

A comparative study between local application of 10% zinc oxide to a combination of 10% zinc oxide and tocopherol in treating infant's diaper dermatitis

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Abstract

Background Tocopherol is known to have an anti-inflammatory effect, thereby reducing erythema, edema, and skin irritation, which are the main pathologies observed in diaper dermatitis.

Objective To compare the effect of local application of a combination of 10% zinc oxide and tocopherol in the treatment of infant diaper dermatitis with plain 10% zinc oxide.

Methods A single-centric, prospective interventional study was conducted in a tertiary care hospital for 18 months where all children aged <1 year newly diagnosed with diaper dermatitis were selected. They were divided into two groups; one group received only 10% zinc oxide, while the other group received a combination of 10% zinc oxide and tocopherol for local application. Patients were assessed for rash dimensions, severity score of diaper dermatitis, and pH of the rash prior to starting treatment and at the end of 5 days. Statistical analysis was done using students paired two-tailed T-test.

Results Out of 115 infants with diaper dermatitis, 88 were included in our study. The decrease in rash dimensions was greater in the study group ($P=0.004$). A mean diaper dermatitis severity score of 1.96 (SD 0.76) cm in the study group was noted on day five of the assessment ($P<0.001$).

Conclusion The healing process in diaper dermatitis is accelerated when a combination of 10% zinc oxide and tocopherol is used. This study supports the evidence of expediting healing by tocopherol, which can be considered in treatment recommendations for diaper dermatitis. [Paediatr Indones. 2024;64:113-9; DOI: 10.14238/pi64.2.2024.113-9].

Keywords: *diaper dermatitis; zinc oxide; tocopherol; vitamin E*

Diaper dermatitis is one of the most common dermatological conditions in the pediatric age group, accounting for approximately 20% of dermatological visits during childhood.¹ Literature estimates of diaper dermatitis rates vary greatly, ranging from 16% to 65%, and given the short duration of diaper dermatitis (typically 2-4 days), most cases are not seen by medical professionals.² Various etiologies have been identified, including maceration, friction, and constant contact with urine and feces.³ These increase susceptibility to skin barrier disruption, absorption of irritants, overhydration, and alterations in skin pH.⁴ Management often includes aeration, barrier preservation, cleansing, using absorbent diapers, and education.^{5,6}

Treatment of diaper dermatitis has been widely studied and includes topical agents aimed at repair and/or barrier creams, some with anti-inflammatory components. Zinc salts (e.g., zinc oxide, zinc gluconate), taurine, dexpanthenol, and petrolatum are the active ingredients found to be effective in

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most barrier creams.^{4,7-9} While modern topical agents such as corticosteroids and antimicrobials are known to have potent and rapid effects on reducing diaper dermatitis symptoms, their excessive, prolonged, and irrational use is associated with adverse effects like skin atrophy, pigmentary changes, suppression of hypothalamic-pituitary-adrenal axis, and bacterial resistance. Hence, newer approaches and combination medications have been constantly explored as replacements.⁴

Tocopherols are a group of naturally occurring chemical compounds that show vitamin E activity. They are commonly used in skin care products because of their ability to protect the skin from free radical damage and to toughen the skin barrier. It is known to scavenge free radicals, act as a reducing agent, decrease oxidative stress, and suppress inflammation.¹⁰ The properties of tocopherol have been analyzed in the treatment of skin diseases in newborns and in the treatment of surgical wounds with pre- and post-surgery administration either for the management of lesions or for the maceration of the skin due to the rubbing on the surface of the diaper or stagnation of material, such as feces and urine, in the areas most prone to the onset of dermatitis.¹¹ When combined, zinc oxide and tocopherol are expected to work synergistically to provide a more powerful tool to treat diaper dermatitis. Given that tocopherol has no known contraindications and few side effects, using this in treating diaper dermatitis would be relevant. However, the use of tocopherol for diaper dermatitis has not been extensively studied. Despite its known anti-inflammatory effects, there are no recommendations for using tocopherol in treating diaper dermatitis.

This study aimed to determine the effect of local application of 10% zinc oxide with tocopherol in comparison with 10% zinc oxide alone in the treatment of infants' diaper dermatitis.

Methods

This single center, prospective interventional study was conducted in a tertiary care teaching hospital for a period of 18 months (November 2018 to April 2020) after obtaining approval from the institutional ethics committee. All children aged < 12 months who were

newly diagnosed with diaper dermatitis were eligible for inclusion in this study. The exclusion criteria were as follows: children with skin lesions in the perianal region and were diagnosed to be other than diaper dermatitis, children on systemic corticosteroid therapy, children already on treatment with topical agents for diaper dermatitis, diaper dermatitis persisting for more than six weeks, known cases of psoriasis/allergy, and dropouts who did not follow up after five days.

Informed consent was obtained from the participants' parents prior to enrolment. Relevant history included the history of diaper dermatitis, type of diaper used, frequency of diaper use, wiping technique, history of allergy, and use of corticosteroid were taken. At the time of first contact, an examination (1st assessment) was performed where rash dimensions, severity score of diaper dermatitis, and pH of the rash were recorded.

Rash dimensions of the largest lesion were measured in centimeters of its length and breadth and recorded along with the presence of ulcers and redness. Rash was scored according to the severity score for diaper dermatitis (DDSS) by Buckley *et al.*¹² in which four domains were studied: severity of erythema and irritation, the extent of diaper dermatitis, papules or pustules, and open skin. The total score was calculated by adding the individual scores obtained in each domain (**Table 1**).

Skin pH was measured using a *Hydriion Insta-Chek Mechanical* pH pencil. The affected site was cleaned using sterile water and pat-dried using a sterile cotton pad. The area was allowed to air dry for 5 minutes. Once the area has dried, two drops of distilled water were placed at the center of the largest lesion onto which a few gentle strokes with the pH pen were made. The change in the color of the area at the end of 20 seconds was matched to a pH colorimetric scale to determine the corresponding pH values.

The subjects were then allotted to one of the two treatment groups by simple random allocation using a web-based electronic system. Subjects in one arm (Group A) received a standard treatment protocol of 10% zinc oxide (Treatment A) for local application. Zinc oxide paste (1 teaspoon of zinc oxide powder mixed with 5 mL sterile water) was advised to be applied topically three times a day for five days. Subjects in the other arm (Group B) received the study

Table 1. Severity score for diaper dermatitis¹²

Parameter	Clinical feature		Score
Severity of erythema and irritation	None	Clear skin	0
	Mild	Skin not clear, some irritation detectable, but may not be obvious	1
	Moderate	Skin irritation obvious, but not severe or intense	2
	Severe	Skin irritation intense, bright red, looks painful	3
Extent of diaper dermatitis	< 50% of the perianal-perineal-gluteal area and of the diaper area affected		0
	≥ 50% of the perianal-perineal-gluteal area or of the diaper area affected		1
Papules and pustules	Papules and pustules are present but few, would be practical to count them		0
	Many or clustered papules or pustules present, would not be practical to count them		1
Open skin	Superficial open skin involving only the epidermis, any erosion on the mucosa; any open skin judged to be caused by friction, injury, or etiology other than diaper dermatitis		0
	Any deep dermal open skin with damage to the dermis not caused by friction, injury, or etiology other than diaper dermatitis		1

treatment protocol of a combination of 10% zinc oxide and tocopherol (Treatment B) for local application. These subjects applied zinc oxide and tocopherol paste (1 teaspoon of zinc oxide powder mixed with 2 capsules of tocopherol) topically three times a day for five days. One capsule of tocopherol used contained 400 mg of alpha-tocopherol acetate.

All subjects were advised to follow the standard diapering guidelines which included washing the diapered region with water, pat-drying with a cotton cloth/paper wipe, frequent changing of diapers (once every 3 to 4 hours), and having a diaper-free period for at least an hour between diaper changes. All subjects received treatment for a standard period of 5 days. After 5 days of treatment, the subjects were reassessed under similar parameters (2nd assessment). Thereafter the data between the two groups were compared and studied. The primary outcome was the improvement in the diaper dermatitis severity score at the end of five days of treatment. Secondary outcomes were the improvement in the extent of rash as measured by the dimensions of the largest rash and improvement in skin pH.

Statistical analyses were done using SPSS version 17.0. All parameters were analyzed using their means and standard deviations. Student's paired two tailed T-test was used for the subgroup analysis. A significance level was set at $P < 0.05$.

Results

One hundred and fifteen children under 12 months of age were diagnosed with diaper dermatitis during the study period, of which 90 subjects fulfilling the inclusion criteria were included in this study. After allotting them to the treatment group, 43 subjects were assigned to group A and 45 to group B. Baseline characteristics of patients in both groups were compared and found to be similar as depicted in **Table 2**. Diaper dermatitis was more commonly seen in the male gender and children less than 3 months of age. The use of disposable diapers for the entire day was more associated with diaper rashes compared to others. The wipe method was also considered for almost equal numbers of infants using water with cloth, wipes, or a combination of the two ($P=0.636$). None of the children had a previous history of allergy or corticosteroid use in either group. Other anthropometric measurements including weight, length, and head circumference, were comparable in each group as shown in **Table 2**.

Outcomes were mainly compared in terms of dimensions (maximum length and breadth) of the largest rash on the day of initiation of treatment and improvement with therapy at the end of 5 days. The day 1 dimensions were almost similar in both groups. The length decreased similarly in both groups, with a larger drop seen in Group B ($P=0.0004$). However, the breadth decreased more in group B than in group A, again showing a larger drop in group B ($P<0.001$).

Table 2. Comparison of baseline characteristics (N=88)

Characteristics	Group A (n=43)	Group B (n=45)	Total (N=88)	P value
Sex, n(%)				0.089
Female	25 (58.1)	18 (41.9)	43	
Male	18 (40)	27 (60)	45	
Mean age (SD), months	4.32 (4)	3.04 (3)	3.67 (3.5)	0.092
Age, n(%)				0.222
<1 month	10 (23.3)	14 (31.1)	24	
1-3 months	11 (25.6)	15 (33.3)	26	
3-6 months	7 (16.3)	9 (20)	16	
6-12 months	15 (34.9)	7 (15.6)	22	
Past history of diaper dermatitis, n(%)				0.926
Present	7 (16.3)	7 (15.6)	14	
Absent	36 (83.7)	38 (84.4)	74	
Type of diaper, n, (%)				0.231
Cloth	4 (9.3)	4 (8.9)	8	
Diaper	29 (67.4)	23 (51.1)	52	
Cloth and diaper	10 (23.3)	18 (40)	28	
Use of diaper, n, (%)				0.499
Occasionally	10 (23.3)	6 (13.3)	16	
Daily at night	7 (16.3)	10 (22.2)	17	
Whole day	26 (60.5)	29 (64.4)	55	
Mean anthropometry (SD)				
Weight, kg	5 (2.2)	4.6 (2.2)	4.82 (2.2)	0.396
Length, cm	60.1(9.78)	55.68 (9.62)	57.9 (9.9)	0.04
Head circumference, cm	39.1 (4.69)	37.9 (4.66)	38.6 (4.7)	0.23

A mean reduction in dimensions from day one to day five was by 4.31 x 4.84 cm in the study group, whereas a reduction of only 3.16 x 3.3 cm was seen in group A. Both groups showed a decrease in severity score at the end of five days, with group B having an overall lower score than group A (P=0.001). When each component was analyzed separately, it was found that a reduction in the ulceration and erythema was similar in both groups, but the reduction in papules and extent of diaper dermatitis was better in group A. A comprehensive comparison of rash dimensions, severity scoring, and skin pH in both groups is presented in **Table 3**. There were no side effects of the treatment noted in either group.

Discussion

Diaper dermatitis results from changes in the physical, enzymatic, chemical, and microbiological factors in the diaper milieu. The spectrum of diaper dermatitis ranges from simple irritant contact dermatitis to allergic contact dermatitis, infection, or psoriasis.

The severity of diaper dermatitis varies from patient to patient based on several etiological factors. The frequent contributing factors for the etiology of diaper dermatitis are the period of diaper wearing, frequency of stools, the role of humidity, the role of feces, the role of heat, the role of pH, seasonal variation, etc. The main goal of diaper rash management lies in accelerating the healing process and prevention of diaper rashes. Various recommendations of a large variety of therapeutic agents are available for the management of diaper dermatitis, which includes zinc oxide, petrolatum, cod liver oil, dimethicone, lanolin, dexpanthenol, and Burow solution; a mixture of aluminium acetate in water. However, a set of standard protocol is not available.¹³⁻¹⁵

Topical vitamin E has emerged as a popular treatment for several skin disorders owing to its antioxidant properties. It has been seen that reactive oxygen species can alter the biosynthesis of collagen and glycosaminoglycans in the skin.¹⁶ However, topical tocopherol has not been widely studied in pediatric patients. Although other vitamins (A, D, and B5) have been studied in their pure form, vitamin

Table 3. Comparison between dimensions of rash, severity scoring, and skin pH, in both treatment groups

Parameter	Group A	Group B	P value
Mean dimensions (SD), cm			
Day 1 length	7.32 (2.68)	7.93 (2.75)	0.295
Day 5 length	4.42 (2.1)	3.67 (2.3)	0.118
Difference in length	3.16 (1.2)	4.31 (1.7)	0.0004
Day 1 breadth	8.07 (2.65)	8.24 (3.16)	0.786
Day 5 breadth	4.77 (2.5)	3.4 (2.3)	0.01
Difference in breadth	3.30 (4.84)	4.84 (1.84)	<0.001
Mean SCDD score, (SD)			
Day 1 DDSS	4.53 (1.14)	4.89 (1.0)	0.118
Day 5 DDSS	2.72 (1.27)	1.96 (0.767)	0.001
Difference on day 5			
Total DDSS	1.84 (0.721)	2.91 (0.733)	<0.001
Erythema	0.98 (0.51)	1.20 (0.59)	0.061
Ulcer	0.07 (0.34)	0.22 (0.52)	0.107
Papules	0.26 (0.82)	0.80 (0.40)	<0.001
Extent	0.42 (0.50)	0.69 (0.47)	0.010
Mean pH (SD)			
Day 1 pH	6.77 (0.78)	6.96 (0.88)	0.287
Day 5 pH	4.88 (0.44)	4.78 (0.517)	0.308
Difference in pH	1.88 (0.793)	2.18 (0.777)	0.083

SD=standard deviation, SCDD=severity score for diaper dermatitis

E has been studied only through sunflower oil which contains significant amounts of vitamin E.¹⁷⁻¹⁸ One of the studies using topical acetate tocopherol in neonates who had skin lesions in the NICU was conducted by Manzoni and Gomirato in 2005. They compared it with a commonly used skin ointment (emollient type, water-in-oil category) and assessed the dermatological severity score. They showed that the mean severity score decreased drastically on day 4 and day 7 in the study group (mean of 4.6 and 3.1). A complete recovery occurred after 9.1 mean days, and the rate of therapeutic failures was significantly lower in that group. They concluded that acetate tocopherol proved to be safe and more effective than the commonly used skin ointments in the topical treatment of ulcerative skin lesions in NICU neonates.¹⁹

In our study, the efficacy of healing of diaper dermatitis was observed in terms of reduction in the length and breadth of the largest rash on day 5 of treatment, which was noted to be significantly reduced with a mean measurement of 3.67 x 3.4 cm ($P < 0.05$). While comparing the DDSS in our study, the scores were similar in both groups prior to the start of treatment. By day 5, there was an overall reduction in the DDSS in both groups. However, the study group treated with tocopherol showed a better

rate of improvement when compared to the standard group. If each component of the score was assessed independently, it is evident that this reduction was largely due to the reduction in erythema and open skin as compared to the presence of papules or pustules and the extent of the rash reduction when treated with a combination of zinc oxide and tocopherol. There was only one other study that compared 10% zinc oxide to the use of 30% zinc oxide and tocopherol in the treatment of diaper dermatitis in children less than 24 months.¹¹ However, in their study, while comparing the severity scores, it was noted that although the scores were clearly decreased in both groups by the end of the trial ($P < 0.01$), there was no statistically significant difference between the groups ($P = 0.860$).¹¹

Changes in the skin pH also play an essential role in the etiology of diaper dermatitis. An increase in pH around the diaper area from the breakdown of urinary urea can increase the fecal enzyme activity and further damage the skin. The combination of these processes results in colonization and infection from bacterial/fungal organisms.²⁰ Technically, as improvement in the diaper dermatitis is seen, improvement in the pH is also expected. In our study, both groups showed improvement and restoration of skin pH; however, one group was not better than the other ($P = 0.083$).

Our study shows that treatment with a combination of zinc oxide and tocopherol was more efficacious than plain zinc oxide in the healing of diaper rashes. The use of a combination of zinc oxide and tocopherol in addition to standard diapering practices can help the recovery of diaper rashes, thus reducing the distress of the child and worry of the parents.

The study was not blinded and it could be considered as one of the limitations of this study. Topical application of vitamin E can rarely cause contact dermatitis, erythema multiforme, and xanthomatous reaction.¹⁶ However, the adverse effects of either group were not studied among the outcomes of this study. The target days for diaper dermatitis to heal are 2-3 days.²⁰ The mean number of days taken for each group to heal was not noted, which may be considered a limitation. Although many commercial ointments used for diaper dermatitis contain vitamin E in varying amounts, the ideal dose has not been established. In our study too, we did not compare different doses or effects seen with increasing doses of tocopherol.

In conclusion, this study helps to understand that the healing process in diaper dermatitis is facilitated by the combination of 10% zinc oxide and tocopherol when used along with the standard diapering guidelines. As evidenced by this study, we can conclude that the addition of tocopherol in topical applications reduces the rash size, thereby decreasing the severity of the diaper dermatitis and restoring the skin pH by the end of five days and can be considered in the treatment regimen for diaper dermatitis. This study helps to form a base for further study on tocopherol formulation for the treatment of diaper dermatitis in infants.

Conflict of interest

None declared.

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