RESEARCH ARTICLES

Topical Pimecrolimus 1% Cream in Treatment of Oral Lichen Planus

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Abstract

Oral lichen planus (OLP) is a common inflammatory disease of unknown etiology. The immunopathogenesis is T-cell mediated autoimmune disease. Various treatments have been tried to treat OLP but complete cure is difficult to achieve. Pimecrolimus is a new calcineurin inhibitor which can inhibit T-cell and mast-cell activation. We presented three cases of OLP patients treated with pimecrolimus 1% cream 2 times daily for 4 weeks. All of the lesions showed improvement with nearly complete remission. No side effects were observed during 6-12 months follow-up in all cases.

Key words: oral lichen planus; pimecrolimus; treatment
ผลของยาท้ารีมไฟฟ้าโครลีมัส 1% ในการรักษาโรคเล.non พลันสิ้น

ในช่องปาก

ภักษาภู แต่งบุตรภูผิว, พรพรรณ จันทะ, พีรพงษ์ จันทะ, ของปัญจน ทองธรรม

1 ภาควิชาศัลยศาสตร์และเวชศาสตร์ช่องปาก, คณะแพทยศาสตร์, มหาวิทยาลัยศรีนครินทรวิโรฒ
2 ภาควิชารังสีเวชศาสตร์, คณะแพทยศาสตร์, จุฬาลงกรณ์มหาวิทยาลัย
3 ภาควิชาเวชศาสตร์ช่องปาก, คณะแพทยศาสตร์, จุฬาลงกรณ์มหาวิทยาลัย

บทคัดย่อ

ระบบโรคเล.non พลันสิ้นในช่องปาก เป็นโรคที่เกี่ยวของกับการลักษณะของเนื้อเยื่อภายในและภายนอก
พบได้บ่อย สาเหตุการเกิดโรคยังไม่ทราบแน่นอน แต่เชื่อว่าเป็นโรคที่เกี่ยวของกับภูมิต้านทานแสดงและฟิส-เซลล์
มีรายงานการรักษาโรคเล.non พลันสิ้นในช่องปากด้วยวิธีต่าง ๆ แต่ยังไม่มีวิธีการใดที่สามารถทำให้โรค
หายขาดได้ ยาฟลูตาโกลมิแกมไม่สามารถรักษาโรคที่เกิดจากอันตรายตั้งแต่เซลล์บริเวณ ซึ่งสามารถยับยั้งการทำงานของฟิส-เซลล์
และฟิส-เซลล์ ไม่สามารถทำให้โรคหายได้ บางทีการรักษาผู้ป่วยโรคเล.non พลันสิ้นในช่องปากจำนวน 3 ราย ดังนี้
ภักษาภู คริณ์ ไฟฟ้าโครลีมัส 1% รัศมี และ 2 ครั้ง เป็นระยะเวลา 4 ้สัปดาห์ พบปวดผู้ป่วยทั้ง 3 รายมีอาการเจ็บต่อเนื่องและโรค
ก็ยังหายไม่สิ้นสุด ทำให้การรักษาเม็ดยาที่ผู้ป่วยในระยะเวลาระหว่าง 6-12 เดือน

คำสำคัญ: โรคเล.non พลันสิ้นในช่องปาก, ไฟฟ้าโครลีมัส, การรักษา
Introduction

Oral lichen planus (OLP) is a chronic mucocutaneous inflammatory disease that affects 0.5-2.2% of the population and is mainly found in women in their fifth or sixth decades of life. The etiology is still unclear. The immunopathogenesis of OLP is complex, involving T-cells, mast cells, intercellular adhesion molecule-I and HLA class II antigens and may be associated with some drugs and dental materials. Various clinical forms of OLP have been recognized. Reticular and plaque type of OLP are often asymptomatic. Whereas atrophic and erosive forms are often painful, interfere with patients’ quality of life and require some treatments. Various treatments have been attempted to improve the symptomatic OLP. Corticosteroids in topical form are safe and effective treatments for OLP. The response rate has been reported to range from 30-70%. Pimecrolimus is one of the new class of novel ascomycin immunomodulating macrolactams, and has been developed for the treatment of inflammatory skin diseases such as atopic dermatitis, psoriasis and contact dermatitis. The mechanism of the drug is inhibiting T-cell and mast-cell activation. Recently, there have been few reports using this medication in the treatment of OLP but there were no reports of pimecrolimus in the treatment of Thai patients with OLP. The aim of the present study was to assess the efficacy and side-effects of pimecrolimus 1% cream in treatment of Thai patients with symptomatic OLP.

Case report

Three patients with atrophic OLP attending the Oral Medicine clinic, Faculty of Dentistry, Chulalongkorn University were asked to participate in the study. None of patients has systemic disease and taking systemic medication. Each subject gave written informed consent and the study was approved by Committee on Experimental Procedures Involving Human Subjects of the Faculty of Medicine, Chulalongkorn University Ethics Committee. Any topical medications previously prescribed for treatment of OLP were stopped for two weeks and systemic therapy for at least four weeks before starting this study. All the lesions were diagnosed by oral examination and confirmed by histopathology. The patients were instructed to apply pimecrolimus 1% cream (Elidel®, Novartis, Mexico) on dried lesions twice a day for four weeks. Transparent grids were used to measure the size of erythematous lesions of the most severity area in mm², while discomfort scores were assessed using a visual analogue scale (VAS). The OLP lesions were also evaluated before and after treatment to the criteria set by Thongprasom et al.

- Score 5: white striae with erosive area > 1 cm².
- Score 4: white striae with erosive area < 1 cm².
- Score 3: white striae with erythematous area > 1 cm².
- Score 2: white striae with erythematous area < 1 cm².
- Score 1: mild white striae only.
- Score 0: no lesions, normal mucosa.

The first patient was a 67-year-old woman with atrophic lesion and white striae at lower lip (Figure 1). Pimecrolimus 1% cream was administered topically twice daily for four weeks. The pain and the size of the lesion were evaluated. After four weeks, the patient reported 78.79% reduction of pain and almost complete absence of OLP (Figure 2). No side-effects were observed (Table 1).

The second patient was a 35-year-old woman with an 11-year history of burning atrophic lesion at buccal gingival of all quadrant extended to mucobuccal fold. Pimecrolimus 1% cream was administered topically twice daily for four weeks. The pain and the size of the lesion were evaluated. After four weeks, the patient reported 78.79% reduction of pain and almost complete disappearance of OLP. No side-effects were observed except the bad taste of the drug.
The third patient was a 28-year-old man with a history of 8-year burning sensation on the left and right buccal mucosa. Pimecrolimus 1% cream was administered topically twice daily on both buccal mucosa. After four weeks, the symptoms reduced 81.63% and only white hyperkeratotic striae was seen. No side-effects were observed.

Discussion

Various regimens have been tried to treat OLP but complete cure has been difficult to achieve. Corticosteroids are the first-line drugs for the treatment of OLP and are effective in managing symptomatic OLP. Fluocinolone acetonide 0.1% in orabase (FAO) has been shown to be more effective than triamcinolone acetonide 0.1% in orabase (TAO) with no serious side effects. Moreover, the effectiveness of various forms of topical fluocinolone acetonide applications in patients with OLP in a 2-year treatment resulted in complete remission of 77.3%, 21.4%, and 17.0% of patients in the FAO, fluocinolone acetonide in solution (FAS), and FAS/FAO groups, respectively.

Acute pseudomembranous candidiasis is the only common side-effect from topical corticosteroid which can be prevented or treated with topical antifungal agent. Although there are some reports of systemic absorption and adrenal suppression from using super-potent topical steroids in treatment of skin disorders, but there has been no report about adrenal suppression from long term oral application of topical corticosteroids.

Other immunosuppressive drugs such as cyclosporine and topical tacrolimus has been reported in treatment of OLP. Cyclosporine is a polypeptide that inhibits the transcription of several cytokine genes, thereby suppressing T-cell cytokine production. Some studies have been reported benefit from applied cyclosporine topically or in form of mouth rinse but others have reported little benefit or no significant improvement. Cyclosporine may be used as an alternative therapy from conventional treatment of OLP but should not be use as a first drug of choice because of the high cost of long term treatment and the availability of effective alternatives. Severe side-effects of systemic cyclosporine, such as hypertension and nephrotoxicity, preclude its use for OLP.

Tacrolimus is an immunomodulating agent inhibiting T-cell activation at 10-100 times lower concentration than cyclosporine. This drug used topically to control symptoms and has been shown to be effective in treatment of OLP. However, local irritation is the most common side-effect.

Pimecrolimus is a topical immunosuppressant calcineurin inhibitors that is applied to many skin diseases such as atopic dermatitis, psoriasis and contact dermatitis. It is related to tacrolimus and shares the same cellular binding targets and mechanism of action. There are some reports about the efficacy of topical pimecrolimus when treating OLP lesions with adhesive ointment two times daily in patients with OLP. After four months, lesions nearly disappear and patients experience only a slight burning sensation immediately following the application of pimecrolimus. Other studies have also been shown partial or complete remission in OLP patients treated with pimecrolimus 1% cream.

Consistent to previous reports, in our study, improvement in both subjective and objective assessment occurred in all three patients treated with topical pimecrolimus 1% cream. Following the administration of pimecrolimus for four weeks, nearly complete resolution of OLP together with symptom improvement were documented in all patients. Moreover, there are no serious side-effects in all cases during 6-12 months follow-up. Therefore, pimecrolimus 1% cream has a potential role to be a novel alternative treatment of symptomatic OLP in patients who do not respond to conventional therapy. However, further studies, are also necessary to evaluate the relapse rate of patients with symptomatic OLP upon discontinuation of pimecrolimus therapy. Long term follow-up of topical pimecrolimus treatment in OLP should be considered both beneficial and unwanted effects.
Figure 1 The first patient with atrophic OLP and white striae at lower lip

Figure 2 After 4 weeks of treatment with pimecrolimus 1% cream, the lesion was almost complete disappearance

Table 1 The VAS, clinical score and size of the erythematous lesion in each OLP subject before and after four weeks treatment with pimecrolimus 1% cream

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<thead>
<tr>
<th>Subject</th>
<th>Before treatment</th>
<th>After 4 weeks treatment</th>
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<tbody>
<tr>
<td></td>
<td>VAS (1-10)</td>
<td>Score (0-5)</td>
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<tr>
<td>1</td>
<td>3.3</td>
<td>2</td>
</tr>
<tr>
<td>2</td>
<td>4.5</td>
<td>2</td>
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<td>3</td>
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References


