Review Article

Strategies used to inhibit postoperative swelling following removal of impacted lower third molar

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ABSTRACT

Postoperative swelling following different surgical strategies is an area of great interest. The main part of literature on the topic deals with swelling after extraction of low impacted third molar. In this review, we have analyzed publications of the last 20 years with a pubmed search using the following key words: impacted third molar, swelling third molar, wisdom tooth, edema jaw, corticosteroids and extraction third molar, antibiotic prophylaxis and tooth extraction. Attention has often been focused on corticosteroid therapy administered by diverse routes (orally, IV, IM, topically) and at different time schedules (before or after surgery or both). This investigation revealed how the use of different molecules and dosages makes the obtained results hardly comparable. Similar conclusions can be drawn from studies aimed at evaluating the efficacy of antibiotic therapy administered either before or after surgery. A complete review has also to take into account different surgical strategies used including various flaps, no traumatic osteothomy, and primary or secondary closure. The use of pharmacological therapy and application of an ice pack is critical in the postoperative period and has always provided positive results. However, even if it is difficult to come to definite conclusions, due to the variability of the design of studies analyzed, the postoperative discomfort identified with edema, pain and trismus following wisdom tooth removal is influenced by various factors such as the difficulty of the surgical procedure involved, age and gender of the patient, and experience of the surgeon. The pharmacological therapy when performed with corticosteroids seems to improve control of the postoperative swelling related with this kind of surgeries.

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INTRODUCTION

A surgical trauma in the oral cavity always causes tissue injury characterized by hyperemia, vasodilatation, increased capillary permeability with liquid accumulation in the interstitial space and granulocyte and monocyte migration,^[1,2] due to the increased osmotic pressure in capillaries (Starling law). Edema is the expression of exudates or transudation, and in surgery, probably both the events

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occur.^[3-5] Transudation in fact is secondary to blood flow slowing (i.e. hyperemia, vasodilatation, stenosis, etc.), while a superimposed infection is responsible for exudates.^[3]

Extension of the incision as well as tissue manipulation and length of surgery could affect the entity of swelling. According to previous published data, postoperative swelling and pain are significantly lower following a smaller incision.^[4,6-9]

When impacted third molars are removed, postsurgery is characterized by limitation in the mouth opening, pain, reduced masticatory capability and swelling of variable degree. The latter represents a serious issue as it affects the ability of the patient to interrelate and to return to the routine working life, especially during the first 3 days following oral surgery.^[10-14] The postoperative period of a patient treated for impacted third molar is hardly predictable. According to Akadiri et al., [15] gender, weight and body surface affect postoperative swelling. However, it is difficult before surgery to predict the entity of edema to occur as this will be the result of several components. In fact, different issues deserve consideration when evaluating the difficulties of one surgical approach versus another, as suggested by Akadiri et al., [16] in a review article. Much attention is given to radiography, dental morphology and depth of impaction, but age of the patient as well as experience of the surgeon should also be taken into account. Postoperative events (pain, trismus, swelling, mouth opening limitation) are usually treated with pharmacological and/or surgical and/or various strategy interventions. To this purpose, different surgeons treat postoperative swelling in the preoperative period or in the postoperative period or in both the periods or, in some cases, even during surgery. The objective of this article is to investigate the most recent literature on methods utilized to control and reduce swelling that occurs after removal of impacted third molar.

Postoperative discomfort may be considered a used term that can nevertheless cause misunderstandings due to its ambiguity. This topic is very much debated in the current international literature. This review will focus on the technical and pharmacological parameters influencing postopertative pain, swelling and trismus after third molar surgery.^[17-20]

A search of the literature of the last 20 years was carried out on Pubmed-Medline using the following key words: swelling third molar, wisdom tooth, edema jaw, corticosteroids and extraction third molar, antibiotic prophylaxis and tooth extraction. In the literature examined, all the methods used for measurement of swelling following impacted third molar removal were analyzed and divided on a temporal basis of intervention in preoperative, intraoperative and postoperative surgery.

PHARMACOLOGIC STRATEGIES

Antibiotics

Antibiotic therapy to treat established infection or as prophylactic strategy to prevent distance site infection or to control postoperative discomfort in third molar surgery is today a broadly accepted indication with documented efficacy.^[18] However, the great variability in the pharmacologic administration related to parameters like time and way of administration, posology and chemical structure seems to influence the effectiveness of the postoperative discomfort.^[19,20]

Surgeons use antibiotic prophylaxis, even if some controversies exist in this regard. In a study reported by Halpern *et al.*,^[21] reduction of both alveolar osteitis and inflammation was observed in patients treated with penicillin (15,000 UI/kg bw, IV) or clindamicin (600 mg in subjects allergic to penicillin), 1 h before surgery versus placebo-treated control patients.

Administration of amoxicillin (2 g orally), 1 h before surgery, did not result in any improvement in the postoperative period versus untreated controls.^[22] According to Martin et al.,^[23] parenteral antibiotic prophylaxis should be applied only in the case of osteotomy, whereas oral surgeons are suggested to limit the use of second- and third-generation antibiotics in maxillo-facial surgery and systemic pathologies.^[24] In patients treated with amoxicillin/ clavulanic acid (1 g, twice a day, for 5 days before surgery), no significant differences were observed versus patients treated with the same drug for 5 days following surgery.^[25] Several authors discussed the effectiveness of antibiotic prophylaxis, and it seems to be highly recommended for patients who present with a high risk of infection or when traumatic surgical procedures have been performed.^[26-30] Antibiotics are largely used in the postoperative period.^[31,32] They can be applied topically or administered systematically, but the efficacy of antibiotic treatment in the preoperative period is also highlighted. According to some authors, to obtain results with the antibiotic treatment, they must be administered preoperatively to act when the bacterial infection starts.^[31]

Topical endoalveolar application of minocyclin [10 mg in bioresorbable poly (D, L-lactide-co-glycolide) lactide sustained-release microspheres] following extraction of third molars, significantly reduces the risk of postoperative infection.^[33]

In contrast, no significant difference as regards to pain, swelling and trismus was reported in a study which compared no antibiotic therapy with administration of clindamycin 300 mg, three times a day, for 5 days, and amoxicillin/clavulanic acid 1 g, two times a day, for 5 days.^[32]

Sekhar *et al.*,^[34] using metronidazole, 1 g, 1 h before surgery, and 400 mg every 8 h for 5 days after surgery, reported that antibiotic treatment is not efficacious either in the pre- or postoperative period.

However, topical application of covomicyn D resulted in a good control of postoperative swelling in a study carried out in the same patients treated for extraction of the impacted third molars with or without antibiotic therapy.^[35]

According to the literature review, the use of the antibiotics before surgery could be considered a predictable procedure to avoid and control the possible infection related to the surgery. If infection and inflammation are present in the surgical area, an antibiotic therapy seems to give a better clinical compliance of the tissues undergoing surgery. The antibiotic administration before, during and after surgery seems to be a better therapeutic choice for controlling the infection arising in the postoperative period.

Corticosteroids

Most surgeons utilize corticosteroids based on the recognized efficacy to control surgery outcomes and to yield a comfortable post-surgery period.^[36] However, there are no definite protocols relative to different molecules or regimens, time and route of administration.

Corticosteroids are known to reduce inflammation, fluid transudation and edema.[36-37] They represent the most efficacious anti-inflammatory agents and to this purpose can be used in several different conditions.^[38] However, important adverse effects limit their use in all patients.^[39] The mechanism of action of corticosteroids has been largely reviewed by several authors,^[7,9,39,40] and those that are preferentially utilized in dentoalveolar surgery include dexamethasone (administered orally), dexamethasone sodium phosphate (IV or IM), dexamethasone acetate (IM), methylprednisolone (orally), methylprednisolone acetate and methylprednisolone sodium succinate (IV or IM). In the past, betamethasone has been used as well.^[41-43]

Milles and Desjardins^[44] obtained good results with the administration of methylprednisolone (16 mg, orally, 12 h before; and 20 mg, IV, immediately before surgery) against placebo administration as one oral tablet 12 h preoperatively. They also suggested continuing administration of the latter for at least 3 days following surgery.

Tiwana *et al.* reported data on patients undergoing surgery for extraction of four impacted molars.^[45] Patients were divided in two groups: the first group was administered with 8 mg desamethasone IV and the second one with 40 mg methylprednisolone IV.

It was concluded that preoperative administration of corticosteroids IV has a better outcome, even in the absence of antibiotic therapy, as suggested by 8% of patients with slight swelling versus 28% in the control untreated group.

In contrast, by evaluating the swelling by ultrasonography and CT, Esen *et al.*^[46] observed a significant reduction with preoperative administration of 125 mg methylprednisolone IV, and 500 mg penicillin orally, for 5 days following surgery.

In the same study, adrenal activity was analyzed by measuring plasma cortisol concentrations before surgery and 2 and 7 days post-surgery, leading to the conclusion that corticosteroid therapy was well tolerated if no absolute contraindications were present, did not affect adrenal activity for short period administration, and showed the ability to reduce edema by 42%. However, it is recommended not to exceed the dose of 125 mg and to avoid long-term treatment to preserve adrenal function, as also suggested by Beirne and Hollander.^[2] Likewise, Bystedt and Nordenram^[47] suggested avoiding very high dosages, and a maximum 5-day therapy. In contrast, Helhag *et al.*^[48] suggested that 10 mg dexamethasone, two times a day, reduces plasma cortisol levels.

A significant 62% reduction of edema has been reported after orthognathic surgery when 1 mg/kg methylprednisolone was administered IV for 24 h, but not for 48 h.^[49]

The efficacy of preoperative administration of 1.5 mg/ kg methylprednisolone sodium succinate IV versus that of 3 mg/kg followed post-surgery by 2 million IU oral penicillin V, plus acetoaminophen 500 mg, was evaluated in patients operated for extraction of the lower third molars, bilaterally.^[50] No significant differences were observed in inflammation, pain and swelling between the two dosage regimens.

Good results were also obtained with 32 mg methylprednisolone and 400 mg ibuprofen administered 12 h before and 12 h after surgery respectively.^[51]

Often used in oral surgery are long-acting corticosteroid compounds. Among these, the most frequently used is dexamethasone that is about 25–30 times more potent than cortisol.^[1] It is available in oral, parenteral and topical formulations and is largely used in oral surgery pre- or only post-surgery due to its high efficacy and long half-life.

Postoperative edema can also be controlled with

dexamethasone administered in the submucosa.^[11] Submucosal administration of 4 mg dexamethasone 1 h before surgery has been compared with that of 8 mg dexamethasone plus 2 g amoxicillin/clavulanic acid two times a day. Both dosages improved swelling versus untreated groups, but no differences were observed between the two dosage regimens.

In striking contrast with this observation, Laureano Filho *et al.*^[52] reported that in patients undergoing surgery for impacted third molars, administration of 8 mg dexamethasone 1 h before surgery, followed by 750 mg paracetamol every 6 h for 4 days produced a better control of swelling compared to treatment with 4 mg dexamethasone. Dexamethasone has also been administered 1 h before surgery (4 mg orally) and 12 h after surgery (4 mg IV), along with antalgic agents (30 mg ketorolac IV), when pain was present.^[43] In this study, treatment with dexamethasone always produced a good control of swelling, as measured 24 and 48 h after surgery.

Elhag *et al.*^[48] reported that administration of 10 mg dexamethasone IM, 1 hour before surgery and 10–18 h later together with antibiotic therapy (400 mg oral metronidazole, administered pre- and post-surgically), significantly reduces swelling when compared to only postoperative treatment, without corticosteroids.

Although a significant reduction (50%) of swelling was observed 2 days after surgery in patients treated with 4 mg dexamethasone IM, no effect was present after 7 days.^[4] However, when administered 5–10 min before surgery, 4 mg dexamethasone IV was not effective in controlling edema when no antibiotic therapy was associated with it.^[53]

Several authors report the use of corticosteroids only in the postoperative period. A detailed review of the literature has been reported by Markiewicz *et al.*^[54] in which all corticosteroids have been compared to methylprednisolone. The effect of treatments administered either immediately or later after surgery has been analyzed. Data obtained report a reduction of 0.6 mm and of 0.5 mm of swelling at 1–3 and 7 days, respectively. However, no significant difference was observed due to the high standard deviations, leading the authors to conclude that corticosteroid administration causes only a slight reducing effect on edema.

In a different study,^[55] patients were divided into three groups: untreated or treated after surgery with 25 mg prednisolone IM or 25 mg prednisolone IM together with diclofenac. Both treatments produced a reduction

of swelling on the 2^{nd} day post-surgery, but it was recommended to reserve this therapy only to those cases in which edema of soft tissue was expected.

In line with this, Vegas-Bustamante *et al.*^[56] reported that following extraction of lower impacted third molar, a single treatment of methylprednisolone, 40 mg IM, through intrabuccal injection in the masseter muscle, together with amoxicillin 750 mg, every 8 h for 7 days, and 575 mg metronidazole, orally, every 6 h for 3 days, significantly reduced postoperative swelling when compared to control, untreated group.

A similar treatment strategy had already been proposed in 1975 by Messer and Keller,^[1] who administered 4 mg dexamethasone in three different parts of the masseter muscle and reported a significant reduction of pain, swelling and trismus. In this study, however, it was not mentioned whether antibiotics were used.

The intramasseter muscle injection has also been adopted by Montgomery *et al.*^[57] The authors did not report any advantage of this versus systemic administration.

Finally, Graziani *et al.*^[58] analyzed 43 patients undergoing surgery for double impaction of lower third molars and administered with (i) dexamethasone, 4 mg endoalveolar; (ii) dexamethasone, 10 mg endoalveolar; and (iii) dexamethasone, 4 mg in the oral submucosa. Amoxicillin and clavulanic acid, 1 g every 12 h, were added for 5 days. The best control of edema was observed in the group treated with 4 mg dexamethasone endoalveolar.

The investigated studies showed how the effectiveness of the corticosteroid administration before surgery could not be considered as a predictable therapy in order to control the postoperative swelling and edema of the surgical area. However, corticosteriod administration during the surgeries or in the postoperative period seems to give a great benefit for reducing the swelling and postoperative edema.

Surgical techniques

Different surgical strategies have been reported in the literature to reduce the postoperative discomfort after the third molar surgeries. They can be used either separately or in association with pre- or postoperative strategies. Different kinds of flaps have been used during extraction of impacted third molars, specifically to assess whether a marginal flap could control postoperative swelling better than a paramarginal one.^[59] No significant difference in the entity of swelling was observed after using the two kinds of flaps. However, there were no significant differences between the marginal and paramarginal flaps in terms of swelling.

In contrast, Kirk *et al.*^[60] reported significant differences, particularly for swelling and pain, during the 2nd day post-surgery between a group with a buccal flap and a group with a triangular flap modified by Szmyd.^[61] In the latter case, an increased swelling was observed.

Based on the hypothesis that the flap shape could affect postoperative swelling, the response to surgery was analyzed in the same patient undergoing germectomy of the third molars and treated with a triangular marginal and a paramarginal flap.^[62] However, no significant difference between the two treatments was observed.

In other studies, attention has been focused on the effect of primary or secondary healing on swelling. Pasqualini *et al.*^[63] have compared 100 patients treated with tight suture with 100 patients sutured after removal of 5–6 mm of mucosa distally to second molar to allow draining. Using this procedure, postoperative swelling was reduced especially on days 2 and 4, while in the group treated with tight suture, the peak of swelling was observed on day 3.

According to several authors,^[64-66] tight closure favors edema formation by creating a unidirectional valve that allows fragments of food to reach the cavity, but not to leave it easily. This can be the origin of local infection, inflammation, edema and potential alveolar osteitis and pain for difficult draining.^[67]

According to other authors,^[68,69] different factors such as edema, pain and trismus that follow extraction of impacted third molars can be related to suture technique and to surgery length, and the use of a draining tube can be helpful in reducing or preventing postoperative swelling. This has been confirmed in a study specifically designed to compare postoperative responses in two groups, one treated with suture and the other with draining. In the latter, a clear reduction in edema formation was observed. Rakprasitkul and Pairuchvej^[70] obtained similar results. They reported reduced swelling with suture in the presence of a draining tube when compared to the primary suture.

In a different study, the effect of draining has been compared with methylprednisone treatment.^[71] Although no significant differences were reported,

pharmacological treatment reduced swelling and was better tolerated by patients. It is then reasonable to conclude that most authors prefer secondary healing and/or draining rather than primary closure.

Different surgical procedures have also been related to postoperative swelling. Osteotomy through piezosurgery has given positive results on tumefaction compared to traditional techniques. However, often, the studies analyzed did not involve extraction of impacted third molars, but general osteotomy of the jaws.^[72-74]

Cryotherapy

Therapeutic effects of ice applied on a surgery wound are due to changes of hematic flow and consequent vasoconstriction and reduced metabolism.^[75,76] In surgery and orthopedics, in fact, the main function of ice on the treated area is to produce vasoconstriction and to control bleeding, resulting in reduced metabolism and control of bacterial growth.^[77-79]

It has to be taken into account that ice applied on an area such as the jaw angle produces rapid chilling in the cutaneous layer, but the effect is much lesser and occurs much later in deep tissues such as the bone.^[80-82] The application of ice does not have to be too long as this may be responsible for tissue death due to prolonged vasoconstriction, ischemia and capillary thrombosis.^[83]

The first physiological response of tissues to cryotherapy is reduction of local temperature that causes reduced cellular metabolism. In this way, cells consume less oxygen and resist longer to ischemia.^[84] In the treatment of impacted third molars, the use of ice shows a good efficacy in reducing post-surgery swelling and pain as demonstrated by several authors.^[69,80,81,84]

In contrast, van der Westhuijzen *et al.*^[79] state that there is no scientific evidence to support the use of an icepack in oral and maxillo-facial surgery and report that a slight, but not significant, difference in swelling was observed in patients in whom ice was applied continuously for 24 h after extraction of third molars compared to untreated controls. Similar lack of efficacy has also been reported by other authors.^[85]

Moore *et al.*^[86] report that the application of ice pack following surgery of impacted third molars causes a reduction of 3°C in the oral mucosa, while Nusayr^[87] underlines the importance of the right length of time of cold application.

It is interesting to note that low laser dosage (4 J cm²),

applied soon after surgery, produces a good control of swelling, especially in patients treated with 4 mg dexamethasone IM.^[88]

DISCUSSION

A large body of investigations have been performed on the control of postoperative edema in oral surgery. The use of drugs or strategies adopted for extraction of impacted third molars is presently a very hot topic.

Post-surgical facial swelling affects the daily life of the patient. Many authors have advocated the use of corticosteroids to limit postoperative edema due to their suppressive action on trasudation, but few have made definitive recommendations supported by randomized clinical trials.^[89,90]

In most of the studies, the use of corticosteroid drugs has been analyzed. Specifically, corticosteroids include compounds with short, intermediate and long duration of action. In the last years, compounds that are more frequently used in oral surgery are dexamethasone and methylprednisolone that are 4–5 times more efficacious than the natural compound cortisol^[9,78] and can be administered orally or IM or IV. Dexamethasone has a longer duration of action and is more efficacious.^[11,39]

All the studies reported in literature have utilized different molecules, dosages, routes and time of administration. While using corticosteroids in the postoperative period, it is preferable to administer drugs 1 h before surgery, if they are administered parenterally, or 2–4 h in advance, if taken orally.^[89] It is also important to continue therapy for more than 24 h in order to obtain a long lasting postoperative effect.^[44,53,73]

In the studies examined, dexamethasone has been administered in the submucosa^[11,74] orally,^[40,52] IM^[42,48] and IV,^[11,40,45,53] whereas methylprednisolone has been administered orally,^[44] IM in the masseteric muscle and IV.^[44,45,50] However, results obtained cannot be compared as, although studies often had an internal control, as they analyzed in the same patient, in independent excisions, treatment versus no pharmacological intervention, the timing, dosage and route of administration differed in independent studies.

In some cases, a single pre-operative administration has been adopted,^[44-46,50-53] whereas in others, the treatment has been administered before and after surgery^[40,48,51] or associated with antibiotics after surgery.^[11,46,48,50] In all these studies, positive results were obtained, confirming the general antiinflammatory properties of corticosteroids irrespective of specific compound, dosage and timing.

The immediate postoperative endoalveolar or submucosal administration of dexamethasone produces a beneficial effect in preventing inflammatory sequelae of lower wisdom tooth removal. In particular, the topical application of 4 mg dexamethasone gave rise to less edema and trismus, and lower patient pain perception after both 2 and 7 days of the surgical removal.^[88,90]

The use of antibiotic therapy has been analyzed in several studies. Either topical or systemic application has been used and again results obtained in all the studies are not comparable due to the different molecules, routes of administration and timing used. As mentioned earlier, corticosteroids have been used sometimes in association with antibiotic therapy.^[91]

Covomicyn D and minocyclin^[33,35] have been administered topically, endoalveolarly. Positive results on postoperative swelling were obtained following treatment with 15,000 UI/kg penicillin administered IV, 1 h before surgery. In contrast, clindamycin at a dose of 300 mg orally, three times a day for 5 days post-surgery, and amoxicillin/clavulanic acid at a dose of 1 g orally, two times a day for 6 days did not produce positive effects.^[32]

Similarly, metronidazole given 1 g pre-surgery and 400 mg three times a day for 5 days post-surgery, as reported by Sekhar *et al.*,^[34] and amoxicillin/clavulanic acid at a dose of 1 g, two times a day for 5 days, either before of after surgery,^[25] failed to cause effects on postoperative swelling.

Finally, the importance of wound draining and suture,^[59-62] the specific flaps used, second intention healing or the application a loose closure^[63-67] have to be taken into account. In addition, some studies support the effect of osteotomy with piezosurgery on postoperative swelling.^[72-74]

More controversial are data concerning the effect of cryotherapy on swelling. In fact, while according to some authors, the use of ice pack after surgery is efficacious, it does not affect postoperative edema as reported in other studies.^[79,80,84]

CONCLUSIONS

Postoperative swelling is a common event after surgery of impacted third molar and may affect, only for a few days, the social and working life of the patient. Clinicians should manage the postoperative discomfort after the surgery as well as they can.

While most surgeons adopt antibiotic therapy in the postoperative period, more questionable is the use of antibiotics administered pre-surgery. Again, in this case, a great discrepancy among different studies exists due to the variety of molecules, timing and routes of administration used.

The intraoperative strategies have been less analyzed. Surgical flaps do not seem to have a major role on edema and piezosurgery has not been applied extensively enough to support a positive effect on the control of edema. A primary intention healing and the use of a draining tube seem instead to provide valuable scientific results. Also, in this case, however, accompanying pharmacological interventions have not been standardized.

In the postoperative period, the use of ice pack is largely recognized to provide good results and it helps the patient to cooperate with pharmacological treatments and/or intraoperative strategies in the prevention of edema. All pharmacological therapies used post-surgery are valid although they differ in the compounds used and their ways of administration.

This review clearly investigated all the ways and treatment used for controlling the symptoms and signs related to the surgery of wisdom third molar. A large number of reports were analyzed.

Although clinical conditions associated with retained third molars are well understood, little is known about the impact of those conditions on the quality of life among affected patients. There is growing recognition that the impact of oral conditions on quality of life is an important outcome that can be quite useful in making treatment decisions. All the data developed by this review could be useful for the clinicians in order to show all the surgical and pharmacologic parameters that may influence the postoperative discomfort in the third molar surgeries.

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