Efficacy of topical sucralfate versus topical zinc oxide in diaper dermatitis: a randomized, double blind study

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Background: Diaper rash is a common but non life threatening condition during infancy. Different modalities of treatment are suggested. Sucralfate acts as a physical barrier to irritants and has antibacterial activities. Promising reports of the effect of topical sucralfate on wound epithelialization along with its bacteriostatic properties led us to carry out a trial to evaluate its role as a topical agent in the treatment of diaper dermatitis and compare its efficacy with topical zinc oxide.

Method: This double blind randomized clinical trial was conducted in Shariati hospital from April 2008 to September 2009. Sucralfate and zinc oxide were formulated as 20% ointments with the same excipients. All patients were randomly treated topically with either sucralfate (N=25) or zinc oxide (N=21) for 7 days. Diaper severity scores were obtained before treatment and at days 3, 5, 7 by the authors.

Result: A total of 46 infants (54.3% female and 45.7% male) with mean age of 4.4±6.5 months entered the study. The mean age, sex, frequency of diaper change (per day) and severity of diaper rash showed no statistically significant difference between two groups. Sucralfate 20% ointment was significantly superior in healing diaper dermatitis at days 5 and 7 ($p < 0.05$ and 0.01 respectively) and showed a significantly shorter healing time (3.24+/-2.02 days) in comparison with zinc oxide 20% ointment (5.42+/-2.39 days) ($P = 0.002$).

Conclusion: Since sucralfate in topical formulations acts as a physical barrier with proved safety and no noticeable absorption, it may be used as a potential treatment for diaper dermatitis.

Keywords: sucralfate, zinc oxide, diaper dermatitis

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INTRODUCTION

Diaper dermatitis is one of the most common skin disorders during infancy. Although it is not a life threatening disorder, it may affect the quality of life in both young children and their parents. The reported incidence and age of onset vary worldwide, related to differences in diaper use, toilet training, hygiene and child-bearing practices in different countries [1].

The exact etiology of diaper dermatitis has not been known. The interaction of many inciting factors, including increased skin hydration, exposure to chemical irritants, and friction beneath the diaper, contributes to the pathogenesis of irritant diaper dermatitis [2-4].

Increased skin hydration develops in the diaper region because it is an occluded moist environment. The wetness of the skin beneath the diaper increases the susceptibility to frictional damage from the

diaper, which impairs the normal skin barrier function [5].

The altered skin barrier then permits increased permeation of chemical irritants and microorganisms. The primary chemical irritants in the diaper area are derived from the synergistic action of urine and fecal bacteria that produce the enzyme urease, which interacts with urine to increase the pH level beneath the diaper [6,7]. Elevated pH levels activate fecal enzymes (protease and lipase) that directly irritate and damage the skin, causing an inflammatory skin eruption [7]. Once the skin beneath the diaper is inflamed, microorganisms (mainly Candida albicans) are able to invade and colonize, often worsening the severity of the diaper dermatitis.

Clinical manifestations of irritant diaper dermatitis range from asymptomatic erythema to painful scaling papules and superficial erosions. Irritant diaper dermatitis typically occurs on convex skin surfaces that are in direct contact with the diaper [8]. These locations include the buttocks, lower abdomen, genitalia, and upper thighs. The skin folds (areas not in direct contact with the diaper) are classically spared [1].

The most effective way to treat irritant diaper dermatitis is to eliminate direct skin contact with urine and feces (e.g. by discontinuing or limiting the use of diapers). Different modalities of treatment are suggested like topical corticosteroid, zinc oxide and topical antifungal preparations [9].

Sucralfate is a synthetic, water insoluble, sulfated disaccharide conjugated with Aluminum salt. It was developed in the early 1980s as an orally effective mucoprotective agent for the treatment of gastric and duodenal ulcers [10]. It also acts as a physical barrier to irritants and has antibacterial activities [11].

The drug adheres to the epithetical proteins at the ulcer site. This then forms a protective coating against the environment. Sucralfate increases both epidermal growth factor and basic fibroblast growth factor concentrate in the wound [12].

After the initial work with topical sucralfate in the management of resistant peristomal and perineal excoriations, various investigators tried this drug in stomatitis, healing of decubitus ulcer, and second and third degree burns [13,14]. Topical application of sucralfate has been reported to be useful in the management of severe or recalcitrant irritant diaper dermatitis [15]. The only common side effect was the constipation. However, a patient with aluminum toxicity was also reported.

Promising reports of the effect of topical sucralfate on wound epithelialization along with its bacteriostatic properties [2,3] led us to carry out a trial to evaluate its role as a topical agent in the treatment of diaper dermatitis and compare its efficacy with topical zinc oxide in diaper dermatitis.

PATIENTS AND METHODS

This was a double blind randomized clinical trial. The study population consisted of 46 inpatient infants who were admitted to Shariati hospital from April 2008 to September 2009.

Sucralfate and zinc oxide were formulated as 20% ointments with the same excipients and after passing all needed tests such as stability, pH, homogeneity and microbial tests, two formulations were coded and dispensed for use. Informed consent was obtained from the parents as ordered by the ethics committee.

All patients were randomly treated topically with either sucralfate (N=25) or zinc oxide (N=21) for 7 days. Diaper severity scores [6] were obtained before treatment and at days 3, 5, 7 by the authors.

The exclusion criteria were secondary infectious dermatitis, use of any injectable or oral steroid, any previous sensitivity to zinc oxide, any topical usage in the previous 2 weeks and a history of atopic dermatitis, candidiasis or seborrheic dermatitis. Patients' demographic data such as age, sex, weight, frequency of diaper change and severity of diaper rash were recorded.

Continuous variables were reported as mean and standard deviation while between-gender comparisons of continuous variables were performed using independent sample *t*-test. For comparison of sucralfate efficacy in treatment of diaper rash, we use non parametric Wilcoxon signed rank test. Data analysis was done with SPSS version 16 and a p-value < 0.05 was considered statistically significant.

RESULTS

A total of 46 infants entered the study with a mean age of 4.4±6.5 months. About 54.3% of them were female and 45.7% were male.

Age, sex, mother's education level, family income and frequency of diaper change showed no significant correlation with diaper rash. The mean age, sex, frequency of diaper change (per day) and severity of diaper rash showed no statistically significant difference between the two groups.

After termination of the study and decoding, it was found that there were significant differences in diaper rash severity after treatment at days 3, 5, 7 in the sucralfate group ($P < 0.001$). There was no significant difference in diaper rash severity after zinc oxide application at days 3, 5, 7 (P value = 0.81, 0.72, and 0.86, respectively).

It was concluded that sucralfate 20% ointment was significantly superior in healing diaper dermatitis at days 5 and 7 ($P < 0.05$ and 0.01, respectively) in comparison with zinc oxide 20% ointment. This superiority was not observed in day 3 (P value = 0.72). Also, complete healing was seen after 3.24 ± 2.02 days in the sucralfate and 5.42 ±2.39 days in the zinc oxide group, indicating a significant shorter healing time in the former (P value = 0.002). Tolerability was excellent in both groups and no adverse effect was reported in either group.

DISCUSSION

Diaper rash is a common but non-life threatening condition during infancy and so an effective and short course therapy with few side effects is an ideal goal.

Zinc oxide is categorized and approved for the treatment of diaper rash and is the most common ingredient in over-the-counter diaper rash products. Zinc oxide also enhances the healing of the skin and has been used as a barrier cream [4]. Sucralfate is a cytoprotective agent, an oral gastrointestinal medication primarily indicated for the treatment of active duodenal ulcer, gastroesophageal reflux and stress ulcer.

Sucralfate, a common anti ulcer medication, is a basic salt of sucrose octasulfate. It has been shown to act as a mechanical barrier because of the strong electrostatic interaction of the drug with proteins at the ulcer site.

It also has an antibacterial activity and is structurally similar to heparin with antigenic properties. All three of these actions would account for its healing action in erosive dermatitis. Vaginal ulceration has previously been treated successfully with vaginal douches of 10% sucralfate suspension twice daily [2]. Sucralfate, prepared as either a powder or as an emollient and applied every 4 to 6 hours, has been used to manage resistant peristomal and perineal excoriation [3]. More recently, a sucralfate suspension was used successfully in the treatment of oral and genital ulceration of Behcet disease [16].

The present study showed that topical sucralfate 20% could cure diaper dermatitis in a short period in comparison with zinc oxide which has been used for the treatment of this problem for a long time.

In a study performed by Banati, it was shown that sucralfate promoted rapid epithelialization of second degree burns with minimal side effects and therefore, it was suggested as an effective topical agent in burn care [13].

Tumino evaluated the efficacy, safety and tolerability of topical sucralfate in healing chronic venous leg ulcers in 50 patients by a double-blind, placebo-controlled, randomized study. A significant improvement was achieved in the sucralfate treated patient group with regard to local tissue inflammation as well as pain, burning sensation, and the ulcer size and it was concluded that sucralfate was an effective therapy for chronic venous ulcers [17].

Lyon investigated the effectiveness of topical sucralfate in the management of periostomal dermatose in adults using an open study design. Topical sucralfate represented a safe, inexpensive and effective therapeutic intervention, particularly for those patients with high output or short stomas. In eight out of nine patients with fecal or urine erosion, daily topical sucralfate treatment was associated with healing within 4 weeks [18].

In a double-blind, randomized controlled study, Gupta et al compared topical application of sucralfate and placebo. At 6-week follow-up, complete wound healing was achieved in 37 patients (95%) in the sucralfate group and 27 patients (73%) in the placebo group. The placebo ointment contained petroleum jelly ($P = 0.009$). The results of this study add support to the evidence that topical sucralfate is a safe and effective method for promoting healing and for providing analgesia during wound treatment. Patients who undergo anal fistulotomy can benefit from the use of topical application of sucralfate [19].

Iraji specifically compared the efficacy of topical sucralfate 4% versus topical hydrocortisone cream

every two weeks in the treatment of diaper rash until complete healing. More than 50% improvement was noted in 90-96% and partial healing (20-25% improvement) in the rest of the patients. Their study showed that topical sucralfate was an effective inexpensive therapeutic intervention for diaper dermatitis with efficacy equal to topical hydrocortisone cream. The duration of study was 8 weeks and the patients were evaluated [20].

The complete healing time in the sucralfate group in our study was significantly shorter than the study conducted by Iraji. It may be due to the use of sucralfate 4% in the latter. In our study, we applied sucralfate ointment 20% and all our patients were hospitalized to make sure of receiving the full course of therapy and to follow the healing time carefully.

The complete healing time in the sucralfate group was significantly shorter than the zinc oxide group, showing that sucralfate seems to be more effective than zinc oxide in the treatment of diaper rash. Since sucralfate in topical formulations acts as a physical barrier with proved safety and no noticeable absorption, it may be used as a potential treatment for diaper dermatitis.

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