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Critical Appraisal of Reports on the Treatment of Perioral Dermatitis

Klaus Weber[a] Rudolf Thurmayr[b]

[a]Private Practice and Krankenhaus der Missionsbenediktiner, Tutzing, and [b]Department of Medical Statistics and Epidemiology, Technical University of Munich, Munich, Germany

Key Words
Erythromycin · Evidence-based medicine · Metronidazole · Perioral dermatitis · Tetracycline

Abstract
Background: Presently, problems exist with the rationale of oral therapy and the nature and indication of topical and accompanying treatment of perioral dermatitis. ***Objective:*** Providing the basis to overcome these problems by a quality evaluation of treatment reports and assessment of the consistency of treatment experience. ***Methods:*** Sources were Medline (1964–2004), Embase (1966–2004), the Cochrane Central (1971–2004) and 526 references of 3 textbooks, 2 recent reviews and 30 papers on perioral dermatitis. Thirty English and German articles were selected. These studies were evaluated according to principles of evidence-based medicine and related criteria. Evaluation of 28 papers was carried out by the authors and of our own 2 papers by 2 other reviewers. Consistency of results was qualitatively assessed by the authors. ***Results:*** There were only 2 therapeutic trials of medium-range quality. The other studies were of low quality. Consistency was noted concerning treatment with oral tetracycline (with 1 exception), discontinuation of topical corticosteroids and cosmetics and, to a lesser extent, regarding no therapy. There was inconsistency in respect to topical therapy. ***Conclusion:*** The presented data help to interpret and conduct studies on the treatment of perioral dermatitis.

Introduction

Perioral dermatitis (POD) consists of erythematous papules, papulopustules or papulovesicles, usually not larger than 2 mm in size, frequently accompanied by a diffuse erythema. POD is predominantly seen in the perioral, paranasal and/or periorbital region. The disorder is sometimes observed in men and children but can be found particularly often in women during the young and middle ages [1–3].

Many authors favour oral tetracycline for the treatment of POD. Certain topical antibiotics and metronidazole have been regarded as treatment of second choice [1–3]. Some dermatologists recommend no therapy [1, 4]. The discontinuation of topical corticosteroids and cosmetics is said to be important [1–8]. However, several problems are encountered. Since the rationale of oral therapy is doubtful, it might be preferable to use effective topical regimens instead of oral tetracycline. Yet, the efficacy of a topical regimen has not been proven apart from one possible exception [6]. Moreover, the nature and in-

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Dr. Klaus Weber
Eichgrabenstrasse 17
DE–82340 Feldafing (Germany)
Tel. +49 8157 7112, Fax +49 8157 922995
E-Mail Dr.KlausWeber@t-online.de

Table 1. Quality evaluation of randomised studies according to principles of evidence-based medicine

Quality criteria[1]	Schubert et al. 1973 [4]	Veien et al. 1991 [5]	Weber et al. 1993 [6]
Randomisation (1)	1	1	1
Concealing of randomisation list (1)	0	0	0
Sufficiently long and complete follow-up (1)	1	0.5	0.5
Intention-to-treat analysis (1)	0	0	0
Blinding (1)	0	1	0
Similarity of pretreatment parameters (1)	0	0	0.5[3]–1[4]
Similarity of accompanying treatment (1)	0.5	0.5	1
Other factors limiting the validity of study (1)[2]	0	1	0.5[4]–1[3]
Total (8)	2.5	4	4

Figures in parentheses indicate maximal scores.
[1] Seven criteria according to Sackett et al. [36].
[2] Additional criterion (courtesy of Prof. F. Porzsolt).
[3] Score of Dr. Fässler.
[4] Score of Prof. Breit.

dication of accompanying treatment need clarification. The purpose of the present paper was to critically appraise the literature, thereby providing the basis to overcome these problems.

Methods

Sources and Identification of Studies

Up to February 2004, sources for this study were Medline (1964–2004), Embase (1966–2004), the Central Register of Controlled Clinical Trials (Central) of the Cochrane Library (1971–2004) and the 526 references of 3 textbook articles [1–3], the 30 papers cited in this study [4–33] and 2 recent reviews [34, 35]. In Medline and Embase, 125 out of 215 and 296 out of 454 articles, respectively, were found referring to 'perioral (and) dermatitis and therapy'. Out of the 526 references mentioned, 183 references found by hand-searching referred to therapy of POD. A systematic review was not found in the databanks.

Selection of Studies

Search was for studies containing any information on the therapy of POD based on at least 9 patients, but smaller case series were also selected if they had been mentioned frequently in the literature [11, 19, 25] or in the Cochrane Central [28]. In the Cochrane Central, only 6 out of 8 articles referred to treatment of POD [5, 6, 11, 12, 27, 28]. For Medline/Embase, the selection process was as follows: from 125/296 articles, 36/160 articles were excluded in a first step (28/105 with diagnoses other than POD, 8/42 dealing with corticosteroids, 0/13 dealing with therapeutics in general) amounting to 89/136 papers; excluded were 64/107 additional articles (36/51 referring to non-therapeutic aspects of POD, 5/12 describing patients with granulomatous POD, 16/33 with languages other than English or German, 7/9 small series and case reports of POD, 0/2 other publications: a paper by A.F. Nikkels and G.E. Piérard because of uncertain diagnosis and 1 POD paper [18] listed twice) amounting to 25/29 articles, respectively. Four papers had to be added to the 25 Medline articles because they were listed in Embase [6–8, 27] or in the Cochrane Central [6, 27], but not in Medline, amounting to 29 databank papers. Another article [21] was extracted from the cohort of 183 articles mentioned above. This amounted to the total number of 30 papers to be evaluated.

Quality Evaluation

To quantify the evaluation of these 30 articles according to the *principles of evidence-based medicine* outlined in table 1, we decided to award 1 score point for fulfilment of each of the 8 criteria, half a point for partial fulfilment and 0 for lack of fulfilment. Seven criteria stemmed from the publication of Sackett et al. [36]. The criterion 'other factors limiting validity of study' was added following the suggestion of Prof. F. Porzsolt, University of Ulm, Germany; it included question changes within the paper, problems with the validity of methods and lack of essential information such as tiny size of paper, omission of important baseline criteria and poor definition of efficacy parameters.

In addition, a *quality evaluation for rosacea studies* was applied to the 30 articles selected [37]. POD is similar to rosacea and has sometimes been called rosacea-like dermatitis [31]. This evaluation included 12 criteria (table 2). Each criterion obtained a score of 0 for failure and 1 or 2 points for fulfilment of the criterion. Two points were allocated for more important and 1 point for less important criteria. Following these guidelines, a study was regarded to be of high quality if it received a score of 15–20 points [37].

Investigators. Twenty-eight out of the 30 papers were evaluated by the two authors, first independently and then by consensus discussions. The authors reached agreement on each question discussed. Two own papers [6, 26] were independently evaluated by Prof. Dr. R. Breit, Pullach, and Dr. Margrit Fässler, Munich, Germany. However, we cannot rule out a publication bias.

Table 2. Quality evaluation of randomised trials according to Gupta and Chaudhry [37]

Quality criteria	Schubert et al. 1973 [4]	Veien et al. 1991 [5]	Weber et al. 1993 [6]
Randomisation (2)	1	1	2
Blinding (2)	0	2	0
Clearly defined aims (1)	1	1	1
Prior sample size calculation (2)	0	0	1
Inclusion/exclusion criteria (2)	1	2	1[1]–2[2]
Baseline patient age and sex (1)	0	1	1
Baseline patient characteristics (2)	0	1	2
Statement of intervention (1)	1	1	1
Definition of efficacy parameters (2)	1	2	2
Assessment of compliance (1)	0	1	0
Intention-to-treat analysis (2)	0	0	0
Statistical analysis (2)	1	2	2
Total (20)	6	14	13[1]–14[2]

Figures in parentheses indicate maximal scores.
[1] Score of Prof. Breit.
[2] Score of Dr. Fässler.

Consistency of Results

Following the suggestion of Sackett et al. [36], we assessed the publications for consistency of results. Consistency of results means results pointing in the same direction (of effects).

Assessment of Data

Data could only be assessed qualitatively. A reasonable statistical analysis was not possible because of lack of pertinent data and the low level of evidence found in most papers [4, 7–33] and since the 2 papers with medium-range quality [5, 6] were different in several respects.

Results

We found 30 studies [4–33] to contain at least partly appropriate information about the treatment of POD (table 3). The quality evaluation based on principles of evidence-based medicine [36] only revealed 2 studies with a medium-range score of 4 [5, 6] and the remaining 28 studies with scores between 0.5 and 2.5 (tables 1, 3) which we regarded to be of low quality. According to the other evaluation system [37], 2 trials [5, 6] received above average scores of 13–14 and the other 28 papers obtained scores of 3–7 (tables 2, 3). Both evaluation systems yielded rather similar scores (correlation factor r = 0.88).

Randomisation

Only 3 investigations [4–6] were randomised justifying 1 point (tables 1, 2). One paper [6] remarked that the randomisation procedure followed a 'predetermined order' (awarded with a second point in table 2). The randomisation list was not concealed in any study (score of 0). In 1 study, only 2 of 3 rather small groups of patients were randomly selected [14] so that this paper was not separately considered and was awarded with 50% score points. All other papers obtained a score of 0 for randomisation.

Follow-Up

The follow-up of the randomised studies was 68–76 days [4], 8 weeks [5] and 50–80 days [6]. We regarded this to be a sufficiently long period of time awarded with half a point in table 1. The follow-up seemed to have been complete in 1 investigation [4] awarded with another half point. According to the other randomised studies, 9% [5] and 18% [6] of the patients did not return for follow-up. The other papers received 1 point [12, 13, 18, 22, 24–26, 29], 0.5 point [7–10, 14–17, 19–21, 23, 28, 30, 32, 33] or a score of 0 [11, 27, 31].

Intention-to-Treat Analysis

An intention-to-treat analysis was not carried out (score of 0 for all papers). Veien et al. [5] stated that they employed the intention-to-treat-principle in all statistical evaluations, but they did not present the results of the analysis addressing the 10 drop-out patients (tables 1, 2).

Table 3. Quality evaluation and pertinent data of 30 reports on the treatment of POD

Reference No.	Number of patients	Therapeutic regimen	Discontinuation of corticosteroids/cosmetics		Disappearance of papules, weeks	Evaluation score	
						table 1	table 2
4	25	no therapy	yes	yes	7.7[1]	2.5	6
	25	oral T	yes	yes	7.3[1]		
5	54	topical metronidazole	yes	no	up to >8*	4	14
	54	oral T	yes	no	up to >4*		
6	31	oral placebo	yes	yes	up to >11**	4	13–14
	35	oral T	yes	yes	up to 5.7**		
	33	topical E	yes	yes	up to 7**		
7	21	sulphonated shale oil paste	yes	yes	>6	1	6
8	25	sulphonated shale oil paste	yes	yes	3.7 (2–6)[2]	1	6
9	29	oral T + various topicals	yes (?)	no	8–12 (?)	0.5	4
10	73	oral T	yes	no	?	0.5	5
11	8	oral T + topical cort.	yes	no	?	0.5	6
12	56	oral T + topicals	no	yes	>4	1	6
	50	various topicals	no	yes	?		
13	206	(oral T)[3] + topicals	yes	no	>12 (?)	1	4
14	14	oral T + topical hydrocort.	no	no	12 (?)[4]	1	5
	11	oral T + topical desonide	no	no	12 (?)[4]		
15	43	oral T + topical cort.	yes	no	>6–12 (?)	0.5	4
16	30	topical T	yes	no	>1–4 (?)	0.5	4
17	116	oral T	yes	no	>6 (?)	0.5	4
18	29	hexachlorocyclohexane[5]	yes	no	5 (?)	1	5
19	6	topical cort. + topical E	yes	no	5 (2–8) (?)	0.5	5
20	82	oral T or oral E + topicals	yes	no	8–12 (?)	0.5	5
21	92	antimalarials	no	no	(?)	0.5	4
22	49	sulphur ointment	no	no	>2 (?)	1	4
23	50	less cosmetics + (oral T)[3]	yes	yes	>4 (?)	1	7
24	14	various topicals	yes	no	5 (1–8) (?)	1	5
25	7	topical metronidazole	yes	no	16 (?)	1	5
26	10	topical E	yes	yes	5 (3–12)	1.5	7
27	21	topical cort. + oral T[3]	yes	no	?	0.5	7
28	3	oral T + placebo[6]	yes	no	>6–8 (?)	1	5
29	32	no therapy	yes	yes	8 (2–24) (?)	1.5	5
	34	various topicals	yes	yes	12 (?)		
30	17	oral metronidazole	no	no	>2–5 (?)[7]	0.5	3
31	42	topical cort.	yes	yes	?	0.5	5
32	32	oral T + topical cort.	yes	yes	>2–4 (?)	1	5
33	9	oral T + oral cort. + topicals	yes	no	12 (?)	0.5	4

Evaluation score according to the criteria of tables 1 (left lane) and 2 (right lane). * $p < 0.01$; ** $p < 0.001$. E = Erythromycin; cort. = corticosteroids; hydrocort. = hydrocortisone; T = tetracycline; ? = not or not clearly described.

[1] No significant difference.
[2] Nine patients with recurrence.
[3] In some patients only.
[4] No statistical analysis.
[5] Plus various topicals in 8 patients.
[6] Cross-over approach.
[7] (Almost) no improvement in 3 patients.

Blinding

One investigation was double-blind and double-dummy [5] (tables 1, 2). Three other studies reported on some degree of blinding and were awarded with 50% score points [11, 27, 28]. Otherwise, there was no blinding.

Similarity of Pretreatment Parameters

Only 1 paper [6] elucidated the similarity of the pretreatment groups but only evaluated 99 out of 120 patients who returned for follow-up (table 1).

Similarity of Accompanying Treatment

Avoidance of topical corticosteroids and avoidance or occasional usage instead of overuse of cosmetics [4, 6–8, 23, 26, 29, 31, 32] were awarded with 0.5 point (tables 1, 3). These measurements and the transient application of topical corticosteroids of rather low potency for about the first 2 weeks after initiation of therapy [11, 12, 14, 15, 19, 20, 27, 33] (not justifying a point by itself) were regarded to represent appropriate accompanying treatment. The similarity of accompanying therapy was evaluated regarding avoidance of both cosmetics and topical corticosteroids in 1 paper [6] and concerning avoidance of topical corticosteroids but not of cosmetics in another trial [5] justifying 0.5 point. Application of topical corticosteroids for more than 2 weeks and lack to discontinue cosmetics and/or topical corticosteroids (table 3) were considered as failure of accompanying treatment (score of 0).

Other Factors Limiting Validity

In 2 randomised trials [5, 6], no other important factors were found to limit validity. However, various factors limited validity in all other studies (score of 0). Schubert et al. [4] used a wash-out period of 1 week in oral tetracycline but not in no therapy recipients and applied lotio alba in patients who were said to undergo no therapy (see discussion); in addition, the size of the paper was limited to 1 page and only received a score of 6 in table 2.

The following criteria refer to table 2.

Clearly Defined Aims

The aim of the study was more or less clearly defined only in some papers [4–8, 10, 12, 16–20, 22–32] awarded with 1 point.

Prior Sample Size Calculation

Prior sample size calculation was not reported by any study group (score of 0) [4, 5, 7–33]. However, a pre-set trial size was presented in 1 investigation [6] justifying 1 point.

Inclusion and Exclusion Criteria

One point was awarded for inclusion criteria and another point for exclusion criteria. The diagnosis of POD was regarded as inclusion criterion in all papers. A definition of POD was hardly ever presented. Nevertheless, we assumed that the authors made the correct diagnosis in case of a lacking definition. Five papules [5] – too small a number of papules in our opinion – or at least 15 papules [26] were required for the diagnosis. Patients with rosacea, seborrhoeic dermatitis or pregnancy were excluded [5, 6], but the other papers did not mention any exclusion criterion. In 1 paper, patients with pruritus were unduly excluded [5].

Baseline Patient Age and Sex

Baseline patient age and sex were listed in most papers (1 point) [5–16, 18–21, 23–29, 31–33].

Baseline Patient Characteristics

Baseline patient characteristics included duration of POD, number of papules and previous application of topical corticosteroids and cosmetics. One trial [6] listed all 4, and other studies included 1–3 of these baseline characteristics [5, 7–15, 17–27, 29, 31–33]. One point was awarded for the inclusion of at least 1 baseline parameter mentioned.

A comparison of pretreatment parameters justified another point [6].

Statement of Intervention

All studies made statements about the type of treatment applied or administered and were awarded with 1 point. However, details about the therapeutic regimens were not always presented [10, 13, 21, 24, 31, 33].

Efficacy Parameters

Eight studies using the papules (papulopustules, papulovesicles) as efficacy parameter obtained 1 point [4–8, 12, 26, 27]. Counting the papules before and after initiation of therapy and allocating the results to the therapeutic groups was awarded with an additional point [5, 6]. We felt that papers claiming resolution or complete resolution of POD although no definition of resolution was presented did not deserve a point. Since a pretreatment erythema is not present in all POD patients [14, 31, pers. observations of K.W.], the inclusion of erythema [5, 7, 27] does not appear to be an appropriate efficacy param-

eter meaning an undue exclusion of POD patients without accompanying pretreatment erythema (score of 0). On the other side, the posttreatment erythema found in all patients was reported to disappear after 10 and 11 weeks [4], >6 weeks [7], >8 weeks [5], up to 8 weeks [22] or after few more than 5 (range 3–12) weeks [26], respectively.

Compliance

Rather detailed data on non-compliance with the treatment guidelines were presented only in 3 papers [5, 23, 26] awarded with 1 point. The other papers made no statements about compliance or provided quite limited information on non-compliance (with the use of cosmetics in about 12 patients [6], with topical corticosteroids in some patients [10, 17, 27] or with the recommended therapy in 1 patient [12]) not justifying a point.

Statistics

Detailed statistical analyses justifying 2 points was provided by 2 papers only [5, 6]. One point was awarded if a single statistical test was performed [4, 11, 23].

Consistency of Results

Consistency of results rested on a qualitative assessment of therapeutic experiences [4–33]. Accordingly, consistency was observed regarding treatment with oral tetracycline (with 1 exception), the discontinuation of topical corticosteroids and cosmetics and, to a lesser extent, in respect to no therapy (table 3). Inconsistency was noted concerning topical therapy.

Discussion

We have used guidelines of evidence-based medicine [36] and a related system [37] to evaluate the quality of studies on the treatment of POD. The principles outlined by Sackett et al. [36] provided the basis of the evaluation. Gupta and Chaudhry [37] have discussed in some detail criteria for the conduct and interpretation of therapeutic trials in general using rosacea as an example. Such a debate appears to be of value for investigations on the treatment of POD as well.

However, there are limitations with these two evaluation systems. Accordingly, the criterion 'other factors limiting validity' was added to the guidelines of Sackett et al. [36]. In the other system [37], follow-up and accompanying treatment seemed to be underrepresented. By using two systems, we tried to overcome the limitations.

We have found that only 2 articles on the treatment of POD were of medium-range quality [5, 6] and the remaining 28 articles were of low quality. This comparably low level of evidence limits statements about the consistency of results. Consistency of results among various therapeutic trials, especially if they are of high quality, indicates a treatment effect [36]. If the studies are of medium-range or low quality as found in the present investigation and their results point in the same direction and are therefore consistent, a therapeutic effect may be possible but the evidence is more or less vague.

There are some hints for consistency about no therapy providing information about the natural course of POD. Röckl and Schubert [29] noted that no therapy in 24 out of 32 hospitalised patients led to clearing of POD within 2 months (range 0.5–6 months). In another paper, the same group reported that no therapy cleared 'all papules, pustules and scales' in 25 patients within 54 days [4]. No therapy in these mainly hospitalised patients included avoidance of topical corticosteroids and cosmetics, but lotio alba was applied [E. Schubert, pers. commun.]. It appears to be doubtful whether the application of lotio alba really means no therapy. Nevertheless, these findings are to some extent in agreement with the clearing of papules within more than 80 days in 31 oral placebo recipients in whom topical corticosteroids and cosmetics were also forbidden [6]. Recently, placebo treatment has been found to lack clinically important effects [38]. Placebo treatment appears therefore to be comparable to no therapy. These observations taken together provide hints that POD is a self-limited disorder because it spontaneously clears in most patients within approximately 3 months and does not represent a chronic disease persisting for years as has been indicated by experts [1–3].

There is consistency regarding therapy with oral tetracycline apart from 1 exception. Oral tetracycline has been found to be superior to oral placebo in a randomised controlled trial of medium-range quality [6]. Oral tetracycline clears the papules of POD in most patients within 4 weeks [5, 6]. Oral tetracycline has been found to have a beneficial therapeutic effect in non-controlled studies [9–12, 14, 15, 17, 20, 23, 26–28, 32, 33] and is regarded by most experts as treatment of choice [2, 3] or has been recommended [1, 35]. The sole exception to this widely held view is the randomised controlled trial of Schubert et al. [4] claiming that oral tetracycline is not superior to no therapy. However, low quality and inconsistency with other experiences limit the value of this study. Thus, oral tetracycline is presumably effective, and no therapy does not appear to be a reasonable alternative compared to oral tetracycline.

However, the rationale of oral therapy in a local disease like POD is doubtful. There are several reasons to avoid oral tetracycline for the treatment of POD: pregnancy and early childhood [5, 12, 14, 16, 17, 19, 24, 25], a tendency for a higher rate of side-effects compared with topical therapy [6, 12, 19] and last not least effective topical therapy.

Unfortunately, we have noted inconsistency concerning topical therapy. A randomised controlled trial provided some evidence that an erythromycin emulsion might be effective because it was found to be superior to oral placebo [6]. There were hints in the same publication that the erythromycin emulsion was similarly effective as oral tetracycline [6]. In another randomised controlled trial, Veien et al. [5] claimed but did not demonstrate efficacy of a metronidazole cream; this preparation was inferior to oral tetracycline [5]. Sulphonated shale oil preparations [7, 8], a topical tetracycline preparation [16], a hexachlorocyclohexane emulsion [18], 10% sulphur mixed in unguentum emulsificans aquosum [22], metronidazole preparations [24, 25], an erythromycin ointment [26], various drying substances [29] or topical corticosteroid preparations [31, 32] may or may not be effective but were not evaluated in controlled trials. Surprisingly, several of these preparations were well tolerated by most or all patients treated [5–8, 16, 22, 25, 26]. Agreeable topical preparations applied without topical corticosteroids and cosmetics were found to clear the papules of POD in most patients within 4–7 weeks [6–8, 26], in compliant patients using an erythromycin ointment usually within 5 weeks [26].

The concept of accompanying treatment is somewhat complex and needs at least partial reconsideration. There are consistent hints that a therapeutic regimen should be accompanied by avoidance of both topical corticosteroids and cosmetics [1–4, 6–8, 23, 26, 29, 31, 32, 34, 35]. Noncompliance with the avoidance of cosmetics [23, 26] or topical corticosteroids [10, 17, 26] might unduly influence outcome. Thus, a prolonged clearing time in patients with POD may be due to disregard of avoidance of topical corticosteroids or cosmetics or both rather than due to insufficiency of the therapeutic regimen itself. Moreover, although most authors agree that previously used topical corticosteroids ought to be discontinued at the first visit, certain topical corticosteroids such as hydrocortisone butyrate have been recommended to mitigate the unpleasant effect of exacerbation for about the first 2 weeks after initiation of therapy [11, 12, 14, 15, 19, 20, 27]. However, the application of topical corticosteroids beyond the exacerbation time of about 2 weeks [11, 12, 14, 15, 19, 20, 27, 31, 32] might be detrimental. In addition, occasional usage instead of overuse of cosmetics has been suggested [23, 39] but the beneficial effect of this recommendation needs confirmation.

In this context, it may be of interest that cosmetics have been found to play a pathogenetic role [12, 40], especially in association with an atopic diathesis [39], and that topical corticosteroids aggravate but usually do not elicit POD [6, 39, 40].

Presently, the lack of high-quality studies leads to a lot of uncertainty. Moreover, there is a need for more plausibility regarding the treatment of POD. More work is needed to overcome these problems. The following hypothetical concept might help in this respect: (1) one or the other effective and agreeable topical regimen (to be determined) is the treatment of choice for POD; an erythromycin preparation may be a possibility [6]; (2) oral tetracycline is indicated in severer disease only [26]; (3) avoid topical corticosteroids; possible exception: low-potency topical corticosteroid in case of exacerbation (if there is any) during the first 2 weeks after initiation of therapy; (4) avoid cosmetics, fatty lip stick and other external substances; possible exception: application of an ointment such as Eucerin cum aqua hand-made by a pharmacist [6, 26, 29] in case of pronounced dryness and occasional usage of cosmetics [23, 39].

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References

1 Braun-Falco O, Plewig G, Wulff HH, Burgdorf WHC: Dermatology, ed 2. Berlin, Springer, 2000, pp 1077–1081.
2 Kerr REI, Thomson J: Perioral dermatitis; in Freedberg IM, Eisen AZ, Wolff K, Austen KJ, Goldsmith LA, Katz SI, Fitzpatrick TB (eds): Dermatology in General Medicine. New York, McGraw-Hill, 1999, vol 1, pp 794–799.
3 Greaves MW: Flushing and flushing syndromes, rosacea and perioral dermatitis; in Champion RH, Burton JL, Burns DA, Breathnach SM (eds): Textbook of Dermatology. Oxford, Blackwell Scientific, 1998, vol 3, pp 2110–2112.
4 Schubert E, Beetz HM, Röckl H: Über den Wert der Tetrazyklin-Therapie bei der perioralen Dermatitis. Hautarzt 1973;24:253.
5 Veien NK, Munkvad JM, Nielsen AO, Niordson AM, Stahl D, Thormann J: Topical metronidazole in the treatment of perioral dermatitis. J Am Acad Dermatol 1991;24:258–260.
6 Weber K, Thurmayr R, Meisinger A: A topical erythromycin preparation and oral tetracycline for the treatment of perioral dermatitis: A placebo-controlled trial. J Dermatol Treat 1993;4:57–59.
7 Nüschel C, Wilbrand G, Altmeyer P: Pilotstudie zur Wirksamkeit und Verträglichkeit einer Rezeptur mit 2% Ichthyol bei perioraler Dermatitis. Akt Dermatol 2000;26:391–394.
8 Dirschka T, Tronnier H, Füsgen I: Periorale Dermatitis im hohen Erwachsenenalter. Eur J Geriatrics 2003;5:195–199.
9 MacDonald A, Feiwel M: Perioral dermatitis: Aetiology and treatment with tetracycline. Br J Dermatol 1972;87:315–319.
10 Sneddon I: Perioral dermatitis. Br J Dermatol 1972;87:430–434.
11 Sneddon I: A trial of hydrocortisone butyrate in the treatment of rosacea and perioral dermatitis. Br J Dermatol 1973;89:505–508.
12 Bendl BJ: Perioral dermatitis: Etiology and treatment. Cutis 1976;17:903–908.
13 Wilsch L, Hornstein OP: Statistische Untersuchungen und Behandlungsergebnisse bei der perioralen Dermatitis. Z Psychosom Med Psychoanal 1976;22:115–125.
14 Cochran REI, Thomson J: Perioral dermatitis: A reappraisal. Clin Exp Dermatol 1979;4:75–80.
15 Coterill JA: Perioral dermatitis. Br J Dermatol 1979;101:259–262.
16 Wilson RG: Topical tetracycline in the treatment of perioral dermatitis (letter). Arch Dermatol 1979;115:637.
17 Wilkinson DS, Kirton V, Wilkinson JD: Perioral dermatitis: A 12-year review. Br J Dermatol 1979;101:245–257.
18 Rufli T, Mumcuoglu Y, Cajacob A, Büchner S: *Demodex folliculorum:* Zur Ätiopathogenese und Therapie der Rosacea und der perioralen Dermatitis. Dermatologica 1981;162:12–26.
19 Bikowski JB: Topical therapy for perioral dermatitis. Cutis 1983;31:678–682.
20 Coskey RJ: Perioral dermatitis. Cutis 1984;34:55–58.
21 Frumess GM, Lewis HM: Light-sensitive seborrheid. Arch Dermatol 1957;75:245–248.
22 Nitzschner H: Akarizide Behandlung der perioralen Dermatitis. Dermatol Monatsschr 1987;173:621–622.
23 Fritsch P, Pichler E, Linser I: Periorale Dermatitis. Hautarzt 1989;40:475–479.
24 Manders SM, Lucky AW: Perioral dermatitis in childhood. J Am Acad Dermatol 1992;27:688–692.
25 Boeck K, Abeck D, Werfel S, Ring J: Perioral dermatitis in children – Clinical presentation, pathogenesis-related factors and response to topical metronidazole. Dermatology 1997;195:235–238.
26 Weber K: How I treat perioral dermatitis: Noncompliance with the treatment guidelines. Dermatology 2003;207:215.
27 Graber W: Zur Behandlung der perioralen Dermatitis – 0,1% Hydrokortison-17-butyrat und 1% Hydrokortisoncreme im Seitenvergleich. Schweiz Rundsch Med Prax 1980;69:967–969.
28 Miller WS: Tetracycline in the treatment of perioral dermatitis. North Carolina Med J 1971;32:471–472.
29 Röckl H, Schubert E: Zur 'Therapie' der sogenannten perioralen Dermatitis. Hautarzt 1971;22:527–531.
30 Stieger M: Metronidazol (Flagyl) als Therapievariante bei 'Rosacea' und 'perioraler Dermatitis'. Z Hautkr 1979;54:671–672.
31 Steigleder GK, Strempel A: Rosaceaartige Dermatitis des Gesichts. Hautarzt 1968;19:492–494.
32 Toyosi JO: Neue Wege der Behandlung therapieresistenter acneiformer Dermatosen, insbesondere der perioralen Dermatitis. Hautarzt 1972;23:79–82.
33 Urabe H, Koda H: Perioral dermatitis and rosacea-like dermatitis: Clinical features and treatment. Dermatologica 1976;152(suppl 1):155–160.
34 Hafeez ZH: Perioral dermatitis: An update. Int J Dermatol 2003;42:514–517.
35 Breit R: Die periorale Dermatitis: eine therapeutische Herausforderung; in Plewig G, Wolff H (eds): Fortschritte der praktischen Dermatologie. Berlin, Springer, 1999, vol 16, pp 545–549.
36 Sackett DL, Straus SE, Richardson WS, Rosenberg W, Haynes RB: Evidence-Based Medicine, ed 2. Edinburgh, Churchill Livingstone, 2000.
37 Gupta AK, Chaudhry MM: Evaluating the quality of rosacea studies: Implications for the patient and physician. Dermatology 2003;207:173–177.
38 Hrobjartsson A, Gotzsche PC: Placebo treatment versus no treatment (Cochrane Review). Cochrane Database Syst Rev 2003;CD003974.
39 Dirschka T, Weber K, Tronnier H: Topical cosmetics and perioral dermatitis. J DDG 2004;2:194–199.
40 Malik R, Quirk CJ: Topical applications and perioral dermatitis. Australas J Dermatol 2000;41:34–38.