Review

Photobiomodulation after Surgical Extraction of the Lower Third Molars: A Narrative Review

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Abstract: The surgical extraction of the lower third molar is widely practiced in oral surgery. Inflammatory complications such as pain, swelling, and trismus can cause discomfort to the patients after third molar extraction. Several methods have been used to reduce these postoperative sequelae, including the use of corticosteroids, nonsteroidal anti-inflammatory drugs, analgesics, antibiotics, less traumatic surgical methods, and the use of photobiomodulation. This narrative review summarizes the current evidence on the effect of photobiomodulation on pain, facial swelling and trismus after third molar surgery. A literature search using MEDLINE (NCBI PubMed and PMC), EMBASE, Scopus, Cochrane library, Web of Science, and Google Scholar was undertaken up to October 2021. Forty-one articles met the inclusion criteria. Photobiomodulation can be considered an alternative and useful method for controlling pain following impacted wisdom tooth surgery. The effectiveness of PBM in reducing swelling and trismus is still controversial. This review highlights the lack of consensus in the literature on protocols used in PBM therapy.

Keywords: photobiomodulation; low level laser therapy; pain; swelling; trismus

1. Introduction

The surgical extraction of the third mandibular molar is the most frequent procedure in oral and maxillo-facial surgery [1].

An impacted third molar can cause different consequences such as pericoronitis, distal caries and periodontal pocket of the second molar, odontogenic abscesses, and the development of follicular cysts [2].

The healing period following the surgical extraction of an impacted third mandibular molar is associated with an intense inflammatory response. This process is responsible for postoperative pain, facial swelling, and trismus, which negatively affect the quality of life of the patients during 7–10 days after the surgery [3]. These signs and symptoms are a consequence of the surgical wound and the duration of the surgery itself [4], as the result of a direct trauma on the blood and lymphatic vessels [5]. After local anesthesia wears off, the pain usually reaches maximum intensity 3 to 5 h after surgery, continuing for 2 to 3 days, and gradually diminishing until the seventh day [6,7]. Swelling reaches peak intensity in 12 to 48 h, influencing facial esthetics and social interactions. It usually resolves between the fifth and seventh days. Trismus may be considered initially as having a protective function by encouraging the patient to rest the surgical site and permit healing. However, it may lead to difficulty in eating and functioning if it persists for more than a few days.

Piezoelectric devices, which can be used instead of conventional burs, may be beneficial for surgeries at complex anatomical sites because they can preferentially cut mineralized structure [8,9]; furthermore, some authors reported a reduction in postoperative sequelae using the piezoelectric surgical technique in third molar extraction [10,11].
The standard therapeutic approach to reduce the postoperative complications is the administration of medications such as nonsteroidal anti-inflammatories (FANS), corticosteroids (CS), and analgesics. However, even if they are effective, these drugs present some important adverse effects such as the tendency to systemic bleeding, gastrointestinal irritation, and allergic reactions. In addition, antibiotics reduce the risk of postoperative infection and alveolitis, but the possibility of developing bacterial resistance makes their administration indicated only in selected cases [12].

These considerations justify the effort to find alternative and innovative methods for the resolution of the symptomatology that follows the surgical extraction of the impacted mandibular third molars, possibly without adverse effects. Non-medication methods used to minimize the postoperative after third-molar extraction include cryotherapy, acupuncture, and photobiomodulation (PBM) [13–15]. PBM is the application of near-infrared (NIR) light for therapeutic purpose. The “optical window” in which the effective penetration of light into tissues is maximized is between approximately 600 and 1200 nm. Low-energy laser light produces photochemical effects whereby it penetrates the mucosa without overheating or producing other side effects [16].

PBM is described in the literature with different terminology starting from 1970: Low Level Laser Therapy (LLLT), Low Intensity Laser Therapy (LILT), and Low Power Laser Therapy (LPLT). Many studies have reported the efficacy of PBM in the wound healing process [17]. PBM could modulate the inflammatory activity and accelerate healing [18]. As primary effects, PBM promote vasodilatation, lymph drainage, and cellular biostimulation, which results in decreasing pain and edema and accelerating tissue regeneration. Secondary effects include the aggregation of many molecules, as endogenous endorphins and encephalins, resulting in the reduction of inflammation and immune response. PBM improves the reparative process and increases the inorganic matrix of the bone and mitotic osteoblastic index. PBM also increases the motility of human keratinocytes and promotes their increase of collagen type I and vascular endothelial growth factor (VEGF) gene expression [19,20]. Moreover, this therapy generally is a safe procedure [21].

PBM has been reported to manage pain, swelling, and trismus following the removal of impacted third molars since the 1980s. However, in the literature, the conclusions are controversial. The aim of this narrative review is to summarize the current evidence on the effect of PBM on pain, swelling, and trismus after third molar surgery.

2. Methods

This narrative review was performed according to the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) guidelines [22]. The focus question was: “Is photobiomodulation useful in reducing pain, swelling and trismus after third molar surgery?” A comprehensive search of MEDLINE (NCBI PubMed and PMC), EMBASE, Scopus, Cochrane library, Web of Science, and Google Scholar was conducted with the following search strategy: (“Low-Level Laser Therapy” OR “Low-Level Laser Irradiation” OR “Laser Biostimulation” OR “Photobiomodulation” OR “Laser Photobiomodulation” OR “Low-Power Laser Therapy” OR “Photobiomodulation Therapy” OR “Laser Phototherapy” OR “Low-Level Light Therapy”) AND “Third molar surgery” for original articles published until October 2021. All studies were selected based on titles and abstracts and all manuscripts that were considered suitable for the revision of the complete text were recovered. In addition, a manual search of references listed in each original article and a revision of each article, to avoid losing potential studies, were performed. Inclusion criteria were (1) studies in the English language; (2) studies involving humans; (3) studies with primary outcomes including pain, swelling, and trismus; and (4) studies in which the types of laser and the laser’s parameters were clearly stated. Exclusion criteria were (1) conference proceedings, letters to the editor, short communications; (2) in vitro or in vivo animal studies; and (3) studies with less than ten subjects. Two investigators (D.P. and F.R.) independently assessed each eligible article, extracted data using a pre-established
form, and collated all data into a Microsoft Excel spreadsheet (Microsoft Corp. Redmond, WA, USA).

3. Results
3.1. Description of the Studies

One hundred and thirty-six studies were obtained from the databases searched. After duplicates were removed, 91 articles were evaluated, of which 50 were excluded after title, abstract and full-text revision. Forty-one studies met the inclusion criteria. A detailed flow chart of the selection process is shown in Figure 1. Thirty-nine studies were RCTs; one was a case-series study. A total of 1833 subjects participated across the 41 studies.

Nine studies did not record participants’ gender; in the other studies, there were 727 female participants and 1106 male participants.

The characteristics of the included studies are presented in Tables 1 and 2.

**Table 1. Characteristics of the studies included.**

| Authors and Year of Publication | Laser Properties (nm) | Laser Properties (mW) | Laser Properties (J/cm²) | Outcomes | Sample Size |
|--------------------------------|-----------------------|-----------------------|--------------------------|----------|-------------|
| Asutay et al. (2018)          | 810                   | 300                   | 4                        | pain, trismus, swelling | 45          |
| Hamid et al. (2017)           | 810                   | 100                   | 32, 86                   | pain     | 30          |
| Landucci et al. (2016)        | 780                   | 10                    | 7, 5                     | pain, trismus, swelling | 22          |
| Sierra et al. (2015)          | 660, 808              | 100                   | 106                      | pain     | 60          |
| Sierra et al. (2016)          | 660, 808              | 100                   | 106                      | pain     | 60          |
| Pol et al. (2016)             | 650, 904              | 8–500, 70             | no reported              | pain, swelling | 25          |
| Abdel-Alim et al. (2015)      | 830                   | 4                     | no reported              | pain, trismus, swelling | 80          |
| Fabre et al. (2015)           | 660                   | 35                    | 5                        | pain, trismus, swelling | 10          |
| Merigo et al. (2015)          | 650, 910              | no reported           | 480, 31                  | pain, swelling | 59          |
| Ferrante et al. (2013)        | 980                   | 300                   | no reported              | pain, trismus, swelling | 30          |
| Koparal et al. (2018)         | 810                   | 300                   | 4                        | pain, trismus, swelling | 45          |
| Raisessian et al. (2017)      | 980                   | 300                   | 18                       | pain, trismus, swelling | 44          |
| Petrini et al. (2017)         | 980                   | 300                   | no reported              | pain, trismus, swelling | 45          |
| Kahraman et al. (2017)        | 830                   | 100                   | 3                        | pain     | 53          |
| Alan et al. (2016)            | 810                   | 300                   | 4                        | pain, trismus, swelling | 15          |
| Eroglu et al. (2016)          | 940                   | no reported           | 4                        | pain, trismus, swelling | 35          |
| Eshghpour et al. (2016)       | 660                   | 200                   | 85, 7                    | pain, swelling | 40          |
| Kazancioglu et al. (2014)     | 806                   | 100                   | 4                        | pain, trismus, swelling | 60          |
| Tuk et al. (2017)             | 660                   | 198                   | 67,5                     | pain     | 163         |
Table 1. Cont.

| Authors and Year of Publication | Laser Properties (nm) | Laser Properties (mW) | Laser Properties (J/cm²) | Outcomes | Sample Size |
|---------------------------------|-----------------------|-----------------------|--------------------------|----------|-------------|
| Pedreira et al. (2016)          | 808                   | no reported           | 2                        | pain, trismus, swelling | 24          |
| Lopez Ramirez et al. (2012)     | 810                   | 500                   | 5                        | pain, trismus, swelling | 20          |
| Amarillas et al. (2010)         | 810                   | 100                   | 4                        | pain, trismus, swelling | 30          |
| Royesdal et al. (1993)          | 830                   | 40                    | no reported              | pain, trismus, swelling | 25          |
| Fernandez et al. (1993)         | 830                   | 30                    | 4                        | pain, swelling          | 52          |
| Markovic et al. (2007)          | 637                   | 50                    | 5                        | swelling              | 120         |
| Aras et al. (2009)              | 808                   | 100                   | 4                        | swelling, trismus      | 32          |
| Aras et al. (2010)              | 808                   | 100                   | 4                        | swelling, trismus      | 48          |
| Feslihan et al. (2019)          | 810                   | 300                   | 6                        | pain, trismus, swelling | 30          |
| Santos et al. (2020)            | 780                   | 70                    | 52, 5                    | pain                 | 32          |
| Lakshmi et al. (2021)           | 980                   | 300                   | no reported              | pain, trismus, swelling | 100         |
| El Saeed et al. (2020)          | 980                   | 300                   | 4                        | pain, trismus, swelling | 20          |
| Nejat et al. (2021)             | 660, 980              | 200                   | 1, 6                     | pain                 | 80          |
| Kanal et al. (2021)             | 980                   | 100                   | no reported              | pain, trismus, swelling | 24          |
| Bianchi de Moraes et al. (2020) | 660                   | 30                    | 10, 30                   | pain, trismus, swelling | 57          |
| Kumar Gulia et al. (2021)       | 940                   | 500                   | 10                       | pain, trismus, swelling | 32          |
| Scaranò et al. (2021)           | 1064                  | 1000                  | 1, 5, 6                  | pain, swelling        | 20          |
| Momenti et al. (2021)           | 940                   | 500                   | 10                       | pain, trismus, swelling | 25          |
| Hadad et al. (2021)             | 810                   | 100                   | 212                      | pain, trismus, swelling | 13          |
| Fraça et al. (2020)             | 808                   | 100                   | 133                      | pain, swelling        | 40          |
| Mohajerani et al. (2020)        | 810, 632              | 500                   | 5, 2                     | pain, trismus, swelling | 40          |

Table 2. Method of evaluation of the outcomes and main results of the included studies.

| Method of Evaluation | Comparison | Pain | Results | Swelling | Trismus |
|----------------------|------------|------|---------|----------|---------|
| [23] VAS, MO, 3dMD FP vs. placebo | Reduction | Not statistically significant | Not statistically significant |
| [24] VAS vs. placebo | Reduction | Reduction | Reduction |
| [25] VAS, NRS vs. placebo | Not statistically significant | Reduction | Reduction |
| [26] VAS, FDM, MO vs. placebo | Reduction | Reduction | Reduction |
| [27] FDM, MO 808 nm vs. 660 nm | Reduction | 808 Reduction | 808 Reduction |
| [28] VAS, FDM vs. placebo | Reduction | Reduction | Reduction |
| [29] MO, Bella’s FSA vs. delayed PBM | Reduction | Reduction | Reduction |
| [30] VAS, FDM, MO vs. placebo | Reduction | Reduction | Reduction |
| [31] VAS, FDM vs. placebo | Reduction | Reduction | Reduction |
| [32] VAS, FDM, MO vs. placebo | Reduction | Reduction | Reduction |
| [33] VAS, MO, 3dMD FP vs. placebo | Reduction | Not statistically significant | Not statistically significant |
| [34] VAS, FDM, MO vs. drug therapy | Reduction | Not statistically significant | Not statistically significant |
| [35] VAS, FDM, MO vs. drug therapy | Reduction | Not statistically significant | Not statistically significant |
| [36] VAS intraoral vs. extraoral | Reduction | Not statistically significant | Not statistically significant |
| [37] VAS, MO, 3dMD FP vs. placebo | Reduction | Not statistically significant | Not statistically significant |
| [38] VAS, FDM, MO vs. placebo | Reduction | Not statistically significant | Not statistically significant |
| [39] VAS, ECE vs. placebo | Reduction | Reduction | Reduction |
| [40] VAS, FDM, MO vs. ozone therapy | Reduction | Reduction | Reduction |
| [41] HR, SR, Questionnaire vs. placebo | Not statistically significant | Reduction | Reduction |
| [42] VAS, FDM, MO vs. placebo | Not statistically significant | Not statistically significant | Not statistically significant |
| [43] VAS, FDM, MO vs. placebo | Not statistically significant | Not statistically significant | Not statistically significant |
| [44] VAS, FDM, MO vs. placebo | Not statistically significant | Not statistically significant | Not statistically significant |
| [45] VAS, FDM, MO vs. placebo | Not statistically significant | Not statistically significant | Not statistically significant |
| [46] VAS, FS, MO vs. placebo | Not statistically significant | Not statistically significant | Not statistically significant |
| [47] VAS, Swelling scale vs. placebo | Not statistically significant | Not statistically significant | Reduction |
| [48] VAS, FS, MO intraoral vs. extraoral | Reduction | Reduction | Reduction |
| [49] VAS, FDM, MO vs. methylprednisolone | Not statistically significant | Not statistically significant | Not statistically significant |
| [50] VAS, ECE vs. placebo | Reduction | Reduction | Reduction |
| [51] VAS, FDM, MO vs. placebo | Reduction | Not statistically significant | Not statistically significant |
| [52] FDM vs. placebo | Reduction | Reduction | Reduction |
| [53] Amin Laskin FS, MO vs. placebo | Reduction | Reduction | Reduction |
| [54] VAS, FDM, MO vs. placebo | Reduction | Reduction | Reduction |
| [55] VAS, FS, MO vs. placebo | Reduction | Reduction | Reduction |
| [56] VAS, FS, MO vs. placebo | Reduction | Reduction | Reduction |
| [57] VAS, MO, 3dMD FP 101/1/cm² vs. 30 J/cm² | Not statistically significant | Not statistically significant | Not statistically significant |
| [58] VAS, FDM, MO vs. placebo | Reduction | Not statistically significant | Reduction |
| [59] VAS, ECE vs. placebo | Reduction | Not statistically significant | Not statistically significant |
| [60] VAS, FS, MO vs. placebo | Reduction | Not statistically significant | Not statistically significant |
| [61] VAS, FS, MO vs. placebo | Reduction | Not statistically significant | Not statistically significant |
| [62] VAS, FS, MO LLLT + aPDT vs. placebo | Not statistically significant | Not statistically significant | Not statistically significant |
| [63] VAS, FS, MO vs. split mouth | Reduction | Reduction | Reduction |

Legend: aPDT, antimicrobial photodynamic therapy; FDM, facial distance measuring; FS, facial swelling; MO, maximum mouth opening; NRS, numeric rating scale; PRS, pain rating scale; VAS, visual analog scale; 3dMD FP, 3dMD face photogrammetric.
3.2. Efficacy of PBM

3.2.1. Pain

Twenty-five studies reported a reduction of pain when compared to placebo [23,24,26,28–37,39,40,52,54–56,58–63]. In these studies, lasers were used both intraorally and extraorally, and the laser’s parameters were as follows: wavelengths ranged from 632 to 1064 nm; powers were between 4 and 1000 mW; energy densities were between 3 and 212 J/cm². Eleven articles reported no statistically significant difference of PBM on reducing pain in comparison with placebo [25,38,41–47,51,57]. The lasers used in these studies were diode lasers with wavelengths of 660 nm, 810 nm, and 980 nm, different powers (30–500 mW) and energy densities (2–60 J/cm²). The most successful wavelengths in reducing pain were 810 and 980 nm (Figure 2).

3.2.2. Facial Swelling

Facial swelling was assessed in 36 studies [23,25,28–35,42–51,53,54,56–63]. Nineteen articles reported significant decrease in facial swelling after PBM application when compared with placebo [25,27–32,39,40,48–50,53,54,56,59,61,63]. The laser’s parameters of the included articles were as follows: wavelengths ranged from 650 to 1064 nm; powers were between 4 and 1000 mW; energy densities were between 2 and 480 J/cm². The wavelength of 810 nm induced the smallest facial swelling reduction (Figure 3).

3.2.3. Trismus

Twenty-eight studies assessed the impact of PBM on postoperative trismus. Eleven studies reported reducing of trismus with PBM [26,27,29,30,32,40,49,50,53,54,56]. In the included studies, wavelengths ranged between 660 and 980 nm, power ranged between 4 and 500 mW, and energy densities were between 2 and 212 J/cm². As for swelling, the wavelength of 810 nm was the one that induced the worst outcome. Instead, the wavelength of 980 nm determined the better reduction of trismus (Figure 4).

Figure 2. Histograms showing the pain outcome according to the wavelengths of the included studies. Legend: NR, no reduction, NSSR, no statistically significant results.
3.2.3. Trismus

Twenty-eight studies assessed the impact of PBM on postoperative trismus. Eleven studies reported reducing of trismus with PBM [26, 27, 29, 30, 32, 40, 49, 50, 53, 54, 56]. In the included studies, wavelengths ranged between 660 and 980 nm, power ranged between 4 and 500 mW, and energy densities were between 4 and 212 J/cm². As for swelling, the wavelength of 810 nm was the one that induced the worst outcome. Instead, the wavelength of 980 nm determined the better reduction of trismus (Figure 4).

4. Discussion

The present narrative review evaluates the role of PBM in the management of pain, facial swelling, and trismus that accompany the postoperative period after the extraction of the third molars. Since the duration of surgeries correlates significantly with trismus and swelling, most surgery protocol was performed by a single oral surgeon, and the duration of the extractions was also recorded. All investigations reported that the duration of surgery was similar between groups, without statistically significant differences. On the other hand, individual pain intensity can vary between operations. In the split-mouth design, both lower third molars of one patient were extracted in two separate operations. Between the two operations, the individual’s pain threshold may change due to the pain-related suffering experienced in the last extraction surgery.

The controversial results from the studies included in our review on the analgesic and anti-inflammatory effects of PBM after the surgical removal of third molars calls into question its efficacy. So far, the parameters of ideal PBM have not been determined due
to the great diversity of variables such as the type of laser wavelength, power, time, and mode of application.

With reference to the effect of the PBM on postoperative inflammation, Marković and Todorović [48] wanted to compare the effect of the PBM used alone or in combination with topical and systemic corticosteroids after the extraction of third molars. In their study, 120 patients were divided into four groups. Group 1 received PBM immediately after the surgery (energy output 4 J/cm² with constant power density of 50 mW, wavelength 637 nm); group 2 also received i.m. injection of 4 mg dexamethasone into the internal pterygoid muscle; group 3 received PBM supplemented by systemic dexamethasone (4 mg i.m. in the deltoid region) followed by 4 mg of dexamethasone intraorally 6 h postoperatively; and group 4 (control) received only the usual postoperative recommendations such as cold packs, soft diet, etc. The best anti-inflammatory effect was obtained with the combination of PBM and local intramuscular (medial pterygoid) dexamethasone (group 2); the authors suggested that this effect was obtained through a summation effect of both procedures. However, with the use of PBM and systemic administration of dexamethasone (group 3), there was a higher anti-edematous effect than with the use of the PBM alone (group 1), although without statistically significant differences between the groups. For this reason, the authors did not justify the use of corticosteroids in case of using PBM.

The choice for intraoral or extraoral application varied between studies, pointing out more beneficial outcomes for intraoral use or associating the two methods of application.

Kahraman et al. [36] in their study on 60 patients used different groups (intraoral LLLT, extraoral LLLT, and control) to compare the two approaches in reducing postoperative pain. They observed statistically significant results for the intraoral group, while the extraoral did not differ from the control. On the contrary, Aras et al. [50] demonstrated that extraoral LLLT is more effective than intraoral LLLT for the reduction of postoperative trismus and swelling after extraction of the lower third molar.

The number and timing of PBM treatments varied greatly among the included studies. Some studies administered the treatment once, whereas others administered it several times. Some treatments were delivered before the surgery, whereas others were delivered at the suture or at different days after surgery. Petrini et al. [35] in their retrospective study on 45 patients demonstrated that a double dose of LLLT, one immediately before and another after the surgery, was effective in reducing pain and edema at 24 h. Although the authors have found no statistically significant differences between the group irradiated also in the pre-surgery phase (group 2) with respect to that irradiated only after the extraction (group 1), for pain and edema, the results gained clinical importance if we considered that the need of Ketoprofen assumption in the first 24 h was statistically significantly lower in group 2 with respect to the controls and group 1.

Abdel-Alim et al. [29] in their study on 80 patients treated one group with PBM therapy immediately after surgery and on the 3rd day postoperatively, and one group on the 2nd and 4th days postoperatively. Statistical results showed a significant reduction in pain, swelling, and trismus in the immediate PBM therapy group compared with the delayed PBM therapy group. In the split-mouth study conducted by Kumar Gulia et al. [58], PBM was applied immediately after the sutures on the test side. The results revealed that pain, swelling, and trismus following surgery were lower on the test side compared to the control side, but only the pain reduction was statistically significant.

The effect of PBM on pain was evaluated in most of the studies included. Most of them showed a positive effect especially in the first days, whereas only some investigations reported no statistically significant results.

López-Ramirez et al. in their study on 20 patients demonstrated that the intraoral application of an 810 nm diode laser did not significantly reduce pain after a surgical extraction of impacted lower third molars. On the contrary, Asutay et al. [23] reported that the pain level in the PBM group was significantly lower than that in the control and placebo groups.
While statistical significance indicates the reliability of the study results, clinical significance reflects its impact on clinical practice. For example, in the study by Amarillas-Escobar on 30 patients, the intensity of pain was lower in the laser group than in the control group, but without statistically significant differences [45].

The role of PBM on swelling was evaluated in 35 of the studies included. Nineteen studies demonstrated swelling reduction with PBM. The measurement of swelling differed across the studies. Most swelling measurements were taken as the distance between two facial points. In the study of Asutay et al., a three-dimensional photogrammetric system was used to measure volumetric postoperative swelling. The results of their study revealed that PBM reduced facial swelling but without significant differences among the three groups (control group, PBM group, and placebo group) [23].

From the twenty-eight studies on trismus, eleven demonstrated a statistically significant reduction in trismus with PBM. For example, in the study conducted by Ferrante et al. [32] on 30 patients, trismus in the LLLT group was significantly less than in the control group at the second and seventh postoperative days ($p < 0.05$). By contrast, the results of the study by Koparal et al. [33] on 45 patients demonstrated no statistically significant difference in the trismus occurring subsequent to surgery in Groups 1 (control group), 2 (single dose of PBM immediately after surgery), or 3 (two doses of PBM, immediately following surgery and on postoperative day 2) when compared with the interincisal opening prior to surgery.

There are some limitations that should be considered regarding the present review. Firstly, the patients in the included studies often used medications, such as analgesics and anti-inflammatories. Therefore, PBM was evaluated as an adjuvant modality, making it impossible to analyze its efficacy in reducing postoperative complications as the only therapy of choice. Secondly, as previously mentioned, pain experience is partly influenced by previous experiences; this is difficult to account for in an investigation and reduces the reliability of the results.

5. Conclusions

Despite the limitations, this narrative review provides a comprehensive synthesis of the topic. PBM is a safe procedure that may not cause adverse effects and shows reduction in pain in patients undergoing the surgical removal of the lower third molar. However, the administration of PBM presents a negligible benefit in reducing swelling and trismus after surgery compared with placebo or no treatment. There is still a need for future studies with a better methodological description to provide a greater quality of evidence.

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