1. Topical application of morphine for wound healing and analgesia in patients with oral lichen planus: is it effective?


Oral lichen planus (OLP) is a chronic inflammatory disorder of the oral mucosa. Prevalence figures are low and vary across different populations. However, more than 60% of patients are women between 30 and 60 years of age. Approximately 1-5% of patients with OLP present with cutaneous lesions. In contrast, 77% of patients with skin lesions also have oral lesions. Asymptomatic variants (reticular and plaque-like types) and symptomatic variants (erythematous, formerly atrophic; erosive; ulcerative; and, rarely, bullous types) may appear singly or in combinations.

Lichen planus is believed to result from an abnormal T-cell-mediated immune response in which basal epithelial cells are recognized as foreign because of changes in the antigenicity of their cell surface. The cause of this immune-mediated basal cell damage is unknown.

As OLP is a chronic, often persisting disorder of immunologic background, treatment is mainly focused on pain reduction and healing of lesions. Cause-related therapies are not available to this date. Topical application of corticosteroids (clobetasolpropionate, triamcinolone, prednisone, and dexamethasone) is the treatment of choice. However, in long-term use, these drugs may, even though rarely, result in systemic adverse endocrine effects (Cushing’s disease, buffalo hump, moon face), adverse metabolic effects (e.g., hyperglycemia, osteopathy), ocular manifestations (e.g., cataract, glaucoma), and electrolyte imbalance (e.g., oedema, hypocalcemia). In view of this, opioids have been considered mainly for topical application as their effectiveness has been demonstrated on wound healing and pain relief. Zaslansky and colleagues (2018) reported on a clinical trial that sought to test the topical application of morphine hydrochloride in patients with symptomatic erosive and/or ulcerative OLP and its effect on healing. The reduction of pain and safety were secondary outcomes.

MATERIALS AND METHODS
This was a single-centre, prospective, double-blind, placebo-controlled, randomized, three arm, phase II study. Patients were eligible if their diagnosis of erosive and/or ulcerative OLP was confirmed by a pathologist; if they were level I–II according to the American Society of Anaesthesiologists (ASA) classification (healthy or minimal systemic disease requiring no treatment), 18–75 years old, either sex, and deemed able to provide assessments of their pain and side effects. Patients were excluded if they had a condition of alcohol abuse or addiction (opioids and/or benzodiazepines), known hypersensitivity to morphine, major renal or hepatic dysfunction, pregnancy or lactation, sleep-apnea-syndrome, diabetes or had participated in other studies. Patients who were included in the trial were then taught how to use a pain diary and how to assess opioid-related side effects using an 11-point item numerical rating scale (NRS) which ranged from score 0 (no side effects) to 10 (worst possible side effects).

After clinical examination of the oral cavity of each of the included patients, the size of the lesion was measured, photographed and scored using the Thongprasom clinical criteria score. Severity of pain was assessed using the NRS. Patients were then assigned to one of three treatment groups using a random log randomization chart and were given a bottle with sufficient medication to last for the duration of the study. Bottles contained 20 ml of either 40 mg (0.2%) or 80 mg (0.4%) morphine hydrochloride dissolved in glycerol 85%. Placebo consisted of 10 mg caffeine dissolved in glycerol (85%). The initial dose of test substance was applied to the lesion(s) by the investigator. Patients were discharged an hour later after confirmation that they experienced no adverse effects.

At home (days 2-5), patients self-applied the test substance three times daily for 5 days. Patients were asked to leave the test substance in the mouth for one min and then spit it out (‘swish and spit’). They were requested to refrain from eating, drinking, or smoking for an hour after application of the test substance. In the event of unrelieved pain, patients were permitted to apply one cm of Volon A Haftsalbe® (= rescue medication) onto the lesions, up to three times a day. As the triamcinolonacetonid in Volon A Haftsalbe® was expected to have an effect on healing, patients taking this medication were excluded from the analysis regarding healing, though not regarding pain.

Monitoring the well-being of patients was carried out by a once daily telephone interview. Patients reported the intensity of pain during this call, whether they experienced side effects and if they had used the rescue medication.
After five days (day six), patients returned to the clinic; their lesions were examined clinically and photographed. Photographs were coded and assessed by a blinded examiner and participation in the study ended.

The primary outcome was the extent of healing of lesions assessed on the return visit.

Secondary outcomes were as follows: (1) pain scores (spontaneous) during the five days of treatment; (2) presence and severity of central (nausea, vomiting, sedation, constipation) and local (burning, dry mouth) side effects; (3) whether patients required ‘rescue medication’ for treatment of pain, the dose, and when it was taken; and (4) total intake of test substance.

RESULTS
Of the 123 OLP patients screened, only 45 fulfilled the inclusion criteria although there had been a recruitment drive of almost three months. Patients were randomized into the three study groups, n = 15 received 0.2% morphine; n = 16 received 0.4% morphine and n = 12 received placebo. Forty-three patients were included in the final analysis. Two patients were excluded because they discontinued intervention.

In the 0.2% morphine group (n=15), there were 12 females and 3 males with an mean age of 58 years, SD 10 years; the 0.4% morphine group (n=16) had 12 females and 4 males with the mean age of 60 years, SD 14 and the placebo group (n=12) had 10 females and 2 males (mean age 65 years, SD 8).

Clinical variants of OLP at the beginning of the study included the following: erosive (n = 23, 53.5%); ulcerative (n = 6, 14.0%), and erosive/ulcerative (n = 14; 32.6%). The most frequently affected location was the gingiva (55%) followed by buccal mucosa (32%) and dorsum of tongue (5%).

There were no differences between the groups with regards to extent of healing (P < 0.686). For the Pain scores, there were no differences between the groups (P < .530) at any time during the observation period. Scores were low (under 3/10) in all groups. None of the patients reported moderate or serious adverse events. None of the patients used the rescue medication. There were no differences in use of the test substance according to amounts (g) remaining in the bottles at the end of the study (P = 0.679).

CONCLUSIONS
The results of this trial suggest that locally applied morphine hydrochloride in a solution of 0.2 and 0.4% used in a period of one week has no clinically relevant benefit compared to placebo treatment based on caffeine and glycerol in OLP.

Implications for practice: This trial provides evidence that morphine should not be considered as a treatment option for OLP. Corticosteroids are still the gold standard for providing symptomatic relief for patients with OLP.

Reference

2. A Comparison of root canal cleanliness using different irrigation activation systems.


The success of any root canal treatment depends on good biomechanical preparation. Irrigation is an essential part of root canal debridement to ensure cleaning in areas that were not touched by mechanical instrumentation.1 These irrigants must have direct contact with the entire canal wall for effective action. Different techniques and irrigant delivery devices have been proposed to increase the effect of chemical disinfection within the root canal system and to improve canal cleanliness following mechanical instrumentation.1 However, thorough cleaning of the entire root canal system is still challenging as mechanical instrumentation of the canal walls always generates a smear layer.

Recently, EDDY, a sonic powered irrigation activation system made of flexible polyamide with a size of 25.04, was introduced (VDW, GmbH, Munich). According to the manufacturer, it allows an efficient cleaning of complex root canal systems without the limitations of ultrasound-activated devices. EDDY is activated to a frequency range of between 5000 and 6000 Hz by an air-driven handpiece (Air Scaler). According to the manufacturer, the instrument is claimed to create a three-dimensional movement that triggers “cavitation” and “acoustic streaming”—two physical effects which up to now have only been caused by passive ultrasonic irrigation (PUI) and to which have been attributed the improved cleaning efficiency of PUI.1 EDDY is a non-cutting, sterile single-use instrument. Another sonic activation system available is the EndoActivator (EA) system, which is a cordless sonic handpiece that activates highly flexible polymer tips in the range of between 33–167 Hz. Hence, with regard to the frequencies, these sonically activated tips differ at least by factor 36 and it is reasonable to assume that this difference may have an impact on the clinical performance of these two sonic devices. However, there are no published data regarding the efficiency of the sonic activation system EDDY. Urban and colleagues (2017)1, reported on an in vitro study that sought to assess and compare the efficacy of EDDY with manual irrigation (MI), EndoActivator (EA), and passive ultrasonic irrigation (PUI) regarding removal of debris and smear layer in the coronal, middle, and apical thirds of straight root canals. The null hypothesis tested was that all activation systems perform equally regarding removal of debris and smear layer.

Acronyms
EA : EndoActivator
ISO : International Standardisation Organisation
MI : manual irrigation
PUI : passive ultrasonic irrigation
MATERIALS AND METHODS
A sample of 58 single-rooted mandibular premolar teeth extracted for periodontal and orthodontic reasons were used in the study. Two digital radiographs were taken in a bucco-lingual and mesio-distal direction to verify root canal anatomy presenting only one central root canal. Inclusion criteria were permanent teeth, intact apices, no previous root canal treatment, or extensive coronal restoration. Exclusion criteria were oval canals (long versus short diameter ≥1.5) root caries, cracks, and fracture lines.

The crowns were not removed in order to preserve the normal trajectory of irrigation instruments. Following access cavity preparation, patency was checked using a size 10 C-Pilot file (VDW GmbH, Munich). Simultaneously, root canal working length was visually determined using a stereomicroscope by subtracting one mm from the measurement taken when the file just passed the foramen major. Additionally, an apical gauging was performed to verify comparable canal diameters and foramen sizes of all samples. This was done using ISO tapered silver points with sizes 20, 25, and 30. Only teeth with an apical size of about size 25 were included in this study.

Prior to canal preparation, all apices were covered with wax in order to guarantee a closed system. Root canal preparation was performed by only one experienced operator with Reciproc R40 instruments using the VDW-Silver motor and the setting “RECIROC ALL.” During instrumentation, all root canals were irrigated after each preparation cycle with 2.5 ml of 3% sodium hypochlorite with a 30-g open-ended needle inserted into the root canal without binding and not deeper than one mm short of the working length. One preparation cycle consisted of three pecks with an amplitude of not more than three mm. When the instrumentation was completed, activation was performed in the following activation procedures with a total volume of 12ml of NaOCl and three activation cycles (4ml of NaOCl per cycle) of 30s:

1. Manual irrigation (volume 12 ml; irrigation time 90 s)
2. EndoActivator (166 Hz, size 25.04)
3. PUI (Irri S size 25; VDW-Ultra device; VDW; setting 30% resulting in about 30 kHz)
4. EDDY (6000 Hz, size 25.04)

One group (n = 10) served as control
5. Negative control group (no irrigation)

The tips of all activation devices as well as the irrigation needle were placed one mm short of the working length without binding. Specimens were prepared for SEM evaluation. After screening of the entire canal wall, three photomicrographs of each specimen were taken to visualize the coronal, middle, and apical portions. Canal areas that were not instrumented were not assessed, and the apical third regions beyond the working length were excluded. For each portion of the canal, always the area showing the greatest amounts of debris and smear layer was selected. A total of 348 images (58 samples × 3 portions, apical, middle, and coronal) were analysed twice at an interval of 48 hours by two blinded and experienced observers who underwent a training process with reference to the scoring system of the SEM evaluations. The following scoring system was used:

- Score 1: clean canal wall, only very few debris particles
- Score 2: few small conglomerations; less than 25% of the canal wall covered
- Score 3: many conglomerations; 25% to 50% of the canal wall covered
- Score 4: 50% to 75% of the canal wall covered
- Score 5: complete or nearly complete (more than 75% of the canal wall) covering of the canal wall by debris

Scoring of debris was performed using a ×200 magnification. Scoring of smear layer was performed using a ×1000 magnification, and the scores were recorded.:

- Score 1: no smear layer, orifices of dentinal tubules patent
- Score 2: small amount of smear layer, some open dentinal tubules
- Score 3: homogenous smear layer along almost the entire canal wall, only very few open dentinal tubules
- Score 4: the entire root canal wall covered with a homogenous smear layer, no open dentinal tubules
- Score 5: a thick, homogenous smear layer covering the entire root canal wall

RESULTS
None of the activation methods completely removed debris and smear layer. With regard to smear layer and debris removal, significant differences between the control group and all experimental groups were obtained (p < 0.001).

Canal cleanliness increased significantly from the apical to the coronal portion of the root canals (p < 0.01). Manual irrigation removed significantly less debris compared with all other groups (p < 0.001). Further significant differences between groups were not obtained (p > 0.05).

Significantly more smear layer was found in the apical portion compared with the middle and coronal thirds of the root canals, independent of the activation method (p < 0.05). PUI and EDDY removed significantly more smear layer than MI (p < 0.01).

Conclusions: Under the conditions of this study, all activation methods were superior compared with manual irrigation regarding debris removal. EDDY and PUI obtained significantly better smear layer scores compared with manual irrigation. Implications for practice: This study has provided evidence that manual irrigation methods used during endodontic treatment can be considered as outdated when compared with the more modern and effective alternatives.

Reference

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