Dermatology Practical & Conceptual

A Comparative Study to Evaluate the Effectiveness between Synergic Activities of 0.1% Polyhexanide and Rigenase® (Fitostimoline® Plus spray) versus a Hydrating Formulation for the Topical Management of Rubbing Injuries Secondary to Atopic Dermatitis

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ABSTRACT

Introduction: Managing rubbing injuries in atopic dermatitis is challenging and has a significant impact on patients' quality of life. Polyhexamethylene biguanide (PHMB) and Rigenase® (a patented Triticum vulgare extract) show promise in tissue repair and antimicrobial activity.

Objective: The aim of this study was to compare the effectiveness of two topical treatments, Fitostimoline® Plus spray and a hydrating formulation with hyaluronic acid, in rubbing injuries secondary to atopic dermatitis.

Materials and Methods: This comparative study enrolled 68 patients with atopic dermatitis and rubbing injuries, randomly assigned to Group A (N=38) receiving Fitostimoline® Plus spray (0.1% PHMB and Rigenase®) or Group B (N=30) receiving a hyaluronic acid spray. The primary endpoint was the clinical lesion response at 10 days post-treatment. Secondary endpoints included pain reduction (Visual Analogue Scale, VAS) and patient satisfaction (Dermatology Life Quality Index,DLQI).

Results: Group A had a significantly higher complete response rate (81.3% vs. 64.3%, P <0.001). Partial response rates were also higher in Group A (P = 0.045). Pain reduction was greater in Group A (VAS: 6.8 ± 1.2 to 2.4 ± 0.8) compared to Group B (7.1 ± 1.3 to 3.9 ± 1.0) (P <0.001). DLQI scores improved more in Group A (12.5 ± 3.5 to 3.2 ± 1.1) than in Group B (13.0 ± 3.2 to 6.5 ± 1.4) (P <0.001). Dermoscopic examinations showed significant skin barrier improvement in Group A (P <0.001).

Conclusion: Fitostimoline® Plus spray, with 0.1% PHMB and Rigenase®, offers superior treatment for chronic lesions in atopic dermatitis, enhancing wound healing and patient quality of life.

Introduction

Patients affected by atopic dermatitis, a common inflammatory skin condition, often present with rubbing injuries that are challenging to manage [1]. Atopic dermatitis predisposes individuals to a variety of complications, including persistent wounds and secondary infections. These chronic lesions significantly impact the quality of life and require effective management strategies to prevent further complications [2,3]. Polyhexamethylene biguanide (PHMB) is a synthetic polymer structurally similar to the naturally occurring antimicrobial peptides (AMPs). The structural similarities between AMP and PHMB suggest that the latter can enter the bacterial membrane cells and kill the bacteria in a similar way to AMP, through a mechanism of action of adherence and destruction of the target cell membranes, causing potassium ions and other cytosolic components to leak, resulting in the bacterial cell death [4,5]. Rigenase®, a specific patented Triticum vulgare extract, exhibits antioxidant capacity through its tissue-repairing activity and moisturizing action; thus, it is used in the formulation of different medication—under the brand name Fitostimoline®—with properties of accelerating tissue repair, improving the restoration of the epidermal barrier and stimulating lipid synthesis [6,7]. A novel formulation based on 0.1% PHMB and Rigenase® (Fitostimoline® Plus spray) has recently been developed for dermatological use [8]. Thanks to its formulation based on Rigenase®, it forms a protective barrier against the external environment, creating favorable conditions for a rapid and proper re-epithelialization of the skin. Additionally, due to PHMB, it helps maintain the microenvironment and control contamination. The aim of this study was to compare the effectiveness of two topical treatments, Fitostimoline® Plus spray and a hydrating formulation with hyaluronic acid, in rubbing injuries secondary to atopic dermatitis.

Materials and Methods

This comparative study enrolled 68 patients aged 18 years or older affected by atopic dermatitis with rubbing injuries willing to participate by signing the informed consent form.

Exclusion criteria include the use of topical therapies two weeks prior to treatment, current systemic therapy for rubbing injuries (corticosteroids, immunosuppressants), lesions suspicious for malignancy, pregnancy, lactation, psychiatric conditions interfering with follow-up, or participation in other clinical trials within 30 days prior to the study. Participants who met the inclusion and exclusion criteria and consented to participate were randomly assigned to one of two groups: Group A or Group B.

- Group A: 38 patients received Fitostimoline® Plus spray containing Rigenase®. This product was applied to the lesions twice daily for 10 days.
- Group B: 30 patients received a hydrating formulation containing hyaluronic acid spray. This product was applied to the lesions twice daily for 10 days.

The primary endpoint of the study was the clinical response of the lesions after 10 days of treatment. Responses were categorized as complete, partial, or no response. Complete response was defined as the total resolution of the clinical lesions, while partial response indicated significant clinical improvement with some residual erythema or scaling. Cases with no response showed no significant improvement in the lesions. Secondary endpoints included pain reduction, which was evaluated using the visual analog scale (VAS) with scores ranging from 0 (no pain) to 10 (worst pain imaginable). Pain levels were measured at baseline and again after 10 days of treatment. Additionally, quality of life was assessed using the Dermatology Life Quality Index (DLQI), with scores ranging from 0 to 30, where higher scores indicate a greater impact on quality of life. Like VAS, DLQI scores were collected at both baseline and after 10 days. Patient compliance and local tolerability were also evaluated based on patient feedback on the ease and comfort of the treatments. At baseline (T0), demographic characteristics and clinical history (including age, sex, family history, precipitating factors, duration of rubbing injuries, previous treatments, and affected areas) were documented. Clinical and dermoscopic examinations were conducted, with photographic documentation. A specific skin area on the face or

body was selected for dermoscopic examination to assess the skin barrier condition. Follow-up visits occurred at 10 days post-treatment (T2), where clinical and dermoscopic evaluations were repeated. Dermoscopic patterns, including erythema, desquamation, and vascular patterns, were assessed and analyzed using a chi-squared test. Changes in VAS and DLQI scores were statistically evaluated using *t*-tests, comparing baseline and post-treatment values.

This study was conducted between April 2023 and April 2024 over a period of 12 months.

Results

Sixty-eight patients affected by atopic dermatitis with rubbing injuries were recruited and randomly assigned to a treatment group (Group A, N=38; Group B, N=30).

The average age of the patients was 41.1 ± 10.2 years for Group A and 35.1 ± 9.8 years for Group B, with 17 males and 21 females in Group A and 13 males and 17 females in Group B. As shown in Table 1, there were no significant differences between the two groups in terms of age, sex, or area of the skin lesion assessed at baseline. The primary endpoint was the clinical lesion response at 10 days post-treatment. The responses were categorized as complete response (CR), partial response (PR), or non-response (NR).

Complete Response: A total of 31 patients (81.3%) in Group A (Fitostimoline® Plus spray) achieved CR, compared to 19 patients (64.3%) in Group B (hydrating formulation containing hyaluronic acid). The statistical analysis showed that the complete response rate was significantly higher in Group A (P <0.001) (Figure 1).

Table 1. Demographic Characteristics of Patients at Baseline.

Characteristic	Group A	Group B
N° patients	38	30
Age (years)	41.1 ± 10.2	35.1 ± 9.8
Sex		
• Male	17	13
• Female	21	17
Lesion Area (cm²)	7.65 ± 2.6	7.85 ± 2.55
Lesion Location		
• Head-neck	4	6
• Trunk	5	7
• Upper limbs	8	4
• Lower limbs	6	5
• Genital/buttocks	1	2
• Acral	2	1
• Widespread	12	5
Dermoscopy Alterations Present (Yes/No)		
• Erythema	34	25
• Desquamation	18	20
• Vascular pattern	22	25
VAS	6.8 ± 1.2	7.1 ± 1.3
DLQI Score at Baseline	12.5 ± 3.5	13.0 ± 3.2

Partial Response: In Group A, six patients (16.4%) exhibited PR, while eight patients (27.3%) in Group B showed PR. The difference in partial response rates between the two groups was statistically significant (P = 0.045).

Non-Response: Non-response was observed in one patient (2.4%) in Group A and in three patients (8.4%) in Group B. The statistical analysis indicated that there was not a significant difference in non-response rates between the two groups (P = 0.112) (Figure 2). The secondary endpoints included the reduction in pain associated with rubbing injuries, patient compliance, and patient assessment of local tolerability and satisfaction with the treatment. The reduction in pain was assessed using the visual analog scale (VAS). At baseline, the mean VAS score was 6.8 ± 1.2 in Group A and 7.1 ± 1.3 in Group B. After 10 days of treatment, the mean VAS score was 2.4 ± 0.8 in Group A and 3.9 ± 1.0 in Group B. The reduction in pain was significantly greater in Group A compared to Group B (P < 0.001) (Table 2). Patient compliance was monitored throughout the study period. In Group A, 35 patients (92.1%) adhered to the treatment protocol, while in Group B, 27 patients (90%) were compliant. The difference in compliance rates between the two groups was not statistically significant (P = 0.637). Patient assessment of local tolerability and satisfaction was evaluated using the Dermatology Life Quality Index (DLQI) questionnaire. The mean DLQI score at baseline was 12.5 ± 3.5 in Group A and 13.0 ± 3.2 in Group B. After 10 days of treatment, the mean DLQI score was 3.2 ± 1.1 in Group A and 6.5 ± 1.4 in Group B. The improvement in DLQI scores was significantly greater in Group A (P <0.001). Dermoscopic examinations were conducted at baseline and after 10 days of treatment to observe changes in the skin barrier. At baseline, the presence of dermoscopic patterns indicative of skin barrier damage was observed in 34 patients (89.5%) in Group A and 25 patients (83.3%) in Group B. After 10 days, the presence of these patterns decreased to five patients (13.2%) in Group A and 15 patients (50%) in Group B. The reduction in dermoscopic changes was more pronounced in Group A, with a statistically significant difference (P <0.001).

Discussion

Patients with atopic dermatitis often suffer from chronic lesions that are difficult to manage [9]. These lesions, compounded by rubbing injuries, significantly impact patients' quality of life [10]. Atopic dermatitis, characterized by chronic inflammation and a compromised skin barrier, predisposes individuals to persistent wounds and secondary

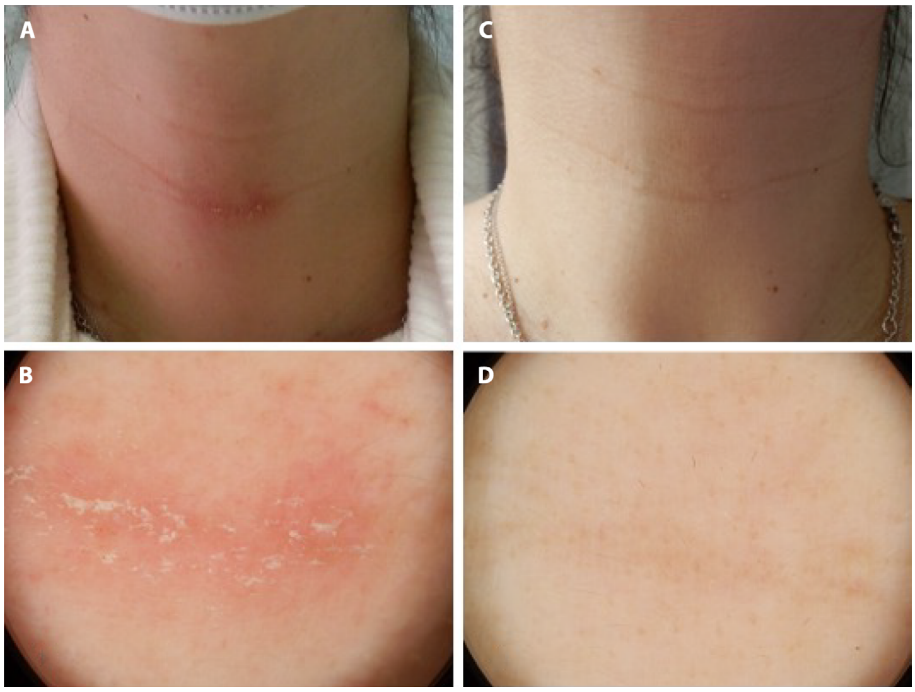

Figure 1. The figure shows a case of complete response of rubbing injuries lesion located on the neck of a 38-year-old woman after treatment with Fitostimoline® Plus spray over 10 days. In Image A, we observe the initial clinical appearance of the rubbing injuries lesion. Image B provides a dermoscopic view of the same lesion, revealing the presence of erythema and desquamation. Images C and D, representing the clinical and dermoscopic views, respectively, show clinical resolution after 10 days of treatment.

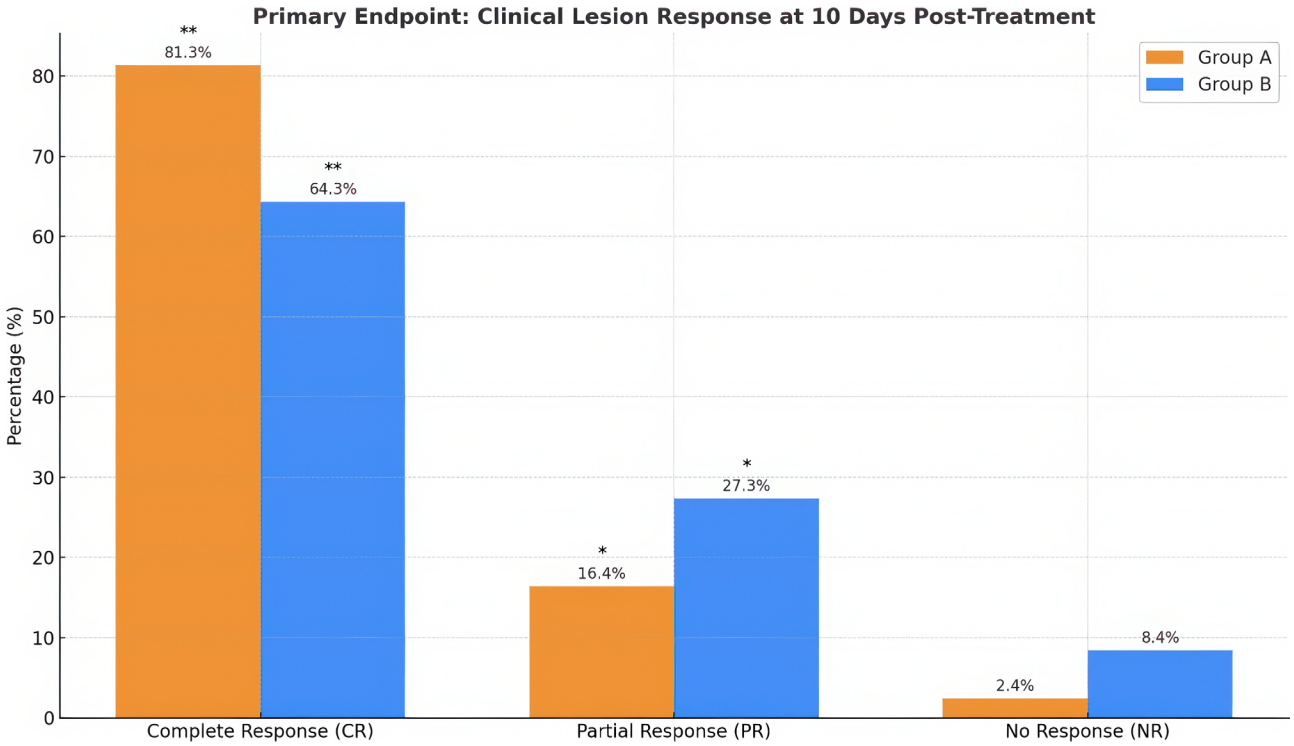

Figure 2. Clinical lesion response at 10 days post-treatment for patients with atopic dermatitis treated with Fitostimoline® Plus spray (Group A) and hydrating formulation containing hyaluronic acid spray (Group B). The percentage of complete response (CR), partial response (PR), and non-response (NR) is shown for each group. Significance levels are indicated as follows: *** P <0.001, ** P <0.01, * P <0.05.

Table 2. Results of secondary endpoints for patients treated with Fitostimoline® Plus spray (Group A) and hydrating formulation containing hyaluronic acid Spray (Group B). Endpoints include pain reduction (VAS), patient compliance, and local tolerability and satisfaction assessment (DLQI). P-values indicate the statistical significance of differences between the groups.

Endpoint	Group A (Fitostimoline® Plus spray)	Group B (hydrating formulation containing hyaluronic acid)	Significance (p-value)
Pain Reduction (VAS)			
• Baseline VAS	6.8 ± 1.2	7.1 ± 1.3	
• VAS at 10 days	2.4 ± 0.8	3.9 ± 1.0	< 0.001
Patient Compliance			
• Patients adhering to protocol	35 (92.1%)	27 (90%)	0.637
Local Tolerability and Satisfaction (DLQI)			
• Baseline DLQI	12.5 ± 3.5	13.0 ± 3.2	
• DLQI at 10 days	3.2 ± 1.1	6.5 ± 1.4	< 0.001

infections [11-13]. Managing these chronic lesions effectively is crucial to preventing further complications and to improving patient outcomes. In contrast, Rigenase® exhibits outstanding skin repair capabilities. This plant-derived polysaccharide can induce the biosynthesis and release of specific proteins from keratinocytes, which are essential for cell communication, tissue repair, and regeneration. Specifically, Rigenase® promotes cell migration and stimulates the synthesis of new extracellular matrix (ECM) components [14-16]. Polyhexanide, a cationic polymer and an active ingredient in Fitostimoline® Plus, disrupts the stability of bacterial cell membranes by binding to anionic phospholipids. Additionally, its interaction with human cells is minimal, making its risk-benefit ratio superior to that of other antimicrobial agents [17].

This study aimed to compare the effectiveness and tolerability of a novel formulation, Fitostimoline® Plus spray, containing 0.1% PHMB and Rigenase®, with a hydrating formulation containing hyaluronic acid in patients with atopic dermatitis and rubbing injuries. The results demonstrate that Fitostimoline® Plus spray significantly outperforms the hydrating formulation in several key areas, including clinical lesion response, pain reduction, patient satisfaction, and dermoscopic improvements. The higher rates of complete response and greater reduction in dermoscopic patterns indicative of skin barrier damage underscore the effectiveness of Fitostimoline® Plus spray. The primary endpoint, the clinical lesion response at 10 days post-treatment, revealed a significantly higher complete response rate in Group A (81.3%) compared to Group B (64.3%). This finding suggests that the combined action of PHMB and Rigenase® in the Fitostimoline® Plus spray facilitates more effective wound healing and skin barrier restoration. The presence of PHMB, known for its antimicrobial properties, likely contributes to this improved outcome by reducing bacterial contamination and promoting a healthier wound environment. Partial response rates also favored Group A, although the difference was less pronounced. Interestingly, non-response rates were low in both groups, with no significant difference, indicating that both treatments provided some level of benefit to most patients. The reduction in pain, as measured by the VAS, was significantly greater in Group A. The mean VAS score decreased from 6.8 to 2.4 in Group A, compared to a reduction from 7.1 to 3.9 in Group B. This significant reduction in pain (P <0.001) highlights the superior pain management capability of the Fitostimoline® Plus spray. The moisturizing and barrier-protective properties of Rigenase® might contribute to this effect by providing a soothing and protective layer over the affected areas, thus reducing irritation and discomfort. High levels of patient compliance were observed in both groups, with no significant difference. This indicates that both treatments were well-tolerated and easy to use. However, patient satisfaction, as measured by the DLQI, showed a more significant improvement in Group A. The DLQI scores improved from 12.5 to 3.2 in Group A, compared to an improvement from 13.0 to 6.5 in Group B (P <0.001). This substantial improvement in quality of life reflects the overall effectiveness and tolerability of the Fitostimoline® Plus spray. Dermoscopic examinations provided further evidence of the superior efficactiveness of the Fitostimoline® Plus spray. At baseline, a high prevalence of dermoscopic patterns indicative of skin barrier damage was observed in both groups. After 10 days of treatment, the presence of erythema, desquamation, and vascular patterns

significantly decreased to five patients (13.2%) in Group A, compared to 15 patients (50%) in Group B. The reduction in dermoscopic changes was more pronounced in Group A (P <0.001), highlighting the enhanced skin barrier repair facilitated by the combined action of PHMB and Rigenase®. Our results agree with the literature, as the superiority of Rigenase® compared to hyaluronic acid-containing formulations has been demonstrated in previous studies. For example, a randomized study involving 60 patients showed that Fitostimoline® Plus was significantly more effective than Connettivina® Bio Plus in healing acute superficial skin lesions and in reducing fibrin in the wound bed [18].

Despite the positive findings, this study has several limitations. The study design may have introduced bias, and the sample size was relatively small. Additionally, the study duration was limited to 10 days, which may not have fully captured the long-term effects and safety of the treatments. Future studies with larger sample sizes, longer follow-up periods, and double-blind designs are needed to confirm these findings and to provide more comprehensive data on the long-term efficactiveness and safety of Fitostimoline® Plus spray.

Conclusion

The findings from this study suggest that Fitostimoline® Plus spray, combining 0.1% PHMB and Rigenase®, offers a superior treatment option for patients with chronic lesions due to atopic dermatitis. Its higher complete response rate, greater reduction in pain, and significant improvement in skin barrier integrity underscore its effectiveness and potential benefits over conventional hydrating formulations. This study supports the use of this novel formulation as an effective strategy for managing atopic dermatitis with rubbing injuries, providing a new avenue for improving patient outcomes and quality of life. Further research could explore the long-term benefits and potential applications of this treatment in other dermatological conditions.

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