SKIN

BRIEF ARTICLE

Reassessing Potential Triggering Factors and Trends in Periorificial Dermatitis: A 12-Year Retrospective Cohort Study

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ABSTRACT

Periorificial dermatitis (POD) has historically been associated with topical corticosteroid use. Despite greater awareness and education on safer corticosteroid use, patients continue to present with POD, prompting a reassessment of risk factors for POD and analysis of whether corticosteroid use remains a dominant factor in POD. This retrospective cohort study characterizes the epidemiology of and risk factors for periorificial dermatitis in an academic medical center from 2008-2023.

A total of 451 subjects with periorificial dermatitis were identified, of whom 79% were women and 80% were White. Age ranged from 4 months to 72 years with a mean of 32 years. Of records with clear steroid use data, 37% reported corticosteroid use within 6 months preceding diagnosis, and 23% reported topical corticosteroid use. Rates of preceding topical corticosteroid use, when excluding unknown cases, increased from 15% in subjects diagnosed 2012-2015, to 19% in 2016-2019, and 29% in 2020-2023 (p=0.03). 25% of subjects reported predisposing factors other than corticosteroids, such as facial sunscreens, whitening toothpastes, and heavy moisturizers. Topical antibiotics were the most prescribed treatment (82%).

As anticipated, the use of corticosteroids commonly precedes the development of POD, however, the 37% rate of use in our study was significantly lower than historical reports, which range from 72 – 96%. A significant proportion of POD was not preceded by corticosteroid use, indicating further research might uncover other predisposing factors and better enable prevention of POD. The remaining association between corticosteroid use and POD indicates an ongoing need for education on corticosteroid risks.

INTRODUCTION

Perioral dermatitis, also called periorificial dermatitis (POD), is a common inflammatory skin condition characterized by papules and pustules with eczematous features primarily distributed in the perioral area but variably involving the periocular and perinasal regions.[1,2] POD predominantly affects children of both sexes and young women between the ages of 20 and 45 years.[3] Histologically, POD shares features with

rosacea and displays marked lymphocyte infiltrate and edema.[1,3,4]

The etiology of POD remains unclear.[2,3] POD was first associated with use of fluorinated corticosteroids in the 1960s. Since then, studies have repeatedly identified associations between POD and the use of corticosteroids,[5,6] which may disrupt the integrity of the skin barrier.[1] Other environmental triggers such as fluoridated toothpaste and cosmetic products have been implicated.[1,3] We hypothesized that the provoking factors in patients today may differ from historical reports due to increased awareness of corticosteroid risks. We performed a retrospective study at our institution to determine current corticosteroid use trends in subjects with periorificial dermatitis.

METHODS

A single center retrospective cohort study was conducted by reviewing electronic records to identify and characterize subjects who were diagnosed with perioral (periorificial) dermatitis by dermatologists in the UMass Memorial Healthcare System between the years of 2008-2023. Subjects with concurrent diagnoses of conditions commonly confused with POD were excluded, including acne vulgaris, allergic contact dermatitis, irritant contact dermatitis, and rosacea. Charts were individually screened by researchers. Study data were collected and managed using REDCap electronic data capture.[7] Thirty records were re-extracted by different researchers for validation.

Demographic and lesion characteristic data were collected as available in medical records. Corticosteroid use was considered positive if use was within 6 months prior to the best approximated date of POD onset, negative if records indicated no use within 6 months prior, or unknown if subject's corticosteroid use could not be definitively established by relevant notes and medication history. Treatments attempted and response were recorded based on follow-up documentation.

Fisher's exact test was used to compare rates between groups. An alpha level of 0.05 was used as a criterion to determine statistical significance. All analyses were conducted using SAS software (version 9.4; SAS Institute, Cary, NC).

RESULTS

A query on TriNetX based on diagnostic codes yielded 1020 subjects. Researchers excluded 569 subjects due to incomplete chart information, unclear diagnosis, treatment by non-dermatologists, or records at outside facilities. Ultimately 451 met inclusion criteria. Subject demographics and characteristics are summarized in **Table 1**. Most subjects were female (79%), White (80%) and non-Hispanic (82%). The mean age of subjects at the time of diagnosis was 32 years, ranging from 4 months to 92 years. 144 subjects (32%) were between 0-13 years old. POD most frequently presented in a perioral distribution, followed by perinasal and periorbital distribution.

In all subjects for whom corticosteroid use was known, the frequency of corticosteroid use prior to development of POD was 37% (143/383), with 23% (90/383) using topical corticosteroids. Of patients using corticosteroids, 63% reported topical corticosteroids use, 20% inhaled, 13% intranasal, and 12% oral corticosteroid use. Percentages sum to over 100% as some subjects used multiple forms. Proportions

Table 1. Demographics, exposures, and disease characteristics of periorificial dermatitis

Sample characteristics	Subjects	Percentage
	n	%
Sex		
Female	358	79
Male	93	21
Years of age at diagnosis a		
0-13 years of age	144	32
14-50 years of age	190	42
51+ years of age	117	26
Race		
White or Caucasian	361	80
Black or African American	27	6.0
Asian American	9	2.0
American Indian or Alaskan Native	1	0.22
Race Other/Unknown	53	12
Ethnicity		
Non-Hispanic	369	82
Hispanic	55	12
Ethnicity Other/Unknown	27	6.0
Steroid use		
Steroid use before POD	143	32
Topical steroid use before POD	90	20
No steroid use before POD	240	53
Steroid use before POD unknown	68	15
Steroid use after POD b	84	19
Location c		
Perioral	399	89
Perinasal	111	25
Periorbital	76	17
Other	37	8.2
Unknown	2	0.44
Non-steroidal predisposing factors d		
Present	114	25
Absent	200	44
Unknown	137	30

Note. N = 451. Subjects were on average 31.78 years old at diagnosis (SD = 22.95). Percentages are calculated subjects / N.

[a] Age is divided into categories approximating to onset and end of menses due to hypothesized hormonal contribution.
[b] Steroid use occurred after the reported onset of perioral dermatitis.
[c] Location is reported as the number of individuals with eruptions in this location; individuals may have disease in one or multiple locations.
[d] Non-steroidal predisposing factors include heavy makeup (foundation, powders, etc.), moisturizers (night cream), facial sunscreens, whitening toothpaste, dental rinses (whitening mouthwash, etc.), other whitening products (whitening strips), dental appliances (braces, Invisalign, retainers, night guards).
[e] Full sample is the total number of individuals in each category.

compared to the entire sample (N= 451) are reported in **Table 1**. In subjects for which steroid use was not unknown, the percentage of subjects reporting prior topical corticosteroid use in the years 2012-2015, 2016-2019, and 2020-2023 was 15% (9/60), 19% (28/147), and 29% (50/172), respectively. Using Fisher's exact test, these groups were found to be significantly different (p=0.03).

Predisposing factors other than corticosteroids were reported in 25% of subjects (**Table 1**). The most frequently reported associated factors other than corticosteroids were whitening toothpastes (15%), moisturizers (6.9%), and sunscreens (4.9%) (**Table 2**). Many subjects (30%) did not have enough information in EMR to identify specific inciting factors. Additionally, 13 (2.9%) identified mask use prior to rash eruption; all were diagnosed between 2020-2022. Upon analyzing predisposing factors versus location, dental rinses were significantly associated with the perinasal location compared to other locations (p = 0.03) using Fischer's exact test. In terms of treatment, topical antibiotics were the most utilized therapy (82%, **Table 3**). Of subjects with known treatments, 34% had complete clearance.

Table 2. Frequency of predisposing factors usage by periorificial dermatitis location

Non-Steroidal Predisposing Factors[a]	Perioral			Perinasal			Periorbital			Total[c]	
	n	%	p-value	n	%	p-value	n	%	p-value	n	%
Other [b]	88	22	0.37	22	20	0.79	11	14	0.13	96	21
Whitening toothpaste	64	16	0.15	18	16	0.76	11	14	1.00	68	15
Moisturizers (night cream, etc.)	29	7.3	0.56	11	9.9	0.19	5	6.6	1.00	31	6.9
Facial sunscreens	21	5.3	0.49	8	7.2	0.21	4	5.3	0.78	22	4.9
Heavy makeup (foundation, powders, etc.)	6	1.5	0.23	1	0.9	0.69	1	1.3	1.00	8	1.8
Other whitening	7	1.8	0.99	0	0.0	0.20	1	1.3	1.00	7	1.6

products (whitening strips)											
Dental rinses (whitening mouthwash, etc.)	6	1.5	0.99	4	3.6	**0.03***	2	2.6	0.27	6	1.3
Dental appliances (braces, Invisalign, retainers, night guards)	4	1.0	0.99	2	1.8	0.25	0	0	1.00	4	0.89

Note. Perioral column N = 399. Perinasal column N = 111. Periorbital column N = 76. Total column N = 451. "*" indicates $p < 0.05$.

[a] Individuals may have used multiple different predisposing factors and have disease in multiple locations. Therefore, cells are not mutually exclusive

[b] Other factors that were commonly reported in subject notes include: Face masks, fluoride containing chewing tablets or water, pacifiers, soap, CPAP, etc.

[c] Total may be less than the sum of row n's due to individuals having POD in multiple locations.

Table 3. *Frequency of therapies used for treatment of periorificial dermatitis*

Treatment	Frequency, (% of sample)[a]	Complete clearance, n (%)[b]	Partial clearance, n (%)	No response, n (%)	Lost to follow up, n (%)
Topical antibiotics (clindamycin, metronidazole, erythromycin)	371 (82.3)	127 (34%)	64 (17%)	7 (1.9%)	173 (47%)
Other [c]	131 (29%)	48 (37%)	29 (22%)	2 (1.5%)	52 (40%)
Negative treatment (recommend discontinuing corticosteroids, whitening toothpaste etc.)	127 (28%)	42 (33%)	26 (21%)	2 (1.6%)	57 (45%)
Oral antibiotics (doxycycline, minocycline, tetracycline, cephalexin, erythromycin)	109 (24%)	133 (34%)	69 (18%)	8 (2.0%)	184 (47%)

Topical calcineurin inhibitors (pimecrolimus (Elidel), tacrolimus (Protopic)	67 (15%)	25 (37%)	15 (22%)	1 (1.5%)	26 (39%)
Moisturizers or emollients	55 (12%)	19 (35%)	15 (27%)	1 (1.8%)	20 (37%)
Topical antifungal: clotrimazole (Lotrimin)	27 (6.0%)	12 (44%)	7 (26%)	0 (0.0%)	8 (30%)
Oral isotretinoin	2 (0.44)	0 (0.0%)	2 (100%)	0 (0.0%)	0 (0.0%)
Topical ivermectin	1 (0.22)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (100%)
Total any treatment	431 (96%)	148 (34%)	72 (17%)	8 (1.9%)	203 (47%)

[a] Percentage in first column is out of whole sample, N = 451. Percentages add up to greater than 100 because some individuals received several treatments.

[b] Clearance percentages are taken category across rows, i.e. reported as the percentage of individuals with clearance who used that treatment.

[c] Other category includes the treatments subjects reported using after the onset of their rash, including OTC products. This included topical hydrocortisone, clobetasol propionate, triamcinolone, and desonide, as well as sulfur-based washes and benzyl peroxide-based washes. Use of corticosteroids post-eruption is reported in Table 1.

CONCLUSION

It is unclear whether increased current awareness of the adverse effects of corticosteroids has resulted in lower rates of inappropriate corticosteroid use. Prior reports have found the percentage of corticosteroid use preceding POD to be 96% (n=203, 1979), 85% (n=80, 1986), and 72% (n=79, 2006).[8,9,10] We found the overall rate of prior corticosteroid use in this study population from 2008 – 2023 was 37%, suggesting alternative factors may now play a larger role in pathogenesis. The percentage of corticosteroid use is lower in our data than historical reports; however, there was a significant increase in corticosteroid use between the 3-year periods, with a 10-point increase in the years coinciding with COVID-19 compared to the prior 3-year period. We hypothesize this may suggest increased over-the-counter use by patients with less medical direction due to COVID-related impacts in medical care access.

Consistent with historical trends, most POD subjects in our study were female. While the pathophysiology of POD remains unclear, hormonal fluctuations may be involved.[2] Although fluoride toothpaste, sunscreen, heavy facial creams, and cosmetic products are putative risk factors for POD, only a minority of subjects in our study reported exposure to these products.[3] Topical therapies were the most utilized treatments, which is consistent with early literature.[6] Study limitations include incomplete data due to high number of unknowns and lack of patient diversity in a single center.

In conclusion, corticosteroid use continues to be the prominent predisposing factor for the development of POD, though there is significantly less use in our study population compared to prior cohorts, and many individuals reported no specific predisposing

factor. Future directions of study could include investigating seasonal fluctuations or comparing if rates of steroid use downtrend post-COVID-19. Continued education of prescribers and the public on safe corticosteroid use is needed, as is more research on the pathophysiology of this common condition.

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