## Original Article:

# Safety and efficacy of topical Crisaborole 2% ointment in the treatment of psoriasis on face, intertriginous and anogenital areas: A vehicle-controlled cross-over study

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## Abstract

**Background:** Psoriasis in some sensitive areas like the face, anogenital and intertriginous areas significantly affects patients' quality of life, and psycho-social and sexual well-being. Due to the special structural and functional characteristics of these areas, all sorts of topical agents are not suitable for use on lesions in these areas. **Objective:** To study the safety and efficacy of crisaborole 2% ointment in treating psoriasis on the face, anogenital and intertriginous areas. **Methods:** It was a randomized vehicle-controlled cross-over study. Thirty-two patients with psoriatic lesions on the face, anogenital and intertriginous areas were enrolled purposively. Selected single lesion was treated with vehicle ointment twice daily for 4 weeks followed by 2 weeks washout period. Then each lesion was again treated with 2% crisaborole ointment twice daily for 4 weeks. Psoriasis disease severity will be measured by the Target Lesion Severity Scale (TLSS) at weeks 0, and 4 during both treatment periods. Changes in TLSS scores were compared between the two groups. **Result:** Topical 2% crisaborole is effective in the treatment of psoriatic plaques as the mean reduction of TLSS score of each treated lesion of the patients was significant after 4 weeks of application compared with baseline and it is significantly better ($p<0.001$) than vehicle ($p=0.257$. Few adverse effects were noted including burning, itching and redness. **Conclusion:** Topical 2% crisaborole ointment is a safe and effective non-steroidal option for treating psoriasis lesions on the face, anogenital and intertriginous areas though for complete lesional clearance a longer treatment period may be needed.
**Key words:** Crisaborole, PDE-4 inhibitor, anogenital psoriasis, intertriginous psoriasis, facial psoriasis

## Introduction

Psoriasis is a common, chronic, recurrent inflammatory disease of the skin, characterized by circumscribed, erythematous, dry, scaly plaques of varying sizes.[1] The prevalence of psoriasis is highly variable from country to country and region to region ranging 0·1% in east Asia and 1·5% in western Europe.[2] The prevalence of psoriasis in Bangladesh is 0.7%.[3]

Sixty-three percent of adults with psoriasis develop psoriatic lesions in the genital and intertriginous area at least once during their lifetime.[4] Though the high prevalence of genital psoriasis, about 50% of patients with genital lesions do not share their problem with a physician.[5] It has a significant negative impact on the

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quality of life and sexual health of patients, especially women who suffer from high levels of sexual distress.[6] Face is involved in 20-50% of cases of psoriasis; it is the most important area of cosmetic concern and social activity and is also considered as a marker of severe psoriasis.[7-8] Inverse or intertriginous or skin-fold psoriasis, is a rare form of psoriasis that affects 3-36% of patients.[9] It typically involves flexural areas – the groin, axillae, umbilicus, intergluteal cleft and external genitalia.[9] Psoriasis in genital and intertriginous areas is remarkably neglected due to a lack of communication and awareness resulting in diagnosis, under-treatment and subsequent risk of inappropriate self-treatment. Treatment of these sensitive areas of the body is challenging and several factors including high percutaneous absorption of topical steroids and alcohol in skin folds and greater potential for local adverse events such as atrophy, striae, and telangiectasia should be taken into account.[10]

Crisaborole ointment is a nonsteroidal phosphodiesterase-4 inhibitor. By inhibiting phosphodiesterase 4 it increases levels of 3′5′-cyclic adenosine monophosphate in inflammatory cells, leading to activation of nuclear factor κB and nuclear factor of activated T-cell signaling pathways and subsequent suppression of inflammatory cytokine release.[11]

It is a safe non-steroidal anti-inflammatory agent for even infants. Initially, topical crisaborole 2% was approved by the FDA for children over two years of age for mild to moderate atopic dermatitis in 2016 and after 4 years the approval was extended further for using children of three months and above.[12]

Apremilast, an oral PDE4 inhibitor has already been approved and is effective for psoriasis though adverse effects restrict its routine use. Roflumilast, a topical PDE4 inhibitor has also recently been approved for psoriasis and shows promise in clinical trials.[13] So it is reasonable to conduct a study to see the safety and efficacy of topical Crisaborole in psoriasis. Initially Lee et al., in 2019 reported two cases of psoriasis treated successfully treated with crisaborole.[14]

Topical crisaborole ointment was found safe and effective in the treatment of facial, anogenital and intertriginous psoriasis in a study by Hashim et al. conducted on 21 patients.[15]

In the current study, we studied the efficacy and safety of this non-steroidal topical agent to treat single plaque psoriasis of the face, anogenital and facial regions.

## Method

It was a vehicle-controlled cross-over study carried out in the dept. of dermatology and venereology, Bangabandhu Sheikh Mujib Medical University (BSMMU), Dhaka, Bangladesh from June 2021 to July 2023 after the approval by IRB (No.BSMMU/2021/3529 Date:06-04-2021). Thirty-two patients of psoriasis having localized and limited plaque on the face, anogenital or intertriginous areas (axillae, groin, gluteal cleft, undersurface of breasts) of ≥6 months' duration. Patients who were on current or past (less than 2 weeks) treatment with any systemic and other topical antipsoriatic medications or phototherapy (PUVA within the last 4 weeks) or Laser therapy were excluded. Patients having plans for lesional sun exposure were also spared from the study. Cases of guttate, erythrodermic, exfoliative or pustular psoriasis were not enrolled. Informed-written consent from patients or their legal guardians were taken.

**Table I: Distribution of the demographic variables (n=32)**

| Variables | Mean (SD), Median (Min-Max) |
|---|---|
| Age (year) | 21.7 (15.3), 19.0 (1-56) |
| Gender | f (%) |
| Male | 20 (62.5) |
| Female | 12 (37.5%) |

f: Frequency

The selected single lesion was treated with vehicle ointment twice daily for 4 weeks followed by 2 weeks washout period and then each lesion was again treated with 2% crisaborole ointment twice daily for 4 weeks. Psoriasis disease severity was measured by the Target Lesion Severity Scale (TLSS) at weeks 0, and 4 during both treatment periods. TLSS was calculated by measuring the redness, thickness, and scaliness of target plaques. Each parameter was graded on a 0 to 4 scale (0 = clear, 1 = slight, 2 = mild, 3 = moderate, 4 = severe), and the sum of the individual scores provides the overall score. The sum score ranges from 0 to 12 points. Changes in TLSS scores were compared between the two groups. Wilcoxon Signed Ranks Test was done to measure the levels of significance of changes of severity with two treatment modalities (Table III).

**Table II: Distribution of the site of involvement (n=32)**

| Site of involvement | f (%) |
|---|---|
| Anogenital | 20 (62.5) |
| Face | 10 (31.3) |
| Intertrginous | 2 (6.3) |

f: Frequency

**Table III: TLSS score after vehicle and Crisaborole at 0 week and 4 weeks (n=32)**

| | 0 week | 4 weeks | p value# |
|---|---|---|---|
| TLSS score treatment with vehicle | | | 0.257 |
| Mean ± SD | 8.1 ± 2.2 | 7.9 ± 2.2 | |
| Min-Max | 4-12 | 4-12 | |
| Median | 8.0 | 8.0 | |
| Q1-Q3 | 7.0-9.8 | 6.0-9.8 | |
| TLSS score after treatment with Crisaborole | | | <0.001 |
| Mean ± SD | 8.1 ± 2.3 | 4.7 ± 1.6 | |
| Min-Max | 4-12 | 2-8 | |
| Median | 8.5 | 5 | |
| Q1-Q3 | 6.3-10.0 | 3.3-5.8 | |

#Wilcoxon Signed Ranks Test was done to measure the level of significance. Q1:First quarter, Q3: Third quarter

**Table IV: Distribution of the adverse event (n=32)**

| Adverse event | f (%) |
|---|---|
| Burning | 4(12.5) |
| Itching | 2 (6.3) |
| Redness | 2 (6.3) |
| None | 24 (75.0) |

f: Frequency

## Result

In this vehicle-controlled cross-over study, 32 patients of psoriasis with a mean age of 21.7(±15.3) were recruited among which 62.5% were male and 37.5% female. Lesions were located at anogenital areas in 20 (62.5%) cases, face 10 (31.3%) and intertriginous area 2 (6.3%) (Table II). The mean Target Lesion Severity Scale score of the patients at baseline was 8.1 ± 2.2. After treatment of each selected lesion with the vehicle for 4 weeks, the mean TLSS score was 7.9 ± 2.2 ranging from 4 to 12 (p=0.257). After 2 weeks washout period lesions were treated with 2% crisaborole ointment, at baseline the mean TLSS was8.2 ± 2.3ranging from 4 to 12 after treatment for 4 weeks mean TLSS was 4.7 ± 1.6 ranging from 2 to 8 (<0.001). Regarding adverse effects 75% had no adverse effects, burning, itching and redness were reported in 12.5%, 6.3% and 6.3% cases respectively.

## Discussion

Psoriasis in some special areas significantly impacts patient's quality of life and there is lack of agreement among practitioners regarding the management of psoriasis these atypical areas which are more resistant to treatment or too sensitive to be treated with strong topical drugs, resulting in more frequent use of systemic drugs.[16] Genital and intertriginous areas are affected in more than sixty percent patients with psoriasis and these areas are involved at least once during their lifetime.[17]

In the current series of patients, the mean age was 21.7(±15.3) ranging from 1 year to 56 years. Psoriasis in genital areas can affect patients of any age from newborns to the elderly, with a bit of predilection for younger males with comparatively more severity.[17] Though genital psoriasis is more common in males, the disease severity is higher in females.[5] Psoriatic plaques involving sensitive private areas of the body significantly reduce their quality of life compared with psoriasis in other areas regarding itching, sexual activities, sexual health, sexual stress, refusal from partners, embarrassment, shame, and psychological depression.[5] In the current study most (63.2%) of participating patients were male, which may be due to females reasonably feel ashamed and neglect to seek treatment for these private part lesions.

In the current study majority of the lesions were located on genital areas. Face is involved in 20% of cases of psoriasis and it is the most important area of cosmetic concern and social activity.

Some studies have even found that facial psoriasis could be considered a marker of severe psoriasis. In the current study, 31% of lesions were located on the face. [18]

Management of psoriasis in these sensitive areas with topical agents deserves a special consideration of the unique anatomical and physiological character of the areas including less thickness of skin, higher

percutaneous absorption and greater potential for local adverse events such as atrophy, striae and telangiectasia. These issues are particularly more problem for infants, who have a high surface area-to-body mass ratio, predisposing them to systemic side effects. However low-to-mid-potency topical corticosteroids are recommended as the first-line treatment for genital psoriasis. The first-line recommended other topical treatments are calcineurin inhibitors and vitamin D analogs. The efficacy and tolerability of topical calcineurin inhibitors tacrolimus are proven in several studies.[19] Calcipotriol and calcitriol, are other non-steroidal treatment modality suitable for prolonged use for genital and inverse psoriasis though less effective compared with topical corticosteroids or TCI.[20] Though the efficacy of these agents is proved however the use of these agents have special safety concern for potential risk for developing malignancy in future.[21] As a novel topical nonsteroidal agent Crisaborole, a phosphodiesterase-4 inhibitor have been reported as effective and tolerable agent for anogenital, intertriginous and facial psoriasis in two available articles.[14-15]

In the current study lesions treated with a vehicle have not achieved significant change of severity (TLSS) after 4 weeks of application. After the application of 2% crisaborole ointment on each lesion the mean TLSS score was reduced significantly from the baseline after 4 weeks of treatment, none achieved complete clearance whereas in the lone previous study by Hashim et al. complete clearance was noted in 70% of patients after treatment of 8 weeks.[15] So for achieving a complete clearance the duration of treatment may be longer. Lesional improvement (TLSS change) was significantly better than a vehicle. Mild adverse cutaneous reactions to topical crisaborole including lesional contact urticaria, irritation, pain, burning, and/or stinging have been experienced among patients treated for atopic dermatitis.[22] In the current study no adverse effects were noted in most of the cases, with lesional burning in 12.5% and equal two persons reported lesional itching and redness. The same kind of mildcutaneous adverse effects were also experienced in using topical tacrolimus for psoriatic lesions on the groin.[19] Topical crisaborole 2% ointment can be considered a tolerable and effective topical treatment option for limited lesions of psoriasis in the face, anogenital and intertriginous areas.

## Conclusion

For treating psoriasis in sensitive areas of the body including the face, anogenital and intertriginous areas topical 2% crisaborole ointment is a safe and effective non-steroidal option but for complete clearance of the lesion a longer treatment period may be needed.

## Limitations

The sample size was small and treatment period should be longer.

## Conflict of interest

None.

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