# Treatment of severe erosive gingival lesions by topical application of clobetasol propionate in custom trays

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***Objective.*** We sought to describe the response of patients with severe erosive gingival lesions to treatment with clobetasol propionate in Orabase paste administered in trays. The adverse effects were also recorded.
***Study design.*** A descriptive pretest/posttest clinical study with no control group (33 patients total) was developed. All patients received repeated applications of 0.05% clobetasol propionate plus 100,000 IU/cc of nystatin in Orabase paste. Over the 48-week period, the pain levels, ulcerations, presence of atrophy, and the patients' daily activities were recorded, and Likert scales were used to classify each outcome as either a *complete recovery*, *excellent*, *good*, *poor*, or *failed*. The presence of any adverse effect was also noted.
***Results.*** At the end of the study period, the pain and ulceration had disappeared (complete response) in 100% of the sample (33/33; 95% confidence interval = 89.4%-100%), and there was a complete recovery of daily activities and remission of atrophy in 93.9% (31/33; 95% confidence interval = 79.8%-99.3%) and 21.2% (7/33; 95% confidence interval = 9.0%-38.9%) of the patients, respectively. No adverse effects related to the treatment were observed.
***Conclusions.*** The application of an Orabase paste of 0.05% clobetasol 17-propionate plus 100,000 IU/cc of nystatin by means of a tray appears to be an efficacious treatment for severe erosive gingival lesions.
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The treatment of severe erosive lesions in the oral cavity represents an important challenge in oral medicine because these lesions are often chronic,[1] rarely spontaneously remit,[2-4] cause intense pain, and interfere with the daily activities of the patients (including eating, drinking, talking, and maintaining normal relationships).[5]

Many factors can increase the severity of these lesions when they appear on the gingiva. The pain and bleeding impede correct oral hygiene practices, which aggravates the gingival clinical symptoms and hastens the onset of periodontal complications, dental caries, and halitosis. Furthermore, ulcerations, reddening, and gingival bleeding can negatively affect patients' appearance, interfere with their daily activities, and diminish their well-being.

The application of topical corticosteroids is a reasonable approach to the treatment of these lesions. It has been reported that severe oral erosive lesions[5,6] can be safely and efficaciously treated with an adhesive paste form of clobetasol propionate, the most potent topical corticosteroid.[7-9] However, it can be difficult to apply the paste to the entire lesional surface in patients with extensive or deep lesions. In addition, normal mouth movements can rapidly displace the paste, precluding good control over the contact time between the corticoid and the lesion, which is critical to the success of this therapy.[10] A tray, which has been used by other researchers[6] to apply and secure the paste, provides an adequate solution to this problem. In this study, we aimed to describe the response of patients with severe erosive gingival lesions to treatment with clobetasol propionate in Orabase paste (Colgate-Palmolive Espana SA, Madrid, Spain) administered in trays. The presence of any adverse effects was also recorded.

## PATIENTS AND METHODS

A descriptive pretest/posttest clinical study with no control group[11] was developed at the Oral Medicine Clinic of the University of Granada (Spain). We recruited all patients referred to our clinic for the diagnosis and treatment of oral erosive lesions from 1998 to 2001 who fulfilled the following criteria: the presence

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**Table I.** Pain response to treatment during follow-up

| *Pain response* | *Week 2 n (%)* | *Week 4 n (%)* | *Week 6 n (%)* | *Week 8 n (%)* | *Week 10 n (%)* | *Week 12 n (%)* | *Week 16 n (%)* | *Week 20 n (%)* | *Week 24 n (%)* | *Week 48 n (%)* |
|---|---|---|---|---|---|---|---|---|---|---|
| Complete | 7 (21.2) | 21 (63.6) | 29 (87.9) | 33 (100) | 33 (100) | 33 (100) | 33 (100) | 33 (100) | 33 (100) | 33 (100) |
| Excellent | 15 (45.5) | 12 (36.4) | 4 (12.1) | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| Good | 10 (30.3) | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| Poor | 1 (3.0) | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| Failed | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| Total | 33 (100) | 33 (100) | 33 (100) | 33 (100) | 33 (100) | 33 (100) | 33 (100) | 33 (100) | 33 (100) | 33 (100) |

of previously untreated autoimmune erosive gingival lesions with extensive gingival ulcerations; a minimum 3-month history of severe and chronic pain; and disease interference in their daily activities, reported as major difficulty in eating, drinking, talking, and maintaining normal relationships.

The study group consisted of 33 patients, 25 women and 8 men; the mean age was 61 years (range, 34-79 years). Twenty-two patients presented with oral mucous membrane pemphigoid. The remaining 11 patients presented with oral lichen planus, with erosive lesions exclusively localized in the gingiva and with painless bilateral reticular lesions in the buccal mucosa. In all patients, the diagnosis was made on the basis of the medical history, a clinical examination, and the results of routine histopathologic and direct immunofluorescence study of a representative biopsy specimen. Three patients had mild hyperglycemia controlled only by diet, and 4 patients were receiving antihypertensive treatment for high blood pressure, which was under control at the time of the study.

A gingival tray was produced for each patient for the application of 0.05% clobetasol propionate plus 100,000 IU/cc of nystatin in Orabase paste. We used 0.10 g of clobetasol 17-propionate (97% purity) and 3.846 g of nystatin (commercially supplied in 5200 units) in 200 g of Orabase paste to achieve the required concentration. After the clobetasol propionate and nystatin were mixed and ground in a mortar, the Orabase paste was slowly added. The mixture was easily produced by using a blender. A good seal was observed between the tray and the gingival tissue. The schedule was in part based on published data on the topical application of corticosteroids in adhesive paste form[6] (Orabase) and was designed as a long-term treatment. The paste was applied with the tray for 5 minutes 3 times daily (after breakfast, after lunch, and after the evening meal). The patients were instructed to remain seated and expectorate excess saliva after the application and not to remove the remains of the paste from their mouth or swallow for at least 10 minutes. When a patient was recorded as having a *complete response* or an *excellent response* in terms of pain, ulcerations, and disease interference with daily life, the treatment was restricted to alternate days, similar to the guidelines for systemic corticosteroid treatment.[1] If continued improvement was observed at follow-up visits, the frequency of the applications was gradually reduced until the patient was on a maintenance dosage of one 5-minute application on alternate days. The patients were warned not to discontinue or modify the treatment themselves, even with the disappearance of pain and lesions, because of the risk of recurrence. Professional oral prophylaxis was performed as soon as the gingival condition of the patient allowed this and was then repeated every 3 or 4 months.[12]

Ten follow-up visits were scheduled for weeks 2, 4, 6, 8, 10, 12, 16, 20, 24, and 48. At each visit, a single experienced clinician (M.A.G.-M.) photographed the lesions and evaluated patients in terms of the evolution of pain, atrophy, ulceration, and disease interference with daily life. The response to treatment in terms of pain and interference with daily activities was assessed by a 5-point Likert-type scale. The follow-up photograph of the lesion was compared with the baseline photograph to assess the response in terms of atrophy and ulceration as *complete* (100% remission/recovery), *excellent* (75%), *good* (50%), *poor* (less than 50%), or *failure* (ie, no response).

The patients were also examined at every visit for the presence of adverse effects related to prolonged clobetasol treatment. Patients were tested for hyperglycemia, and their blood pressure was determined; they were also evaluated in light of the clinical signs and symptoms of candidiasis (erythema and burning) and for the presence of moon face, hirsutism, buffalo hump, liquid retention, and weight increase. Patients were also interviewed with regard to mood changes, gastrointestinal disorders, easy bruising, and taste loss.

## RESULTS

Data on the posttreatment evolution of pain, disease interference in daily activities, atrophy, and ulceration are displayed in Tables I, II, and III, respectively. After 2 weeks of treatment, approximately half of the patients had an excellent response to treatment in all of the

**Table II.** Response of disease interference to treatment during follow-up

| *Response of disease interference* | *Week 2 n (%)* | *Week 4 n (%)* | *Week 6 n (%)* | *Week 8 n (%)* | *Week 10 n (%)* | *Week 12 n (%)* | *Week 16 n (%)* | *Week 20 n (%)* | *Week 24 n (%)* | *Week 48 n (%)* |
|---|---|---|---|---|---|---|---|---|---|---|
| Complete | 5 (15.2) | 24 (72.7) | 27 (81.8) | 31 (93.9) | 31 (93.9) | 31 (93.9) | 31 (93.9) | 31 (93.9) | 31 (93.9) | 31 (93.9) |
| Excellent | 17 (51.5) | 9 (27.3) | 6 (18.2) | 2 (6.1) | 2 (6.1) | 2 (6.1) | 2 (6.1) | 2 (6.1) | 2 (6.1) | 2 (6.1) |
| Good | 11 (33.3) | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| Poor | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| Failed | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| Total | 33 (100) | 33 (100) | 33 (100) | 33 (100) | 33 (100) | 33 (100) | 33 (100) | 33 (100) | 33 (100) | 33 (100) |

**Table III.** Response to treatment during follow-up of atrophic lesions

| *Atrophy response* | *Week 2 n (%)* | *Week 4 n (%)* | *Week 6 n (%)* | *Week 8 n (%)* | *Week 10 n (%)* | *Week 12 n (%)* | *Week 16 n (%)* | *Week 20 n (%)* | *Week 24 n (%)* | *Week 48 n (%)* |
|---|---|---|---|---|---|---|---|---|---|---|
| Complete | 0 | 0 | 2 (6.1) | 7 (21.2) | 7 (21.2) | 7 (21.2) | 7 (21.2) | 7 (21.2) | 7 (21.2) | 7 (21.2) |
| Excellent | 7 (21.2) | 10 (30.3) | 15 (45.5) | 21 (63.6) | 21 (63.6) | 21 (63.6) | 21 (63.6) | 21 (63.6) | 21 (63.6) | 21 (63.6) |
| Good | 7 (21.2) | 12 (36.4) | 15 (45.5) | 5 (15.2) | 5 (15.2) | 5 (15.2) | 5 (15.2) | 5 (15.2) | 5 (15.2) | 5 (15.12) |
| Poor | 19 (57.6) | 11 (33.3) | 1 (3.0) | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| Failed | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| Total | 33 (100) | 33 (100) | 33 (100) | 33 (100) | 33 (100) | 33 (100) | 33 (100) | 33 (100) | 33 (100) | 33 (100) |

variables except for atrophy. At the end of the study period, the pain and ulceration had disappeared (complete response) in 100% of the patients (33/33; 95% confidence interval = 89.4%-100%; Figure), and there was a complete response in terms of the recovery of daily activities and atrophy in 93.9% (31/33; 95% confidence interval = 79.8%-99.3%) and 21.2% (7/33; 95% confidence interval = 9.0%-38.9%) of the patients, respectively.

No patient's symptoms worsened during the follow-up period (data not shown), and no adverse effects related to the treatment were observed.

## DISCUSSION

We treated patients with severe erosive gingival lesions by applying an adhesive paste form of clobetasol 17-propionate in a tray. An important study limitation was the absence of a control group. Although placebo-controlled clinical trials represent the ideal study design,[13] we decided against this approach on ethical grounds in view of the severe clinical condition of the patients. It should also be taken into account that all patients in the study had a minimum 3-month history of chronic pain caused by the atrophy and ulcerations, which would probably not respond to a placebo effect. Therefore, it seems reasonable to assume that any improvements (particularly in clinical signs) were related to the treatment.

These lesions have a very deleterious effect on the health and well-being of the patient, and their successful treatment is an important goal. We present, to the best of our knowledge, the first report on the outcomes and secondary effects of treating this type of patient with topical corticoids applied in a tray. Gonzalez-Moles and Bagan-Sebastian[14] have reported the successful treatment of a large alendronate-induced palatine ulcerous lesion by using the patient's prosthesis as a tray for the application of clobetasol 17-propionate in adhesive paste form.

The pain and ulceration of all 33 patients in the present study had completely disappeared by the end of the 48-week follow-up, and 93.9% had returned to complete normality in their daily activities, with 2 further patients reporting an excellent response. By the sixth week of treatment, 87% of the patients had a complete absence of pain, 93% had a complete absence of ulcerations, and 81% had a full recovery in terms of daily activities. The results of this study indicate that the use of a tray of clobetasol 17-propionate with Orabase paste offers an efficacious and rapid treatment of severe erosive gingival lesions.

Recently, Lo Muzio et al[15] treated oral aphthous lesions and lichen planus by applying clobetasol propionate with a bioadhesive system, which resulted in surprisingly good outcomes. However, their article provides only scant clinical data on the patients with erosive lichen planus, raising the possibility that patients may have had a form of the disease that tends to have spontaneous resolution without treatment. Evidently, the greatest clinical challenge is posed by persistent

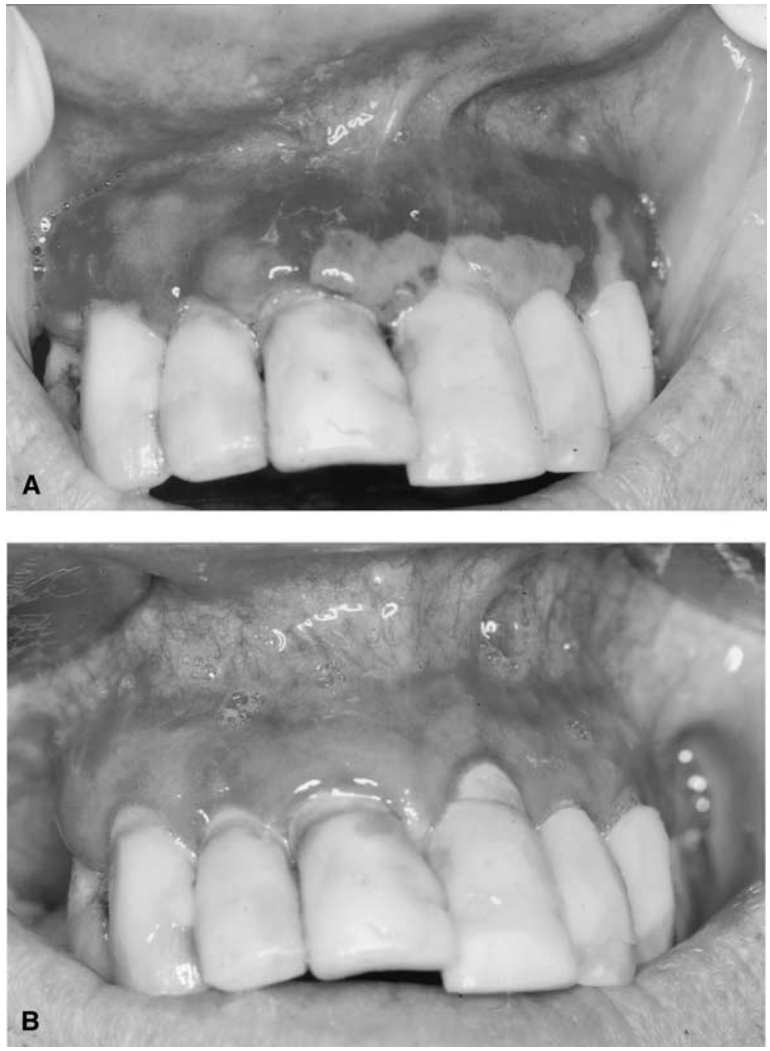


Fig. **A,** A patient with oral mucous membrane pemphigoid and painful severe erosive gingival lesions. **B,** After treatment, the ulceration had completely disappeared, but painless atrophy persisted.

chronic erosive forms of oral lichen planus, especially when severe (ie, extensive, multiple, and very painful), because they do not tend to spontaneously remit and they require sustained treatment with systemic or topical corticoids.[16] Lozada-Nur et al[5,6] used clobetasol-17 propionate mixed in an adhesive paste to treat patients with severe erosive disease of the oral mucosa, reporting a complete response in only 62.5% of patients and an excellent response in 29.7%; they described the treatment as efficacious and safe. Silverman Jr et al[3] used 0.025% fluocinolone in Orabase paste to treat patients with erosive oral lesions produced by oral lichen planus. They concluded that the treatment was of some benefit to 61.9% (96/155) of the patients in their series, even though only 14.1% (22/155) of the patients were symptom-free. Our excellent outcomes are probably related to the following factors: the very high potency of the drug and its improved delivery to all lesions through the use of the tray, the higher concentration used (0.05% vs 0.025%), and the perfect control we achieved over the duration of contact between the drug and the lesion (ie, 15 minutes a day during our initial treatment phase).

Without the use of trays, the clinician cannot be sure that the patient will place the drug on all the gingival lesions or that the desired contact time will be maintained. Although Orabase paste is an adherent vehicle, mouth movements can soon alter the initial placement of the paste if a tray is not used. Gonzalez-Moles et al[10] have published the excellent outcomes of patients with multiple severe, erosive oral lesions treated with a clobetasol propionate mouthwash, another method that

offers excellent control over the contact time between the drug and all lesions.

Atrophy had the least response to the treatment. Most patients had an excellent response (63.7%; 21/33) or good response (15.2%; 5/33) rather than a complete resolution of the atrophy. Nevertheless, the remaining gingival atrophies were not painful and did not interfere with the daily activities of the patients, a similar result to that of the patients given clobetasol propionate mouthwash.[10] In our view, the transformation of severe erosive gingival lesions into a painless gingival atrophy can be considered a therapeutic success.

As mentioned, the adverse effects of topical corticoid treatment in the oral cavity have already been reported.[10] With the present protocol, however, no side effects were present. We therefore decided not to measure the cortisol levels in plasma. There were no increases in blood pressure or episodes of hyperglycemia among our patients with a history of diabetes or controlled hypertension, and no case of candidiasis appeared as a result of our treatment. Lozada-Nur et al[5,6] prevented the appearance of candidiasis by prescribing an antifungal treatment to individuals at risk, who were identified by using pretreatment cultures and counts of colony-forming units. We included 100,000 IU/cc of nystatin in our paste because of the large surface area in contact with the drug and the high concentration of clobetasol used and because the occlusive nature of the tray method could have induced candidiasis in many of our patients. The innocuous nature of nystatin and its low cost are favorable reasons for its use in all patients treated by using the proposed technique.

The application of an Orabase paste of 0.05% clobetasol 17-propionate plus 100,000 IU/cc of nystatin by means of a tray may be an efficacious treatment of severe erosive gingival lesions.

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