descriptive statistics of the clinical assessment

	TP, h	n	Median	Sum	Score			
					0	1	2	3
DM-o-V	1	30	0	15	17	11	2	0
	2	30	0	16	17	10	3	0
	4	30	0	16	19	6	5	0
	6	30	0	11	20	9	1	0
	18	30	0	2	28	2	0	0
DM-o	1	30	2	59	1	4	20	5
	2	30	2	60	1	3	21	5
	4	30	2	60	1	3	21	5
	6	30	2	58	1	3	23	3
	18	30	0	15	16	13	1	0
DM-fo-V	1	30	0	10	20	10	0	0
	2	30	0	9	21	9	0	0
	4	30	0	6	25	4	1	0
	6	30	0	5	26	3	1	0
	18	30	0	1	29	1	0	0
DM-fo	1	30	2	60	0	4	22	4
	2	30	2	59	1	3	22	4
	4	30	2	60	0	3	24	3
	6	30	2	58	0	3	26	1
	18	30	0	14	16	14	0	0
HC 1.0%	1	30	0	9	21	9	0	0
	2	30	0	7	23	7	0	0
	4	30	0	5	25	5	0	0
	6	30	0	2	28	2	0	0
	18	30	0	3	27	3	0	0
BM 0.05%	1	30	2	58	0	5	22	3
	2	30	2	60	0	4	22	4
	4	30	2	60	0	4	22	4
	6	30	2	60	0	2	26	2
	18	30	1	19	11	19	0	0
CP 0.05%	1	30	2	48	4	6	18	2
	2	30	2	50	3	6	19	2
	4	30	2	51	2	7	19	2
	6	30	2	51	0	10	19	1
	18	30	0.5	16	15	14	1	0

DM-o-V = DM-o vehicle; DM-fo-V = DM-fo vehicle; TP = time point.

inferior to BM 0.05%, the difference of mean blanching after treatment with BM 0.05% minus mean blanching after treatment with DM-o was calculated. The upper 95% confidence limit of the difference between both treatments (0.75) should be below 25% of the mean for BM 0.05% (25% of 3.26 is 0.82). DM-o was noninferior to BM 0.05%. The actual upper 95% confidence limit was 23% of the comparator's mean effect. In order to judge whether DM-o was found noninferior to CP 0.05%, the difference of mean blanching after treatment with CP 0.05% minus mean blanching after treatment with DM-o was calculated. It could be confirmed that DM-o was noninferior to CP 0.05% when considering a 25% margin. The actual upper 95% confidence limit was 8% of the comparator's mean effect.

The comparison of DM-fo with its vehicle showed no overlap between the corresponding 97.5% confidence intervals. It could be concluded that DM-fo was more active than its vehicle. In order to judge whether DM-fo was noninferior to HC 1.0%, the difference of mean blanching after treatment with HC 1.0% minus mean blanching after treatment with DM-fo was calculated. The upper 95% confidence limit of the difference between both treatments (–2.45) should be below 25% of the HC 1.0% mean (25% of 0.37 is 0.09). Since –2.45 is below 0.09, it can be confirmed that DM-fo was noninferior to HC 1.0% when considering a 25% margin. In order to judge whether DM-fo was noninferior to BM 0.05%, the difference of mean blanching after treatment with BM 0.05% minus mean blanching after treatment with DM-fo was calculated. The upper 95% confidence limit of the difference between both treatments (0.28) should be below 25% of the BM 0.05% mean (25% of 3.26 is 0.82). It could be confirmed that DM-fo was noninferior to BM 0.05% when considering a 25% margin. The actual upper 95% confidence limit was 9% of the comparator's mean effect. In order to judge whether DM-fo was noninferior to CP 0.05%, the difference of mean blanching after treatment with CP 0.05% minus mean blanching after treatment with DM-fo was calculated. The upper 95% confidence limit of the difference between both treatments (–0.22) should be below 25% of the CP 0.05% mean (25% of 2.73 is 0.68). Since –0.22 is below 0.68, it can be confirmed that DM-fo was noninferior to CP 0.05% when considering a 25% margin (table 2; fig. 2).

Analyses of Secondary Efficacy Variables – Clinical Assessment of Vasoconstriction

For the treatments with DM-o, DM-fo, BM 0.05% and CP 0.05% the score sums were maximal during the first 6 h after the end of the treatment period and ranged between 58 and 60 after treatment with DM-o, DM-fo and BM 0.05% and between 48 and 51 after treatment with CP 0.05% at the different assessment points (table 3). A marked decrease in the score sum was recorded 18 h after the end of treatment (DM-o, score sum: 15; DM-fo, score sum: 14; BM 0.05%, score sum: 19; CP 0.05%, score sum: 16).

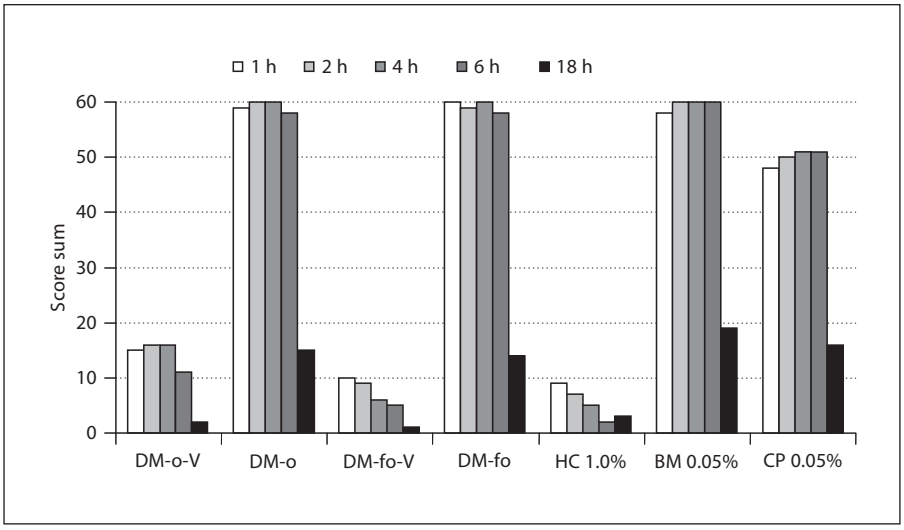

Fig. 2. Score sums of the clinical assessment of vasoconstriction. DM-o-V = DM-o vehicle; DM-fo-V = DM-fo vehicle.

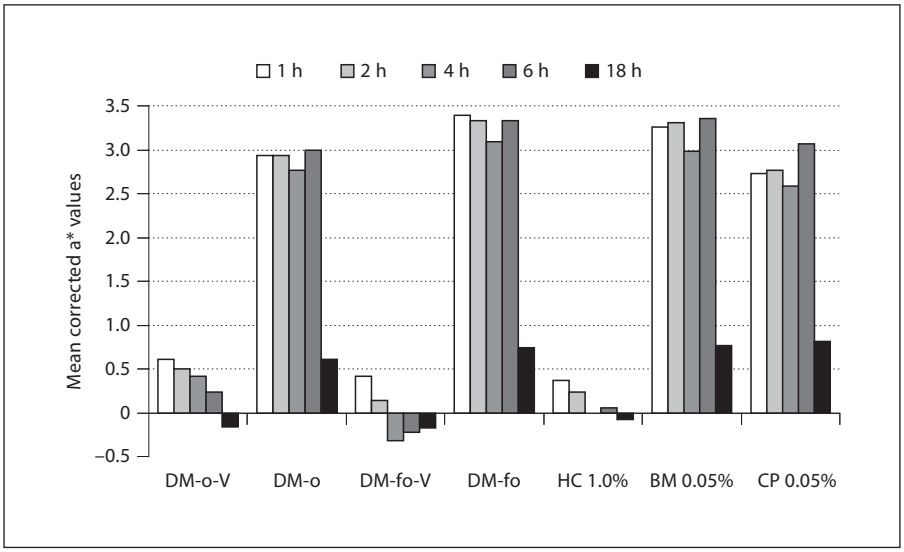

Fig. 3. Mean baseline-corrected, untreated control site-corrected a* values. DM-o-V = DM-o vehicle; DM-fo-V = DM-fo vehicle.

For the DM-o vehicle, the score sums were maximal during the first 4 h after the end of treatment and ranged between 15 and 16. A decrease in the score sum to 11 was observed at the 6-hour assessment point, and to a score sum of 2 at the 18-hour assessment point.

After treatment with the DM-fo vehicle and after treatment with HC 1.0% the highest score sum was assessed 1 h after the end of treatment (score sums 10 and 9, respectively).

As in the analysis of the chromametric data, the description of the clinical assessment is focussed on the data assessed 1 h after the end of treatment. In the fields treated with the DM-o vehicle, some vasoconstriction was observed in 13 subjects, leading to a score sum of 15. In 11 cases, mild vasoconstriction (score 1) and in 2 cases moderate vasoconstriction (score 2) was observed. In the fields treated with DM-o, vasoconstriction was found in 29 subjects (score sum: 59). Mild vasoconstriction was found in 4 cases, moderate vasoconstriction in 20 cases and intense vasoconstriction (score 3) in 5 cases. In the fields treated with the DM-fo vehicle, mild vasoconstriction was observed in 10 subjects, leading to a score sum of 10. In the fields treated with DM-fo, some vasoconstriction was noted in all 30 subjects (score sum: 60). Mild vasoconstriction was observed in 4 cases, moderate vasoconstriction in 22 cases and intense vasoconstriction in 4 cases.

Table 3. Descriptive statistics for baseline-corrected, untreated control site-corrected a* values

	TP h	n	Mean	SD	Min	Max	Lower 95% CL	Upper 95% CL
DM-o-V	1	30	0.61	0.93	–0.98	2.71	0.27	0.96
	2	30	0.50	0.97	–0.92	3.37	0.14	0.87
	4	30	0.41	1.16	–1.67	2.52	–0.03	0.84
	6	30	0.24	1.13	–1.33	3.15	–0.18	0.67
	18	30	–0.16	0.84	–2.60	1.68	–0.47	0.15
DM-o	1	30	2.93	1.46	–1.26	5.38	2.39	3.47
	2	30	2.93	1.38	–0.15	6.14	2.41	3.44
	4	30	2.76	1.14	–0.32	4.61	2.34	3.19
	6	30	3.00	1.32	0.88	6.12	2.51	3.49
	18	30	0.61	1.13	–1.94	2.65	0.19	1.04
DM-fo-V	1	30	0.41	0.81	–1.47	2.56	0.11	0.72
	2	30	0.14	0.92	–1.72	2.45	–0.20	0.49
	4	30	–0.32	0.90	–1.90	2.55	–0.65	0.02
	6	30	–0.22	1.01	–1.84	2.30	–0.60	0.16
	18	30	–0.18	0.78	–1.96	1.10	–0.47	0.11
DM;-fo	1	30	3.39	1.53	–1.05	6.49	2.82	3.96
	2	30	3.33	1.48	0.90	6.99	2.78	3.88
	4	30	3.09	1.05	1.42	5.53	2.70	3.49
	6	30	3.33	1.36	1.16	6.50	2.82	3.83
	18	30	0.74	1.31	–2.22	2.85	0.26	1.23
HC 1.0%	1	30	0.37	1.03	–1.87	2.63	–0.02	0.75
	2	30	0.24	0.93	–2.63	1.79	–0.11	0.58
	4	30	–0.01	0.89	–2.85	1.43	–0.34	0.32
	6	30	0.05	1.22	–3.44	2.40	–0.40	0.51
	18	30	–0.08	0.82	–2.33	1.35	–0.38	0.23
BM 0.05%	1	30	3.26	1.52	1.12	7.23	2.70	3.83
	2	30	3.31	1.73	1.04	6.94	2.67	3.96
	4	30	2.98	1.36	0.70	6.23	2.47	3.49
	6	30	3.36	1.49	1.06	6.46	2.81	3.92
	18	30	0.76	1.25	–2.79	2.87	0.30	1.23
CP 0.05%	1	30	2.73	1.51	–0.09	5.76	2.16	3.29
	2	30	2.77	1.66	–0.03	7.09	2.15	3.39
	4	30	2.59	1.43	–0.14	5.59	2.06	3.12
	6	30	3.07	1.51	0.09	5.73	2.51	3.63
	18	30	0.81	1.13	–1.30	3.72	0.39	1.23

DM-o-V = DM-o vehicle; DM-fo-V = DM-fo vehicle; TP = time point; CL = confidence limits.

In the fields treated with HC 1.0%, mild vasoconstriction was observed in 9 subjects, leading to a score sum of 9.

In the fields treated with BM 0.05%, some vasoconstriction was found in all 30 subjects (score sum: 58). Mild vasoconstriction was noted in 5 cases, moderate vasoconstriction in 22 cases and intense vasoconstriction in 3 cases.

In the fields treated with CP 0.05%, some vasoconstriction was found in 26 subjects, leading to a score sum of 48. In 6 cases, mild vasoconstriction, in 18 cases moderate and in 2 cases intense vasoconstriction was observed (table 2; fig. 2).

Activity Conclusions

Under the conditions in this vasoconstrictor assay DM-o and DM-fo showed clear blanching. Accordingly, topical bioavailability of DM was shown for both Topisolon formulations. In contrast, both corresponding vehicles showed only slight blanching. The comparisons between the Topisolon formulations and the corresponding vehicles showed that the active formulations were obviously more active. The active comparators with similar (BM 0.05%) or higher strength (CP 0.05%) showed similar blanching effects as the DM formulations. Less of a blanching effect was noted for the comparator with lower strength (HC 1.0%).

The chromametric measurements demonstrated clear reduction in skin redness for DM-o, DM-fo, BM 0.05% and CP 0.05%. The mean a* values were similar for these formulations. In the fields treated with HC 1.0%, only a slight reduction in skin redness was observed (mean a* value: 0.37). In the fields treated with the DM-o vehicle and the DM-fo vehicle, the mean a* values were comparable amounting to 0.61 and 0.41, respectively (tables 1–3).

The blanching effects of DM-o, DM-fo, BM 0.05% and CP 0.05% were confirmed by the lower 97.5% confidence limits of the mean a* values being greater than 0. The corresponding 97.5% confidence intervals for the DM formulations and the comparators of similar and higher strength (BM 0.05% and CP 0.05%) showed an overlap in every case. No overlap was seen between the DM formulations and the comparator of lower strength (HC 1.0%) and between the DM formulations and their corresponding vehicles.

Furthermore, both DM-o and DM-fo were noninferior to each of the comparators when considering a 25% margin.

Comparing the data 1 h after the end of treatment, the results of the clinical assessment reflect the chromametric data. DM-o, DM-fo, BM 0.05% and CP 0.05% had a clearly greater effect than both vehicles and HC 1.0%.

The vehicles and HC 1.0% had no clear-cut vasoconstrictive effect. DM-o, DM-fo and BM 0.05% showed a similar vasoconstrictive potential. CP 0.05% was found a little less active. No serious adverse events were reported during the entire study (table 3; fig. 3).

Discussion

The blanching activity of topical corticosteroids is a pharmacodynamic phenomenon which correlates well with clinical efficacy [3, 6]. In this clinical study, the activity of two DM formulations (DM-o and DM-fo) was compared with the activity of their active ingredient-free vehicles and the activity of three marketed active comparators of different strengths (HC 1.0%, BM 0.05%, and CP 0.05%). In this trial, a 6-hour open application for all study medications was chosen since this is an established treatment period for corticosteroids of medium potency such as DM. At baseline, the mean a* values were comparable in all test fields, which confirms correct conditions for chromametric measurement and intraindividual comparison of different test fields.

One hour after the end of treatment, a clear reduction in the mean a*b*c* values was observed in the fields treated with DM-o, DM-fo, BM 0.05% and CP 0.05%. Only a slight reduction in the mean a* values was observed in the fields treated with the vehicles and HC 1.0%. The weak effect in the fields treated with HC 1.0% may be attributed to the study conditions optimized for the moderate-potency glucocorticoids.

According to the classification of the strength of glucocorticoids, it was expected that the highest degree of blanching would be seen in the fields treated with CP 0.05% being the highest-potency corticosteroid. The ranking observed in this study can be explained by the importance of the vehicle composition and subsequent release of the corticosteroid from the vehicle. In this study, all of the vehicles of the study medications were different. It is likely that the release of CP from CP 0.05% was not as good as the release of the actives from the DM formulations and BM 0.05%. The role of the vehicle in the context of cutaneous bioavailability of topical corticosteroids is well established [13]. In principle, vehicles of the ointment type, which are more fatty, may lead to better penetration of the active ingredient due to an occlusive effect and therefore to an amplification of the effect [1, 14]. As ointments are often considered favorable in the treatment of atopic dry skin, the DM formulations tested here look appropriate for initial treatment of manifest atopic eczema.

Conclusion

Topical bioavailability of DM was shown for both formulations by chromametric measurement and clinical assessment in the vasoconstriction assay. DM-o, DM-fo and BM 0.05% showed a similar vasoconstrictive potential. CP 0.05% was found a little less active. HC 1.0% and the DM-o and DM-fo vehicles had no clear-cut vasoconstrictive effect.

References

1 Luger T, Loske KD, Elsner P, Kapp A, Kerscher M, Korting HC, Krutmann J, Niedner R, Röcken M, Ruzicka T, Schwarz T: Topical skin therapy with glucocorticoids – Therapeutic index. J Dtsch Dermatol Ges 2004;2:629–634.

2 Niedner R: Entwicklung der topischen Kortikoide; in Niedner R (ed): Kortikoide in der Dermatologie. Bremen, Uni-med, 1998.

3 McKenzie A, Stoughton R: Method for comparing percutaneous absorption of corticosteroids. Arch Dermatol 1962;86:608–610.

4 Seidenari S, Di Nardo A, Mantovani L, Giannetti A: Parallel intraindividual evaluation of the vasoconstrictory action and the anti-allergic activity of topical corticosteroids. Exp Dermatol 1997;6:75–80.

5 Woodford R, Barry BW: Proceedings: comparative bioavailability of proprietary hydrophilic topical steroid preparations. J Pharm Pharmacol 1973;25(suppl):123.

6 Gorne RC, Greif C, Metzner U, Wigger-Alberti W, Elsner P: Assessment of topical corticosteroid activity using the vasoconstriction assay in healthy volunteers. Skin Pharmacol Physiol 2007;20:133–140.

7 Savin RC: Desoximetasone – A new topical corticosteroid: short- and long-term experiences. Cutis 1978;21:403–407.

8 Hebert AA, Koo J, Fowler J, Berman B, Rosenberg C, Levitt J: Desoximetasone 0.25% and tacrolimus 0.1% ointments versus tacrolimus alone in the treatment of atopic dermatitis. Cutis 2006;78:357–363.

9 Henry M, Hanks G, Whelan A: A randomized, double-blind therapeutic trial of 0.25% desoxymethasone and 0.1% hydrocortisone 17-butyrate in the treatment of varicose eczema. Curr Med Res Opin 1980;6:502–506.

10 Ashton RE, Catterall M, Morley N, Fairris G, Joseph DN: A double-blind comparison of 0.25% and 0.05% desoxymethasone, 0.1% betamethasone valerate and 1% hydrocortisone creams in the treatment of eczema. J Int Med Res 1987;15:160–166.

11 Queille-Roussel C, Poncet M, Schaefer H: Quantification of skin-colour changes induced by topical corticosteroid preparations using the Minolta Chroma Meter. Br J Dermatol 1991;124:264–270.

12 Morgan JF: p Value fetishism and use of the Bonferroni adjustment. Evid Based Ment Health 2007;10:34–35.

13 Krochmal L, Wang JC, Patel B, Rodgers J: Topical corticosteroid compounding: effects on physicochemical stability and skin penetration rate. J Am Acad Dermatol 1989;21:979–984.

14 Korting HC, Maslen K, Gross G, Willers C: Comparison of activity of different topical corticosteroid creams and ointments using a vasoconstriction assay: superiority of hydrocortisone butyrate over hydrocortisone. J Dtsch Dermatol Ges 2005;3:348–353.