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# Zinc-Oxide Eugenol Paste, Antimicrobial Gel, and Ayurvedic Medicament in the Management of Alveolar Osteitis: A Prospective and Comparative Study

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## Abstract

**Objectives:** The objective of this study was to compare the three treatment strategies of zinc oxide eugenol (ZOE), metronidazole gel, and Aloe vera gel in the management of dry socket with respect to pain relief and mucosal healing. **Methods:** This was a comparative study in which 90 patients were recruited and randomly divided into three groups of 30. ZOE dressings were applied in Group A, Metronidazole gel in Group B, and Aloe vera gel was applied in Group C patients on the day of reporting. Patients were followed up for seven consecutive days. Day-wise pain and mucosal healing were assessed in each patient using the visual analog scale and mucosal healing index, respectively. **Results:** The mean age for the 90 patients recruited in the study was 44.02 (9.9). Male: Female ratio was 37:53. Higher values of pain were reported in Group A from day 1 to 6 ($P < 0.01$). However, the difference was not significant among the three groups ($P > 0.05$) on the 7th day. Significant differences were seen among groups ($P < 0.01$) for mucosal healing on days 2–6 with higher mean values in Group A. On day 1 and day 7, a non-significant difference was seen for the values across all three groups ($P > 0.05$). **Conclusion:** Metronidazole and Aloe vera gels were found effective in early pain relief while producing a similar amount of mucosal healing. These gels offer the potential to be used as alternative home remedies, thus reducing the number of dental appointments required in the case of ZOE dressings. However, further randomized and clinical studies are required to evaluate the three strategies for their potential adverse effects.

**Keywords:** Aloe vera, Alveolar osteitis, Dry socket, Metronidazole, Zinc oxide eugenol.

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## Introduction

Dental extractions are routinely performed minor oral surgical procedures which could be associated with certain post-operative complications. Alveolar osteitis or dry socket is one of the most common complications after the extraction of a permanent tooth.[1] It can be defined as "the post-operative pain in and around the extraction site, which rises in severity at any time between the 1st and 3rd days after the tooth extraction, accompanied by a partial or complete disintegration of the blood clot within the alveolar socket, with or without halitosis".[2] The rate of incidence of dry socket has been reported to be variable, ranging from around 0.5–68%.[3] Lower third molars are the most common teeth that are associated with dry socket with an incidence between 25% and 30%.[2]

Dry socket is a painful and annoying condition and since the causes for this condition have not been precisely determined, management is primarily targeted at relieving the symptoms and stimulating the socket to heal itself. The most common dressing reported in the literature for a dry socket is zinc-oxide eugenol (ZOE) which is placed in the socket and changed every day until the pain subsides.[4] The major disadvantage of ZOE dressing in a dry socket is that it has to be freshly prepared, thus requiring the patient to visit the dental clinic every subsequent day until the pain subsides and the socket heals. Other medicaments and procedures have also been suggested in the management of dry socket such as Metronidazole gel, Aloe vera gel, platelet-derived growth factors, topical anesthetic gel, vitamin supplements, and low-level laser therapy, each with a varying degree of clinical success.[5]

This study aims at exploring the potential alternative remedies to the ZOE dressing, which includes aloe vera gel and metronidazole gel in the management of dry socket. A comparison of conventional Zinc-oxide eugenol paste, antimicrobial gel, and ayurvedic medicament has been made in terms of early and final pain relief, and mucosal healing in the management of dry socket.

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## Methodology

### Ethical Approval

Ethical approval was obtained from the Institutional Ethical Committee under proposal 1/9/334/JMI/IEC/2021 before the commencement of the study. Written informed consent was obtained from all participants.

### Study Design

This comparative and prospective study was conducted in the Department of Oral and Maxillofacial Surgery of a central government dental care institute over a period of 3 months. A total of 90 patients were recruited in the study and randomly allotted to the three following groups.

- Group A: ZOE paste dressing was applied daily over the dry socket.
- Group B: Antimicrobial gel (metronidazole) was applied daily over the dry socket.
- Group C: Ayurvedic gel (aloe vera) was applied daily over the dry socket.

### Diagnosis and Eligibility Criteria

Dry socket occurring in any extraction site was included. The criteria of dry socket considered for inclusion in the study were:

a) Symptoms started on the 3rd–5th day after extraction of the tooth.
b) Loss of blood clot from the socket.
c) Severe pain that radiated from the empty dry socket, normally toward the ipsilateral ear and also toward the temporal region.
d) A clot that initially had a dirty gray seeming appearance which later disintegrated to leave a grey or yellowish grayish bare bone socket devoid of granulation tissue.
e) Foul odor
f) Confirmation of the diagnosis was made by smoothly sliding a probe into the socket which was extremely sensitive.

Patients allergic to any component of the drug prescribed in the study and female patients who were pregnant were excluded from the study.

### Details of Intervention

The ZOE paste used in the study is commercially available in powder and liquid form. The composition for each is shown [Table 1].

Commercially available metrohex gel was used as the antimicrobial gel (consisting of metronidazole 10 mg% + chlorhexidine 0.25%). Ayurvedic medicament in the form of a commercially available Aloe vera gel was used that consists of Aloe Barbadensis Gel (Stabilized Aloe Vera Gel), Sorbitol, Hydrated Silica, Glycerin, Sodium Lauryl Sulfate, Chondrus Chrispus (Carrageenan), Flavor (Aroma), Bee Propolis, Sodium Saccharin, Sodium Benzoate, and Chlorophyllin-Copper Complex Contents Net Wt. 4.6 Oz (130G).

### Treatment Protocol

The treatment protocol was determined by a team of oral and maxillofacial surgeons according to the standard care of the management of dry socket. Every dry socket was irrigated with normal saline and dried with gauze, and the drug of intervention was applied. In Group A patients, ZOE paste formed after mixing the powder and liquid form was incorporated into sterile gauze fibers to form a dressing and packed into the socket once a day. In Group B and C, Metronidazole gel and Aloe vera gel was directly applied to the socket once daily by the surgeon. Patients were followed up for a duration of 7 days or till pain lasted, whichever was longer and the outcomes were assessed by two observers for 7 subsequent days. No drugs were given through systemic routes.

### Outcomes

Two main outcomes that were assessed during follow-up were pain relief, which was evaluated using the visual analog scale [Figure 1], and mucosal healing, which was assessed using the standardized mucosal healing index given by Landry *et al*.[6] [Table 2].

### Statistical Analysis

The data obtained from the participants were entered into a computer by giving coding system and proofed for entry errors. The data were compiled on an MS Office Excel Sheet (v 2019, Microsoft Redmond Campus, Redmond, Washington, United States). It was subjected to statistical analysis using Statistical Package for the Social Sciences (SPSS v26.0, IBM). Descriptive statistics such as mean, SD, and medians for numerical data were used. The normality of numerical data was checked using the Shapiro–Wilk test. It was found that the data did not follow a normal curve; hence non-parametric tests have been used for comparisons. Inter-group comparison (>2 groups) was done using the Kruskal–Wallis ANOVA followed by pair-wise comparison using Mann–Whitney *U*-test. Intra-group comparison was done using Friedman's (for >2 observations) followed by pair-wise comparison using Wilcoxon Signed rank test. For all the statistical tests, $P < 0.05$ was considered to be statistically significant, keeping $\alpha$ error at 5% and $\beta$ error at 20%, thus giving power to the study as 80%.

## Results

### Patient Demographics

A total of 90 patients were recruited out of which 37 were males and 53 were females. Male: Female ratio for Group A was 14:16, 12:18 for Group B, and 11:19 for Group C. The mean age for the patients was 44.02 (9.9). For Group A, the mean was 39.13 (9.07), for Group B, it was 46.83 (9.39), and for Group C, it was 46.10 (9.63). The most common arch to be reported with dry socket was the

**Table 1:** Composition of zinc oxide eugenol for dressing in dry socket

| | |
|---|---|
| Powder | |
| Zinc oxide – 69% | Principal agent |
| White rosin – 29.3% | Reduces the brittleness of set cement |
| Zinc stearate – 1.0% | Accelerator, plasticizer |
| Zinc acetate – 0.7% | |
| Liquid | |
| Eugenol – 85.0% | Reacts with zinc oxide |
| Olive oil – 15.0% | Plasticizer to form a paste |

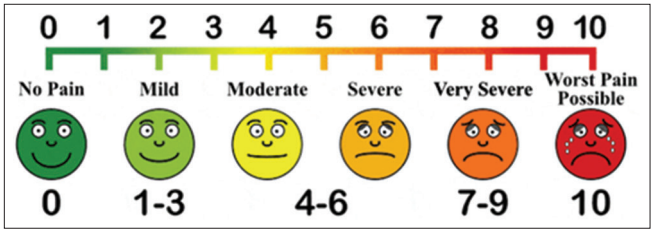


**Figure 1:** Visual analog scale used for measurement of levels of pain

mandible and the most common region was the third molar region. Group-wise, the most commonly reported region of the tooth was the mandibular first molar for Group A, mandibular third molar for Group B, and mandibular third molar for Group C.

## Intergroup Comparison

### *Pain*

There was a statistically significant difference seen for the values between the groups ($P < 0.01$) on day 1–6 with higher values for pain in Group A. However, there was a statistically non-significant difference seen for the values between the groups ($P > 0.05$) on day 7. The comparison between the three groups for estimated pain levels has been represented in the Table 3. Comparison between Group A and B revealed higher values of pain in Group A on all days ($P < 0.01$, 0.05) except for day 7 where the difference was not significant ($P > 0.05$). Similar results were seen between Group A and C where higher values of pain in Group A ($P < 0.01$, 0.05) except on day 1 and day 7. In between Group B and C, the differences were not significant for the values on all the days ($P > 0.05$) except on day 1 where there was a statistically significant difference seen ($P < 0.05$).

## Mucosal Healing

Statistically significant differences were seen for the values between the groups ($P < 0.01$) for mucosal healing index on days 2–6 with higher mean values in Group A. There was a statistically non-significant difference seen for the values across all three groups ($P > 0.05$) for MHI on day 1 and day 7 [Table 4]. Between Groups A and B, there was a statistically significant difference seen for the values on all the days ($P < 0.01$, 0.05) except on day 1 and day 7 ($P > 0.05$). A similar observation was made between Groups A and C. However, there was a statistically non-significant difference seen for the values of MHI on all days ($P > 0.05$) between groups B and C.

## Intra-group Comparison

In Group A, there was a statistically highly significant difference seen for the values of pain ($P < 0.01$) and MHI ($P < 0.01$) within the time interval with the highest values on day 1 and the least on day 7 for pain, and higher values at day 2 and the least at day 7 for MHI. Pair-wise comparison produced Z values of −4.837 for pain, and −4.688 for MHI. The highest values of pain on day 1 and the least on day 7 were observed ($P < 0.01$) for Group B and MHI values were

**Table 2:** Mucosal healing index

| *Grades* | *Tissue color* | *Response to palpation* | *Granulation tissue* | *Incision margin* |
|---|---|---|---|---|
| Very poor 1 | ≥50% of gingiva red | Bleeding | Present | Not epithelialized, with loss of epithelium beyond incision margin |
| Poor 2 | ≥50% of gingiva red | Bleeding | Present | Not epithelialized, with connective tissue exposed |
| Good 3 | ≥25% and<50% of gingiva red | No bleeding | None | No connective tissue exposed |
| Very good 4 | <25% of gingival red | No bleeding | None | No connective tissue exposed |
| Excellent 5 | All tissue pink | No bleeding | None | No connective tissue exposed |

**Table 3:** Intergroup comparison with respect to pain measured using visual analog scale

| *Day number* | *Group* | *Mean* | *Standard deviation* | *Standard error* | *Median* | *Chi-square value* | *P-value of Kruskal–Wallis test* |
|---|---|---|---|---|---|---|---|
| Pain day 1 | A | 5.27 | 1.202 | 0.219 | 5.5 | | |
| | B | 3.97 | 1.351 | 0.247 | 4 | | |
| | C | 4.90 | 1.185 | 0.216 | 5 | 13.014 | 0.001† |
| | Total | 4.71 | 1.351 | 0.142 | | | |
| Pain day 2 | A | 4.13 | 1.634 | 0.298 | 4 | | |
| | B | 2.17 | 2.214 | 0.404 | 2 | 18.692 | 0.000† |
| | C | 1.80 | 2.091 | 0.382 | 0 | | |
| | Total | 2.70 | 2.226 | 0.235 | | | |
| Pain day 3 | A | 2.80 | 2.058 | 0.376 | 3.5 | | |
| | B | 1.07 | 1.874 | 0.342 | 0 | 25.680 | 0.000† |
| | C | 0.40 | 1.221 | 0.223 | 0 | | |
| | Total | 1.42 | 2.011 | 0.212 | | | |
| Pain day 4 | A | 1.37 | 2.025 | 0.370 | 0 | | |
| | B | 0.30 | 0.952 | 0.174 | 0 | 12.360 | 0.002† |
| | C | 0.07 | 0.365 | 0.067 | 0 | | |
| | Total | 0.58 | 1.414 | 0.149 | | | |
| Pain day 5 | A | 0.77 | 1.569 | 0.286 | 0 | | |
| | B | 0.00 | 0.000 | 0.000 | 0 | 12.706 | 0.002† |
| | C | 0.00 | 0.000 | 0.000 | 0 | | |
| | Total | 0.26 | 0.966 | 0.102 | | | |
| Pain day 6 | A | 0.50 | 1.167 | 0.213 | 0 | | |
| | B | 0.00 | 0.000 | 0.000 | 0 | 10.462 | 0.005† |
| | C | 0.00 | 0.000 | 0.000 | 0 | | |
| | Total | 0.17 | 0.707 | 0.075 | | | |
| Pain day 7 | A | 0.10 | 0.548 | 0.100 | 0 | | |
| | B | 0.00 | 0.000 | 0.000 | 0 | 2.000 | 0.368‡ |
| | C | 0.00 | 0.000 | 0.000 | 0 | | |
| | Total | 0.03 | 0.316 | 0.033 | | | |

*Statistically significant difference ($P<0.05$). †Statistically highly significant difference ($p<0.01$). ‡Non-significant difference ($P>0.05$)

**Table 4:** Intergroup comparison with respect to mucosal healing

| *Day number* | *Group* | *Mean* | *Standard deviation* | *Standard error* | *Median* | *Chi-square value* | *P-value of Kruskal-Wallis Test* |
|---|---|---|---|---|---|---|---|
| MHI day 1 | A | 2.23 | 0.626 | 0.114 | 2 | | |
| | B | 2.23 | 0.774 | 0.141 | 2 | 0.681 | 0.711‡ |
| | C | 2.13 | 0.730 | 0.133 | 2 | | |
| | Total | 2.20 | 0.706 | 0.074 | | | |
| MHI day 2 | A | 2.47 | 0.860 | 0.157 | 3 | | |
| | B | 1.50 | 1.456 | 0.266 | 2 | 11.843 | 0.003† |
| | C | 1.27 | 1.437 | 0.262 | 0 | | |
| | Total | 1.74 | 1.370 | 0.144 | | | |
| MHI day 3 | A | 2.17 | 1.510 | 0.276 | 2.5 | | |
| | B | 0.70 | 1.264 | 0.231 | 0 | 27.240 | 0.000† |
| | C | 0.30 | 0.915 | 0.167 | 0 | | |
| | Total | 1.06 | 1.479 | 0.156 | | | |
| MHI day 4 | A | 1.40 | 1.734 | 0.317 | 0 | | |
| | B | 0.30 | 0.915 | 0.167 | 0 | 17.263 | 0.000† |
| | C | 0.13 | 0.730 | 0.133 | 0 | | |
| | Total | 0.61 | 1.321 | 0.139 | | | |
| MHI day 5 | A | 0.90 | 1.561 | 0.285 | 0 | | |
| | B | 0.00 | 0.000 | 0.000 | 0 | 17.337 | 0.000† |
| | C | 0.00 | 0.000 | 0.000 | 0 | | |
| | Total | 0.30 | 0.988 | 0.104 | | | |
| MHI day 6 | A | 0.63 | 1.474 | 0.269 | 0 | | |
| | B | 0.00 | 0.000 | 0.000 | 0 | 10.461 | 0.005† |
| | C | 0.00 | 0.000 | 0.000 | 0 | | |
| | Total | 0.21 | 0.893 | 0.094 | | | |
| MHI day 7 | A | 0.10 | 0.548 | 0.100 | 0 | | |
| | B | 0.00 | 0.000 | 0.000 | 0 | 2.000 | 0.368‡ |
| | C | 0.00 | 0.000 | 0.000 | 0 | | |
| | Total | 0.03 | 0.316 | 0.033 | | | |

*Statistically significant difference ($P<0.05$). †Statistically highly significant difference ($P<0.01$). ‡Non significant difference ($P>0.05$)

higher on day 2 and least on day 7 ($P < 0.01$). Pair-wise comparison for time interval produced Z values of −4.813 for pain, and −4.862 for MHI. In Group C, the highest values of pain were observed on day 1 and least on day 7 within the time interval ($P < 0.01$), and the highest values on day 2 and the least on day 7 were observed for MHI ($P < 0.01$). Time pair comparison produced Z values of −4.832 for pain, and −4.899 for MHI.

The intra- and inter-group comparisons for pain and mucosal healing have been depicted through figures [Figures 2 and 3].

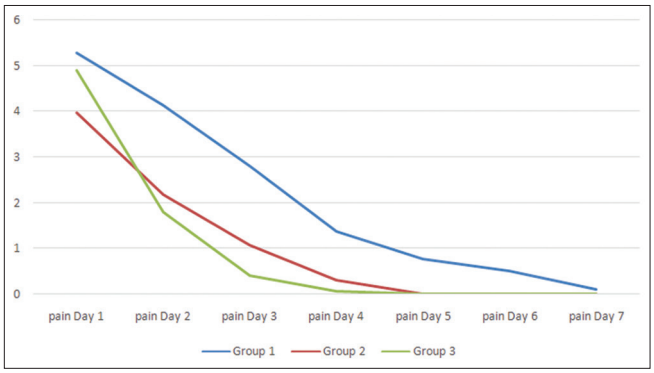


**Figure 2:** Intra and Inter group comparison for values of pain

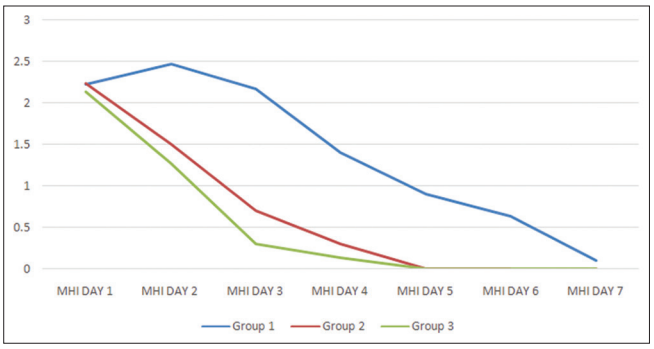


**Figure 3:** Intra and inter group comparison for values of mucosal healing

## Discussion

Several etiological factors have been suggested that contribute to the occurrence of dry socket but a definitive cause for it has not yet been established. Few proposed etiological factors are traumatic extractions, bacterial infection, smoking, medications, and anatomical susceptibility.[3] Non-compliance to post-extraction instructions also plays a crucial role in the incidence of dry socket after extraction.[7] Fibrin deposition and formation of a blood clot are an important step that enables healing of the extraction socket by forming a meshwork that acts as a physical barrier to the invading pathogens. The proposed etiological factors altogether or individually cause the activation of plasminogen into plasmin which results in the degradation of the blood clot and activation of kinins, inducing a state of hyperalgesia.[8]

The management of dry socket usually comprises local preventive measures to initiate healing of the exposed socket and pain control. In routine practice, this is achieved by daily irrigation of the socket followed by dressings soaked in different medicaments. The procedure of forceful irrigation drives out the slough and debris accumulated in the socket and promotes the formation of a new clot. The solutions used for irrigation are normal saline, hydrogen peroxide, or antimicrobial solutions such as chlorhexidine and betadine. The medications used in dressings

are ZOE, Alvogyl, a popular hemostatic surgical dressing, Colloidal silver, or SaliCept. Other antimicrobial intra-socket medicaments such as metronidazole gel, rifampicin, or clindamycin are also used after refreshening of the socket.[9]

Three techniques were utilized in the present study, where one group was provided ZOE-packed dressings as per convention, Metronidazole gel was used in the second, and Aloe vera gel was used in the third. The results showed higher early pain values in the ZOE group compared with the Metronidazole and Aloe vera group for the first 6 days which suggests Metronidazole gel and Aloe vera provided immediate and early pain relief when compared with ZOE. However, for the 7th day, the differences were not significant across the three groups. In addition, no differences were found between Metronidazole and Aloe vera gel in terms of pain relief for the past 6 days suggesting a minimal advantage of one over the other. Thus, all three treatment strategies provided final relief in pain but early pain relief was provided only by Metronidazole and Aloe vera intra-socket medicaments. For healing of the extraction socket, MHI values were highest in the ZOE group for the initial 6 days, after which all three groups showed comparable healing of the extraction wound on the 7th day. Metronidazole and Aloe vera groups showed equivalent healing from the first to the 7th day. No adverse effects or complications after the intervention were reported. Since Aloe vera and Metronidazole provide better early pain relief and almost similar mucosal healing when compared with ZOE, the usage of these home remedies is advisable over ZOE. ZOE has to be freshly prepared by the dentist every day and requires additional patient recalls. Therefore, Metronidazole and Aloe vera can be prescribed to the patient as home remedies without the need for the patient to visit the dentist every day.

Eugenol present in ZOE acts as a potent analgesic, sedative, and obtundent that causes denaturation of the proteins, leading to a reduction in the permeability of sodium channels. This prevents the propagation of action potential across the nerve endings and reduces pain. Zinc, as a micronutrient, promotes healing through the process of angiogenesis and re-epithelialization.[10] Many authors have recommended this conventional modality to be a preferred treatment option in the management of dry socket.[11,12] However, the main disadvantage of ZOE paste is that it requires frequent clinical visits which need patient compliance and effort. Metronidazole gel, on the other hand, has a primary antimicrobial action at the healing site, thus providing an additional advantage of preventing secondary infection due to its bactericidal action against anaerobes. Although the pathogenesis of dry socket remains inconclusive for the involvement of microbes in the incidence of dry socket, studies have shown reduced incidence with Metronidazole prophylaxis after extraction. Thus, the association of anaerobic bacteria in the pathogenesis of dry socket could be said to be positive and the effect of Metronidazole gel to be inhibitory in the progression of dry socket.[13]

Aloe vera is an ayurvedic herb with anti-inflammatory, antibacterial action, mucus-stimulating, and cellular protection properties, reported to be effective in healing burns, skin damage, edema, and pain.[4] In post-extraction management, Aloe vera has been used in various forms. Acemannan is a polysaccharide extracted from Aloe vera, known for its osteoinductive and proliferative properties. In a clinical trial by Vu *et al*., there was no incidence of dry socket in the group treated with Acemannan post-extraction, and a greater reduction in socket volume was observed at all post-operative time points.[14] Another derivative of Aloe vera, Alvogyl has been used which is a hemostatic analgesic paste containing Iodoform as an antimicrobial, Eugenol for pain relief, and Penghawar fibers which provide good adhesion and have anti-inflammatory properties.[15] According to the study by Ali Hatem *et al*., the use of Aloe vera extract showed promising results in terms of pain relief in patients with dry socket when compared with Alvogyl.[16] Additionally, Chaurasia *et al*. found ZOE to be more effective in dry socket management compared to Alvogyl for early as well as final pain relief.[17]

Aloe vera and metronidazole gel could be used as alternative remedies for pain control and mucosal healing. The additional advantage of cost-effectiveness, compliance, and self-application of the gel by the patient could reduce the number of visits to the dental office when compared to ZOE which requires the patient to be present at every appointment for reapplication of freshly prepared ZOE dressing. In view of the rapid increase in antimicrobial resistance over the past few years, the practice of prescribing oral antibiotics to patients for dry socket is deemed irrelevant. Local measures such as gels and dressings provide viable options with the least possible side effects.

### Limitations and Future Recommendations

This comparative study requires further clinical trials with randomizations to accurately assess the potential benefits and possible complications of the stated interventions. Second, there was no region-specific selection of dry socket and the cases were randomly distributed across the whole oral cavity. This could potentially affect the progression and healing of the socket. Future studies could select a specific region of the dry socket to assess the prognosis of different intervention strategies. Moreover, microbiological flora around the extraction socket could be assessed in studies involving local antimicrobial measures to detect the response of intervention to microbes responsible for the initiation and progression of dry socket.

## Conclusion

The management of dry socket is primarily palliative, aimed at controlling pain and initiating healing of the exposed socket. ZOE packs are commonly used surgical dressings for this purpose. However, alternative techniques such as Metronidazole gel and Aloe vera extracts prove to be viable methods to effectively combat dry socket. Although the end-term differences were not significant among the three groups in the present study, metronidazole and Aloe vera gels were found to be effective in providing early pain relief, with comparable mucosal healing. The usage of Aloe vera and metronidazole gels is recommended as effective home remedies which could reduce the number of patient recalls required in ZOE dressings. Further randomized studies are required to accurately evaluate and compare the three strategies for their potential hazards.

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