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RESEARCH ARTICLE

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EFFICACY OF PREOPERATIVE DEXAMETHASONE IN LOWER THIRD MOLAR SURGERIES: A SYSTEMATIC REVIEW

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ABSTRACT

Lower third molar extraction surgery generates pain, edema and trismus as the main postoperative symptoms, which directly affect the patient life quality. The aim of this study is to evaluate the effectiveness of preoperative administration of dexamethasone in lower third molar surgeries to decrease postoperative symptoms. This systematic review followed the PRISMA recommendations. The search was realized in the PubMed, LILACS and Science Direct databases. The inclusion criteria were: patients with lower third molars with a similar impaction degree class II and III (Pell and Gregory classification) and with a standardized duration of surgery, limited to a maximum of 45 minutes. The GRADE tool was used to determine the level of evidence of the articles. Among the 296 articles found in the search and only 3 were included. The included studies evaluated 144 lower third molar surgeries, 72 using dexamethasone and 72 using placebo. In all 3 studies, pain and swelling had the lowest levels in the dexamethasone groups compared to the placebo groups. Only one study showed higher levels of trismus in the test group compared to the control group. In this study, dexamethasone was shown to be effective in reducing the postoperative symptoms analyzed, especially pain and edema.

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INTRODUCTION

The surgery to extract impacted mandibular third molars is a routine procedure in dental clinic Oliveira *et al.*, 2021). The most common postoperative symptoms associated to this surgery are pain, swelling and trismus (Lim *et al.*, 2017); therefore, the effectiveness of managing these symptoms is directly linked to the success of the surgical procedure¹. For this reason, several studies have evaluated the effect of using corticosteroids to reduce pain and inflammation after third molar surgeries (Mojsa *et al.*, 2017). The corticosteroids anti-inflammatory action is linked to different effects such as the reduction of circulating lymphocytes, redistribution of leukocytes and modulation of inducible cyclooxygenase 2 (COX-2). They also cause an increase in lipocortin expression, which leads to a reduction in inflammatory enzymes such as phospholipase A2 (PLA2) (Mojsa *et al.*, 2017; Núñez-Díaz *et al.*, 2019). Consequently, the arachidonic acid cycle is blocked, preventing the production of leukotrienes, prostacyclin and thromboxane A2 (TXA2) (Oliveira *et al.*, 2021; Mojsa *et al.*, 2017). Pain, edema and trismus are common events in the postoperative period, resulting from the inflammatory process generated by tissue injury. These symptoms, especially pain, can increase the patient discomfort and anxiety, delaying the healing

process and thus affecting the patient life quality, limiting their physical and mental well-being (Selvido *et al.*, 2021). The preemptive use of anti-inflammatories is a good alternative, in order to assure the best recovery of the patient and, consequently, the reduction of discomfort caused by the surgery (Falci *et al.*, 2017). In this sense, the corticosteroids dexamethasone and methylprednisolone are a good alternative, which is why they are widely used as a preoperative prescription in surgeries (Lim *et al.*, 2017). In general, dexamethasone is more prescribed in dentoalveolar surgeries because of its dominant glucocorticoid effect, lower sodium retention and longer half-life (Oliveira *et al.*, 2021; Selvido *et al.*, 2021). The preventive use of dexamethasone has been shown to be more efficient than the use of non-steroidal anti-inflammatory drugs (NSAIDs) (Oliveira *et al.*, 2021). In addition, several randomized clinical trials have tested the efficacy of dexamethasone at different concentrations and administration routes (Oliveira *et al.*, 2021; Lim *et al.*, 2017). In view of this context, the present systematic review aims to evaluate the effectiveness of preoperative administration of dexamethasone in surgeries of impacted lower third molars, in order to reducing the painful process, the formation of edema and the emergence of trismus.

MATERIALS AND METHODS

The present systematic review was initially registered in the PROSPERO database under CRD number 42022328839 and followed the recommendations of the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA). This review was designed using the PICO strategy (Population/ Intervention/ Control/ Outcome); and the question that guided the research was “is perioperative dexamethasone administration efficient for the reduction of postoperative symptoms in third molar surgeries?” The searches were carried out in May 2022 in the electronic databases of the National Library of Medicine, USA, in its PubMed interface (www.pubmed.com.br), Latin American and Caribbean Literature in Health Sciences, LILACS (lilacs.bvsalud.org) and Science Direct (www.sciencedirect.com). The MeSH terms used were: “Corticosteroids”, “Dexamethasone” and “Third molar”. Table 1 presents the search delimiter filters according to each database. Randomized clinical studies published from 2017 onwards in English, Portuguese and Spanish were included. The selection was made based on the title and abstract and then by reading and analyzing the full text. All citations were inserted in the bibliographic reference manager Mendeley Reference Manager. From the included studies, data were extracted and tabulated regarding the year of publication, study design, number of participants, gender, number of third molars undergoing surgery with the use of preoperative dexamethasone and with placebo, the degree of impaction of the third molar, the time of the surgical procedure, the drug administration route and the observed postoperative symptoms, such as: pain, edema and trismus. Based on a detailed evaluation of the methodology and results, the following methodological inclusion criteria were defined: patients with lower third molars with a similar impaction degree class II and III according to the Pell and Gregory classification and with a timed and standardized duration of surgery, limited to a maximum of 45 minutes.

occurrence”. The following questions were answered to determine the study value: “Were the results biased?”; “Are there any confounding or distorting factors present or a lack of standardization among study participants?” and “Is there a possibility that the results came about by chance?”. “YES” and “NO” answers were given. If the answers were NO to the three questions, the research was considered reliable with a low bias risk. The evidence level was determined using GRADE (Grading of Recommendations Assessment, development and Evolution). From this tool, the quality of the evidence and the strength of the pharmacological protocol recommendations could be graded. GRADE has four levels of evidence: very low, low, moderate and high; that depend on whether issues such as bias risk, inconsistency, imprecision, and publication bias are serious, very serious, or not serious.

RESULTS

After searching the databases, following the previously mentioned strategy, 296 articles were found, however after reading the abstracts, only 22 articles were selected for full reading, as described in Figure 1. After a complete reading of the 22 articles, 8 were eliminated because they used inappropriate methodologies and/or were outside the proposed objective and/or inadequate results. As a result, only 14 studies were considered eligible for inclusion. Then, the evaluation of the quality of the studies was applied based on the bias risk, confounding factors and random occurrence. Eleven studies were considered of low methodological quality and classified as high bias risk, the other 3 articles were classified as low bias risk, as shown in Table 2. Table 3 shows the main reasons for bias in the eleven surveys classified as high risk. Table 4 presents the details of the studies included, as they are low-risk studies. In total, the 3 included studies evaluated 144 lower third molar surgeries, 72 using dexamethasone and 72 using placebo.

Table 1. Search delimiter filters

Database	Delimiter filters
PubMed	Publication date: 5 years
	Article type: “Clinical trial” and “Randomized controlled trial”.
LILACS	Publication year interval: Last 5 years.
Science Direct	Years: 2017-2022.
	Article type: Research articles
	Subject areas: Medicine and Dentistry.

Table 2. Classification of articles according to bias risk

Study	Were the results biased?	Are there confounding or distorting factors present or lack of standardization among study participants?	Is there a possibility that the results came about by chance?	Bias risk
Oliveira et al(2021)	No	No	No	Low
Lim et al(2017)	No	No	No	Low
Mojsa et al(2017)	No	No	No	Low
Al-Djani(2017)	Yes	Yes	Yes	High
Arora et al(2018)	Yes	Yes	Yes	High
Chug et al9 (2018)	Yes	Yes	Yes	High
Hiriyanna et al(2021)	Yes	Yes	Yes	High
Kaewkumnert et al (2020)	Yes	Yes	Yes	High
Martins-de-Barros et al (2021)	Yes	Yes	Yes	High
Núñez-Días et al (2019)	Yes	Yes	Yes	High
Rodrigues et al (2019)	Yes	Yes	Yes	High
Shad et al (2020)	Yes	Yes	Yes	High
Suleiman et al(2022)	Yes	Yes	Yes	High
Vincentini et al(2018)	Yes	Yes	Yes	High

Articles that presented an approach outside the guiding question and/or that evaluated dexamethasone without a placebo control group and/or did not standardize the positioning of the third molar and/or did not determine the surgical time were excluded; as well as the articles that were in duplicate. The studies selected for full reading had their methodologies and results analyzed in detail in order to avoid the occurrence of “distorted results”, “confusions” and “random

Pain, swelling and trismus were evaluated in the three included articles. There were divergences regarding the form of analysis of each study, however, when evaluating the data, it was possible to compare each postoperative symptom between the three studies. Postoperative pain was assessed by the number of times the patient needed to use analgesics during the first 24 postoperative hours. In all studies, the test groups showed positive indices (Figure 2).

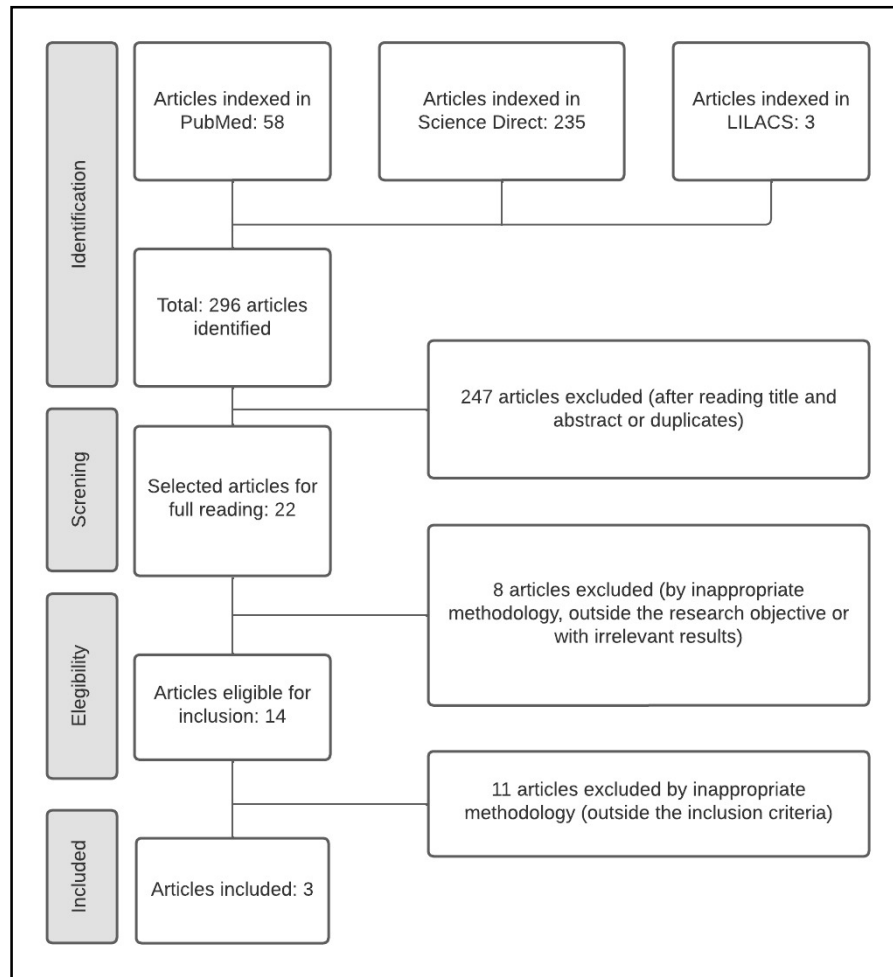


Figure 1. PRISMA flow diagram

Table 3. Reasons for bias in high-risk searches

Study	Excluded by
Núñez-Días et al (2019)	No control group.
	Non-standard impaction degree.
	Surgery duration not standardized.
Suleiman et al (2022)	No control group.
	Non-standard impaction degree.
	Surgery duration not standardized.
Rodrigues et al (2019)	No control group.
	Non-standard impaction degree.
	Surgery duration not standardized.
Shad et al (2020)	Surgery duration not standardized.
Martins-de-Barros et al (2021)	No control group.
	Non-standard impaction degree.
	Surgery duration not standardized.
Arora et al (2018)	Surgery duration not standardized.
Chug et al (2018)	Non-standard impaction degree.
Vincentini et al (2018)	No control group.
Hiriyanna et al (2021)	No control group.
Al-Djani (2017)	Non-standard impaction degree.
	Surgery duration not standardized.
Kaewkumnert et al (2020)	No control group.
	Non-standard impaction degree.

Table 4. Details of included studies

Study	Sample	Gender	Dexamethasone group	Control group	Dosage and administration route
Oliveira et al (2021)	44 lower third molars	15M 7F	22 lower third molars	22 lower third molars	4mg oral
Lim et al (2017)	60 lower third molars	11M 49F	20 lower third molars	20 lower third molars	4mg submucosa
Mojsa et al (2017)	90 lower third molars	32M 58F	30 lower third molars	30 lower third molars	4mg submucosa

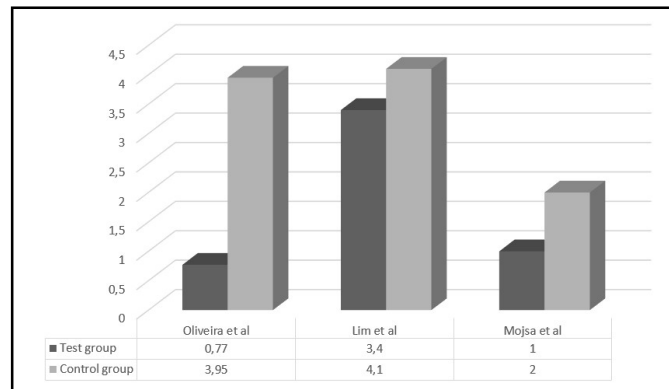


Figure 2. Pain analysis in the first 24 hours after surgery

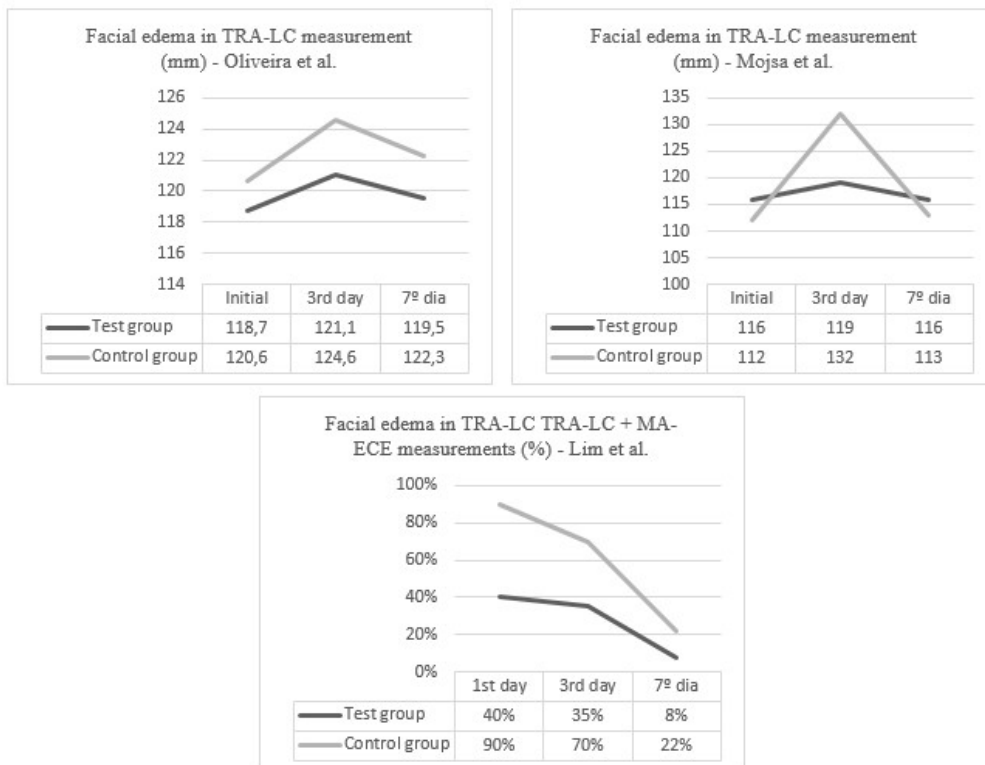


Figure 3. Facial edema analysis

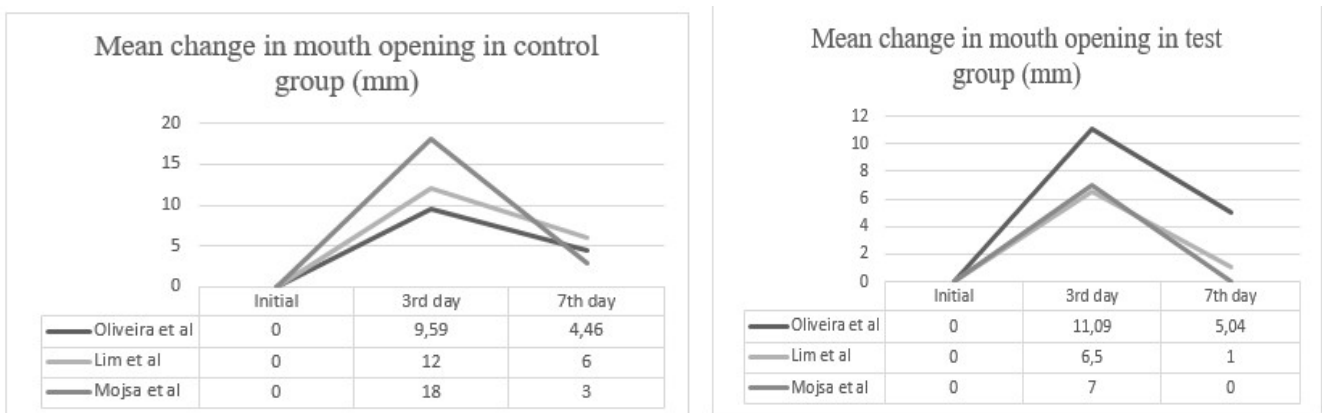


Figure 4. Analysis of trismus

Oliveira *et al* (2021) and Mojsa *et al* (2017) evaluated edema by measuring the imaginary line between the tragus and the labial commissure (TRA-LC). Lim *et al* (2017) evaluated it from the sum of the TRA-LC measurement and the measurement of the imaginary line between the outer corner of the eye to the angle of the mandible (MA-ECE). In all cases, the test groups presented the best indices in relation to the control group (Figure 3).

Trismus was assessed by the degree of change in the opening patients' mouth. The measurement preferred by the studies was between the central incisors. Only in the study by Oliveira *et al* (2021) there was a negative index of the test group in relation to the control group (Figure 4).

DISCUSSION

Inflammation presents itself as an essential process for the defense of the organism in the face of tissue injury, such as a surgical intervention (Lima *et al.*, 2017). This process generates a series of events that contribute to the restructuring and defense of the injured tissue, but which also negatively influence the patient life quality (Lima *et al.*, 2017; Arora *et al.*, 2018). Postoperative pain, for example, is mediated from the release of inflammatory chemical mediators that sensitize peripheral nociceptors at the site of injury. Studies demonstrate a direct relationship between postoperative pain in third molar surgeries and levels of Prostaglandin E2 and Thromboxane B2, related to the corticosteroids action mechanism at the surgical site (Martins-de-Barros *et al.*, 2021). In this sense, corticosteroids, such as dexamethasone, have been shown to be a better alternative in this context in relation to non-steroidal anti-inflammatory drugs (NSAIDs), mainly due to their dual ability to contain the inflammatory process, through a slow-acting genomic mechanism and a fast-acting non-genomic mechanism (Núñez-Díaz *et al.*, 2019), as previously explained. A split-mouth study developed at the University of Pernambuco, in Brazil, compared the dexamethasone action and ketorolac tromethamine in a standardized way and obtained satisfactory results in which dexamethasone was more effective in reducing postoperative symptoms (Martins-de-Barros *et al.*, 2021).

In general, the most used steroids in oral surgery are dexamethasone and methylprednisolone. Both exert an anti-inflammatory response capable of inhibiting vasodilation and, consequently, the formation of edema, from the limitation of leukocyte migration to the surgical site (Shad *et al.*, 2020). Falci's meta-analysis suggests that dexamethasone is more efficient than methylprednisolone in third molar surgeries (Falci *et al.*, 2017). From the literature search, it was possible to identify an initially satisfactory number of studies involving dexamethasone in third molar surgeries. However, the wide variety of methodologies did not allow for a standardization of comparative analysis between studies. These variations were mainly related to comparisons between preoperative and postoperative administration, as well as administration routes. There are divergences in the literature regarding the dosage and administration routes (Núñez-Díaz *et al.*, 2019). In summary, there is a lack of consensus on the best dosage, best administration route, among other factors, which is explained by the lack of standardization of parameters, which generates a shortage of randomized clinical trials with low bias risk and that allow satisfactory conclusions (Núñez-Díaz *et al.*, 2019; Chug *et al.*, 2018). In addition, some studies are dedicated to comparing preoperative administration with postoperative administration. In this sense, a study carried out in Campinas, Brazil, stands out for standardizing the degree of impaction of the third molars, as well as the duration of surgery, and showed satisfactory results for both groups, with a relative decrease in pain, edema and trismus in the group who received dexamethasone before surgery (Vincentini *et al.*, 2018).

In total, Oliveira *et al.* (2021), Lim *et al.* (2017) and Mojsa *et al.* (2017) evaluated 144 lower third molar surgeries, 72 using dexamethasone and 72 using placebo. The standardization of the degree of impaction of the dental elements submitted to surgery allowed the comparison of results, although the evaluating way of the postoperative symptoms has differed. Furthermore, in this study, there was a small variation in the administration route and in the period in which dexamethasone was applied. The dose was the same in all three included studies, 4 mg. In the study by Oliveira *et al.* (2021), the administration route was oral, while in the other two, the administration route was submucosal. In addition, the three studies varied when dexamethasone was administered, in Oliveira *et al.* (2021) the administration took place 1 hour before surgery; in Lim *et al.* (2017), however, it occurred soon after the administration of the anesthetic; and in Mojsa *et al.* (2017), administration took place 15 minutes before surgery. Dexamethasone proved to be effective in reducing pain and swelling. In the evaluation of trismus, only the

study by Oliveira *et al.* (2021) showed negative results compared to the control group. This small divergence can perhaps be explained by the difference between the administration routes. However, the search in the literature did not result in comparative studies between the oral and submucosal routes, although it is considered that the oral route, despite rapid administration and good absorption, requires a repeat dose to maintain blood levels during the postoperative period (Priyanga *et al.*, 2022). Trismus is a reaction generated by the accumulation of edematous fluid inside and around the masticatory muscles (Shad *et al.*, 2020). In the three included studies, the highest levels of trismus were observed between the second and third day. Since trismus is also a result of the formation of edema, we can compare with the levels of this symptom. Among the three studies, the one by Oliveira *et al.* (2021) recorded the highest levels of edema in the test group, mainly on the third day; consequently, he recorded the highest levels of trismus in the same group. However, the inflammatory response after surgery also depends on patient individual characteristics (Oliveira *et al.*, 2021). In general, in this systematic review, it can be considered that all postoperative symptoms were reduced, and that the submucosal administration route showed greater efficiency in relation to the oral administration route.

CONCLUSION

In this systematic review, dexamethasone administered before surgical intervention was shown to be an effective agent for reducing the postoperative symptoms analyzed, especially pain and edema. Thus, it reaffirms the importance of knowing the mechanisms that contribute to the maintenance of the patient quality of life in oral surgeries, such as a extraction of lower third molars, considering that a good surgery procedure must also cover the good patient recovery.

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