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Systematic Review and Meta-Analysis
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Intramuscular injection of dexamethasone for the control of pain, swelling, and trismus after third molar surgery: a systematic review and meta-analysis

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Abstract. This systematic review aimed to answer the following PICO question: Does the intramuscular injection of dexamethasone result in less pain, swelling, and trismus after mandibular third molar removal when compared to other routes of administration or a control group (saline solution injection or no treatment)? An electronic search was conducted in Virtual Health Library, PubMed, and Web of Science, through March 2018. Eligibility criteria included clinical trials. The search strategy resulted in 331 studies. Following the selection process, 15 articles were included in the systematic review; eight of these were included in the meta-analysis. Most of the studies had an unclear risk of bias (Cochrane Handbook assessment). Pain (mean difference (MD) −1.58, 95% confidence interval (CI) −1.99 to −1.16) and oedema (MD −1.76, 95% CI −2.38 to −1.14) were lower in the intramuscular dexamethasone group when compared to the control group. When compared to the submucosal route, the intramuscular route was more effective only for pain on the third postoperative day (MD −0.79, 95% CI −1.38 to −0.20). The results suggest that the intramuscular injection of dexamethasone may be an alternative route of administration, since it is effective at reducing pain and oedema when compared to non-steroidal treatment and has similar results to the submucosal route.

Key words: third molar; dexamethasone; oral surgery; pain; oedema; trismus; intramuscular injections.

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The surgical removal of mandibular third molars is one of the most common procedures performed by dental surgeons. Due to the involvement of connective tissue and the high vascularity of the affected region, a substantial inflammatory response is expected after third molar surgery, which is often expressed as pain, oedema, and trismus; this affects the quality of life of the patients[1]. Many strategies to control these undesirable complications have been reported in the literature, such as cryotherapy and the administration of suitable medications[2].

For several decades, corticosteroids have been one of the drugs most often used to control postoperative symptoms of wisdom tooth surgeries due to their anti-inflammatory, immunosuppressive, and analgesic effects[3]. The therapeutic effect of dexamethasone (a member of the corticosteroid family) in improving the postoperative quality of life of patients undergoing third molar surgeries is scientifically proven[4]. Also, some authors have studied whether different routes of dexamethasone administration can interfere in the development of the pain, swelling, and trismus after mandibular third molar removal[5]. However, the conclusions of these studies have varied from no significant difference between intramuscular (IM) and oral administration of dexamethasone[6], to better results with the submucosal route than with IM injection of dexamethasone[7].

Despite the valuable function of dexamethasone after third molar removal, there is no true agreement regarding the routes of administration of this medication[8]. This is likely due to methodological failures in the published studies, resulting in a lack of good controlled clinical trials and questionable scientific evidence. Recently, increased attention has been paid to the preoperative administration of IM dexamethasone for the management of postsurgical complications[9], since the enteral route has a later onset of effect, may lead to a different biological response in different patients due to pharmacokinetics, and requires the patient's cooperation[10]. Single-dose IM injection of dexamethasone is an easy means of administration and can result in a substantial plasma concentration of this steroid and a more potent anti-inflammatory response[11].

This systematic review aimed to evaluate the current scientific evidence on the efficacy of IM injection of dexamethasone in reducing pain, oedema, and trismus during the postoperative period after mandibular third molar surgeries compared with a control group or other routes of administration of this corticosteroid.

Materials and methods

This systematic review and meta-analysis was performed based on the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement.

The PICO process was used to determine the clinical question (patient, problem, or population; intervention; comparison; outcomes). The population comprised patients undergoing mandibular third molar removal. The intervention was the IM injection of dexamethasone. The comparison was with other routes of administration of dexamethasone or a placebo group. The outcomes were pain, swelling, and trismus after third molar removal. Thus, the question was: Does the intramuscular injection of dexamethasone result in less pain, swelling, and trismus after mandibular third molar removal when compared to other routes of administration or a control group (saline solution injection or no treatment)?

Eligibility

The inclusion criteria encompassed clinical trials that compared the IM injection of dexamethasone to other routes of administration or a control group (saline solution or no treatment). Also, the studies had to have analysed at least one of the three target variables (oedema, pain, and trismus). The following were exclusion criteria: observational studies, case reports, case series, letters to the editor, summaries in proceedings of events, and review articles.

Search strategy

The electronic search was conducted in three databases: PubMed, VHL (Virtual Health Library), and Web of Science. The assessment included studies through March 2018, without language restriction. A combination of medical subject heading (MeSH) terms was used for the search. The terms used in the databases were third molar AND dexamethasone. A search of the grey literature (Google Scholar, OpenGrey, and Digital Library of Theses and Dissertations) and the references lists of the selected studies was performed in order to identify any reference that had not been found in the search strategy and could be included.

After searching the databases and the grey literature, the references were compiled and organized in EndNote X7 software. Titles and abstracts of the articles were read by two authors independently (I.A.F. and G.M.S.). Duplicates were excluded. Studies that could probably be included in the review were identified at this stage. After independent reading, the two authors compared the selected studies that would pass to full-text reading, reaching agreement on inclusion or not. If there was disagreement, a third author (S.G.M.F.) gave his opinion to obtain a consensus. Studies selected after this second stage were read in full. At this point, the studies that met all the inclusion criteria were included in the systematic review.

Quality assessment

The quality of the included studies was assessed by the same two authors (I.A.F. and G.M.S.) independently, using a specific risk of bias assessment form related to the study design (*Cochrane Handbook for Systematic Reviews of Interventions* version 5.0.1). The classification of the potential risk of bias for each study was based on the following criteria: sequence generation, allocation sequence concealment, blinding of participants, personnel, and outcome assessors, incomplete outcome data, selective outcome reporting, and the report of exclusion of patients with pericoronitis, periodontal disease, or other inflammation processes, systemic disorders for which the use of corticosteroids is contraindicated (such as diabetes), and those using other steroidal medications. Each criterion was rated as exhibiting a low, high, or unclear (no information or uncertain) risk of bias. Disagreements between reviewers were resolved by consensus for the final classification.

Data extraction

The following data were extracted: author, year of publication, country where the research was performed, study design, sample size, mean age, follow-up times, therapy protocol for the study groups, time of administration of dexamethasone (pre- or postoperative), Pell and Gregory classification of the third molars, drugs used as supplementary therapy, and muscle into which dexamethasone was injected. Moreover, statistical data (mean and standard deviation of the outcome variables) were extracted when available.

Statistical analysis

Data analyses were performed using Review Manager software (RevMan version 5.3; Cochrane Collaboration, Copenhagen, Denmark, 2014). All included articles had to present the mean and standard deviation values of the variables of inter-

est in this study in order to be included in the meta-analysis. After extraction of the statistical data, a meta-analysis was performed to determine whether IM injection of dexamethasone is better than control treatment (saline solution or non-treatment) and submucosal injection of dexamethasone for pain and swelling variables. It was not possible to analyse trismus and other routes of dexamethasone administration due to the lack of statistical data.

First, data were extracted from the articles and databases were built in Excel (.CSV). Following this, the databases were imported into RevMan and the meta-analyses were performed. For the pain variable, comparisons between groups were performed using the mean difference (MD), because data collection was similar in all of the included studies (visual analogue scale). For the swelling variable, comparisons between groups were performed using the standardized mean difference (SMD), since there were some differences in data collection between the studies; e.g., some used two facial measures[6] and some used three facial measures[12]. Heterogeneity was calculated through I^2 statistics. When the I^2 statistic was equal to 0, the fixed-effects model was used. When it was above 0, the random-effects model was considered. The sensitivity test was performed through subgroup analysis (first postoperative day, third postoperative day, seventh postoperative day, and overall). Tests to verify the presence of publication bias and representation in a funnel plot were not performed, as there were not enough included studies to allow this.

Results

Systematic search

The search strategy resulted in 331 articles (105 in PubMed, 121 in VHL, and 105 in Web of Science). One hundred and seventy of these articles were removed as they were duplicates, leaving 161 articles for analysis. The titles and abstracts of these articles were read by two independent authors to select those that could be included in the study. At this stage, 141 articles were excluded. Therefore, 20 studies were assessed and read in full. From the search of the references lists, one more study was included for full-text reading[13], resulting in a total of 21 studies. One study was excluded as it was a summary in proceedings of an event. Two studies were also excluded due to the absence of IM injection of dexamethasone. Another study was excluded because other dental procedures were included in addition to the third molar surgeries, such as apicectomies, ossifying fibroma removals, and surgeries of retained canines. Another article evaluated muscle activity by electromyography rather than inflammatory parameters, and thus was excluded. Finally, one article had only the abstract available and it was not possible to determine whether IM injection was a route of administration of dexamethasone, so it was also excluded. Fifteen articles were included in the qualitative analyses[6,7,9,11–22], and eight of them were included in the meta-analysis[7,9,12–14,16,17,20] (Fig. 1).

Among the 15 articles included, seven were split-mouth studies[6,9,11,14–16,21]. Dexamethasone was most frequently injected into the masseter muscle[11,12,19,21,22] or deltoid muscle[6,9,13,14,16]. One article injected dexamethasone into the gluteus maximus muscle[15], another into the internal pterygoid muscle[18], and the other three did not report the target muscle[7,17,20] (Table 1).

All 15 studies used antibiotic therapy as supplementary medication. Fourteen studies used amoxicillin[6,7,9,11–18,20–22] and only one used ciprofloxacin[19]. As rescue therapy, two studies used ibuprofen[9,15], one used naproxen[11], three used tramadol[7,13,17], one used aceclofenac[19], and five used paracetamol[6,12,14,16,21]. Moreover, two studies recommended cryotherapy in the postoperative period[9,12], and five used mouth rinse with chlorhexidine[7,11,13,15,17].

Besides the experimental group in which the IM route was used to administer dexamethasone, there was a variety of comparison/control groups among the included studies. All studies except two[6,15], compared IM injection (experimental group) with a control group (injection of placebo, saline solution, or no corticosteroid administration). Five studies compared the experimental group with submucosal injection of dexamethasone[7,13,14,17,20]; six studies compared it with oral administration of dexamethasone in tablets[6,12,13,14,18,22]; three studies used intravenous administration of dexamethasone as the comparison group[13,14,20]; and one study compared IM dexamethasone associated with low-power laser (LPL) therapy to LPL alone, IM dexamethasone plus oral dexamethasone associated with LPL, and a non-treatment group[18].

Five articles found that IM administration of dexamethasone can reduce pain[9,11,16,19], swelling[9,11,16,19,21], and trismus[9,11,19] after surgical extraction of mandibular third molars when compared to a placebo/non-treatment group, and can also be effective in other respects, such as a lower intake of analgesics and faster return to daily activities[9]. Of three articles that compared the IM route to the submucosal route, two found that submucosal injection of dexamethasone is superior in reducing the sequelae after third molar surgery[7,17], and one concluded that IM injection is more efficient[20]. Comparing IM to oral administration, one study found the second route to be superior[22], and two studies reported equal effectiveness of these two routes after surgical removal of third molars[6,12]. Two studies did not find a significant difference between the different routes of dexamethasone administration[14,15]. One study found that local administration of dexamethasone showed comparable effects to systemic routes and was superior in terms of being simple, safe, painless, and more cost-effective[13]. Another study recommended the use of LPL irradiation associated with IM administration of dexamethasone to minimize swelling after third molar removal[18].

Quality assessment

According to the risk of bias analyses, for the criterion random sequence generation, 10 articles had an unclear risk of bias[6,7,12–16,18,19,22], four had a low risk or bias[9,11,17,20], and only one had a high risk of bias[21]. In the last domain, the studies had to have reported the exclusion of patients with pericoronitis, periodontal disease, systemic disorders (such as diabetes), and those using other steroidal medications. Of the 15 studies included, 11 had a high risk of bias[6,9,11,13–16,18,19,21,22], two had a low risk of bias[12,20], and the other two had an unclear risk of bias[7,17]. The quality assessment is presented in Fig. 2.

Meta-analysis

Meta-analysis showed that postoperative pain was lower in the IM dexamethasone group than in the control group (saline injection or non-treatment) on the first postoperative day (MD −1.62, 95% CI −2.31 to −0.94); third postoperative day (MD−2.21, 95% CI −3.19 to −1.22); seventh postoperative day (MD −0.98, 95% CI −1.45 to −0.51); and overall (MD −1.58, 95% CI −1.99 to −1.16) (Fig. 3). On the other hand, when compared with submucosal injection, the IM dexamethasone group showed lower pain only on the third postoperative day (MD −0.79, 95% CI −1.38 to −0.20) (Fig. 4).

Swelling was also lower in the IM dexamethasone group than in the control

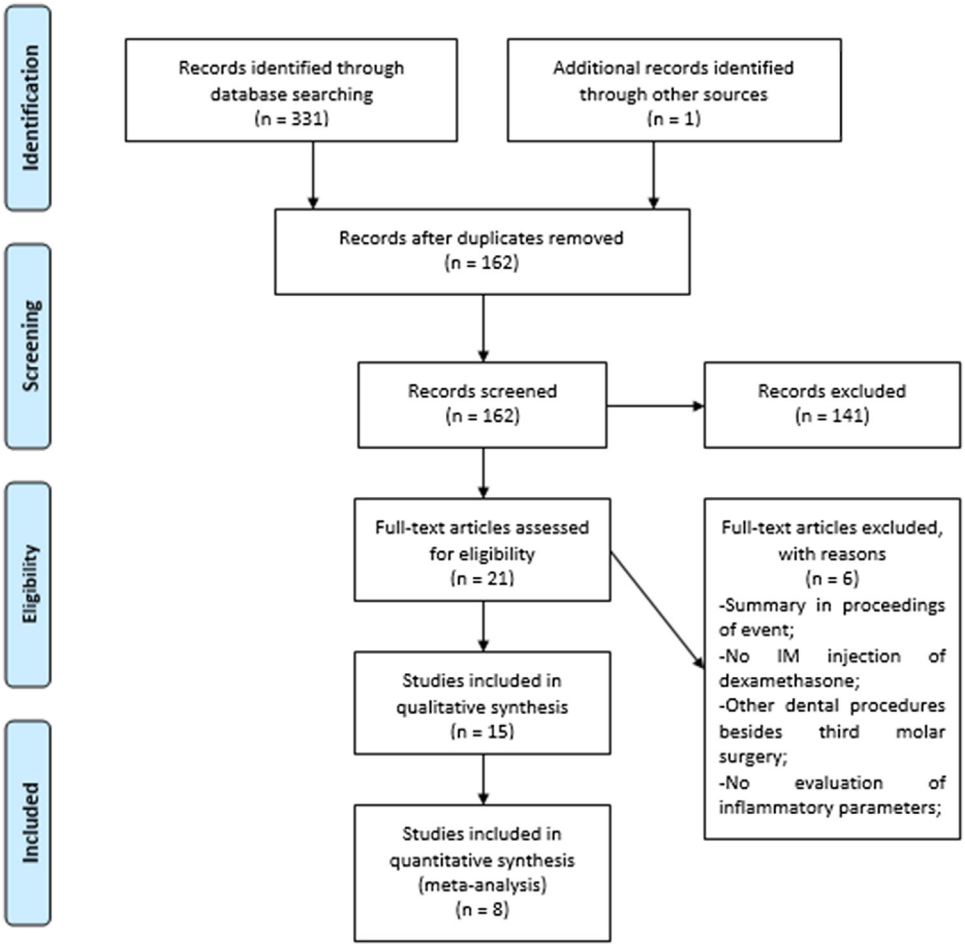

Fig. 1. Flow diagram showing the article selection process.

group (saline injection or non-treatment). A large SMD was observed on the first postoperative day (SMD −2.59, 95% CI −3.33 to −1.85) and third postoperative day (SMD −2.49, 95% CI −3.89 to −1.10); the SMD was smaller on the seventh postoperative day (MD −0.61, 95% CI −1.13 to −0.09). The overall effect also showed lower swelling in the IM group (MD −1.76, 95% CI −2.38 to −1.14) (Fig. 5). On the other hand, when IM and submucosal injection of dexamethasone were compared, a difference in swelling was not shown (Fig. 6).

Discussion

The purpose of this study was to assess whether IM injection of dexamethasone in mandibular third molar surgery is more effective in reducing pain, oedema, and trismus when compared with a control group or other routes of administration of this corticosteroid. It was hypothesized that the IM group would have less pain, swelling, and trismus.

A considerable number of studies support the administration of corticosteroids in third molar surgery[23–25]. Dexamethasone has powerful anti-inflammatory effects by blocking the activation of phospholipase A2 due to the production of endogenous proteins. In this way, the cell membrane does not release arachidonic acid, inhibiting the synthesis of leukotrienes, thromboxanes, and prostaglandins[26]. Moreover, the anti-inflammatory potency of dexamethasone, which is 20–30 times higher than cortisol, and a half-life of 36–54 hours make it an indicated drug as a single dose in managing inflammatory parameters induced by surgical procedures in the maxillofacial region, such as third molar removal[15].

Dexamethasone is available in various formulations and can be administered through different routes. For example, intravenous administration of dexamethasone is usually used in the surgical removal of third molars in the USA, while the IM route is more common in other countries[9]. A single dose of dexamethasone via IM injection is a simple method of administration and can generate high plasma concentrations, enhancing the anti-inflammatory activity of this steroid[11]. Exploring the ideal route of dexamethasone administration to manage pain, swelling, and trismus after third molar surgery is scientifically justifiable in order to assure patient comfort and quality of life and surgeon confidence.

The results of this meta-analysis confirmed that postoperative pain was lower in the IM dexamethasone group than in the non-corticosteroid group at all follow-up times and overall. Seven articles were included in this statistical analysis[7,9,12–14,16,17]. Dexamethasone is a corticosteroid and acts by decreasing pro-inflammatory inducers, resulting in less pain. In contrast to the study of Esen et al.[27], which reported a controversial effect of dexamethasone on pain after third molar removal, this variable was reduced when compared to the control group in the present meta-analysis. Considering that articles from three global regions were included in this review and that pain is a subjective parameter that depends on

Table 1. Data extracted from the articles included in the review.

Author, year	Country	Study design	Mean age ± SD (range)	Study groups	Number	Pell and Gregory classification	Muscle of injection
Al-Dajani, 2017[9]	Saudi Arabia	RCT	NR	Group 1: Dx 0.1 mg/kg (IM)	32	No standardization	Deltoid
				Group 2: Placebo (IM)	32		
Antunes et al., 2011[12]	Brazil	RCT	21 (14–37)	Group 1: Dx 8 mg (IM)	18	Class II B	Masseter
				Group 2: Dx 8 mg (PO)	20		
				Group 3: No corticosteroid treatment	22		
Bhargava et al., 2014[14]	India	RCT	24.1 ± 4.3	Group 1: No corticosteroid treatment	10	Class II B	Deltoid
				Group 2: Twin mix[a] (PMS)	10		
				Group 3: Dx 4 mg (1 ml) (SM)	10		
				Group 4: Dx 4 mg (1 ml) (IM)	10		
				Group 5: Dx 4 mg (1 ml) (IV)	10		
				Group 6: Dx 4 mg (PO)	10		
Bhargava et al., 2016[15]	India	RCT	29.4 ± 6.65	Group 1: Twin mix[a] (PMS)	30	Class I A	Gluteus maximus
				Group 2: 4 mg dexamethasone (IM)	30		
Boonsiriseth et al., 2012[6]	Thailand	RCT	20 (15–23)	Group 1: 8 mg (2 ml) Dx (IM) + placebo tablet	20	NR ''similar difficult indices''	Deltoid
				Group 2: 2 ml normal saline solution (IM) + Dx (PO)	20		
Dereci et al., 2016[11]	Turkey	RCT	21.35 ± 4.18 (15–32)	Group 1: 8 mg (2 ml) Dx (IM)	20	Class I	Masseter
				Group 2: 2 ml sterile saline	20		
Klongnoi et al., 2012[16]	Thailand	RCT	21	Group 1: 8 mg (2 ml) Dx (IM)	20	NR ''similar difficult indices''	Deltoid
				Group 2: 2 ml normal saline solution (IM)	20		
Majid, 2011[7]	Iraq	RCT	26.9 ± 6.1	Group 1: 4 mg Dx (SM)	11	Class II or III; B or C	NR
				Group 2: 4 mg Dx (IM)	11		
				Group 3: No corticosteroid treatment	11		
Majid and Mahmood, 2011[17]	Iraq	RCT	26.7 ± 6.3	Group 1: 4 mg Dx (SM)	10	Class II or III; A, B or C	NR
				Group 2: 4 mg Dx (IM)	10		
				Group 3: No corticosteroid treatment	10		
Majid and Mahmood, 2013[13]	Iraq	RCT	25.6 ± 5.9	Group 1: 4 mg Dx (IM)	12	Class II or III; A, B, or C	Deltoid
				Group 2: 4 mg Dx (IV)	12		
				Group 3: 4 mg Dx (PO)	12		
				Group 4: 4 mg Dx (SM)	12		
				Group 5: 4 mg Dx powder (EA)	12		
				Group 6: No corticosteroid treatment	12		
Markovic and Todorovic, 2007[18]	Serbia	RCT	NR	Group 1: Low-power laser irradiation	30	NR	Internal pterygoid
				Group 2: Low-power laser irradiation + Dx 4 mg (IM)	30		
				Group 3: Low-power laser irradiation + Dx 4 mg (IM) + (PO)	30		
				Group 4: Postoperative recommendations[b]	30		
Nandini, 2016[19]	India	RCT	(18–40)	Group 1: 8 mg Dx (IM)	10	Class A, B, or C	Masseter
				Group 2: No corticosteroid treatment	10		
Pappalardo et al., 2007[20]	Italy	RCT	26.45 ± 4.2	Group 1: 10 mg Dx (EA)	20	Class I B	NR
				Group 2: 10 mg Dx (SM)	20		
				Group 3: 4 mg Dx (IV)	20		
				Group 4: 8 mg Dx (IM)	20		
				Group 5: Sterile saline solution	20		
Rocha-Neto et al., 2017[21]	Brazil	RCT	24.2 ± 3.14	Group 1: 4 mg (1 ml) Dx (IM)	30	NR ''similar difficult indices''	Masseter
				Group 2: No corticosteroid treatment	30		

Table 1 (*Continued*)

Author, year	Country	Study design	Mean age ± SD (range)	Study groups	Number	Pell and Gregory classification	Muscle of injection
Sabhlok et al., 2015[22]	India	RCT	NR	Group 1: No corticosteroid treatment Group 2: 4 mg/day Dx (PO) Group 3: 4 mg Dx (IM)	20 20 20	Class II B	Masseter

Dx, dexamethasone; EA, endoalveolar; IM, intramuscular; IV, intravenous; NR, not reported; PMS, pterygomandibular space; PO, orally; RCT, randomized clinical trial; SD, standard deviation; SM, oral submucosal.

[a] Twin mix: 1.8 ml 2% lidocaine with 1:200,000 epinephrine + 1 ml 4 mg dexamethasone.

[b] Postoperative recommendations: cold pack, soft diet, etc.

several issues such as previous experience, lifestyle, and cultural issues, the results of this variable should be interpreted with caution.

When compared to submucosal injection of dexamethasone, the IM group showed lower pain only on the third postoperative day. Pain is a subjective parameter and the randomization of individuals in study groups is a necessary process to determine the real effectiveness of a medication in a clinical trial when assessing this variable. Most of the included studies obtained an uncertain risk of bias for the random sequence generation criterion. Moreover, unlike IM injection[20], dexamethasone applied submucosally has a rapid onset effect and it is quickly removed from the treated area that is hyperaemic, which may explain the fact that on the third postoperative day, the IM route was more efficient than the submucosal one. On the seventh postoperative day, the difference was not significant, probably because, clinically, the highest levels of postoperative pain in third molar surgery

Fig. 2. Quality assessment of the articles included in the review.

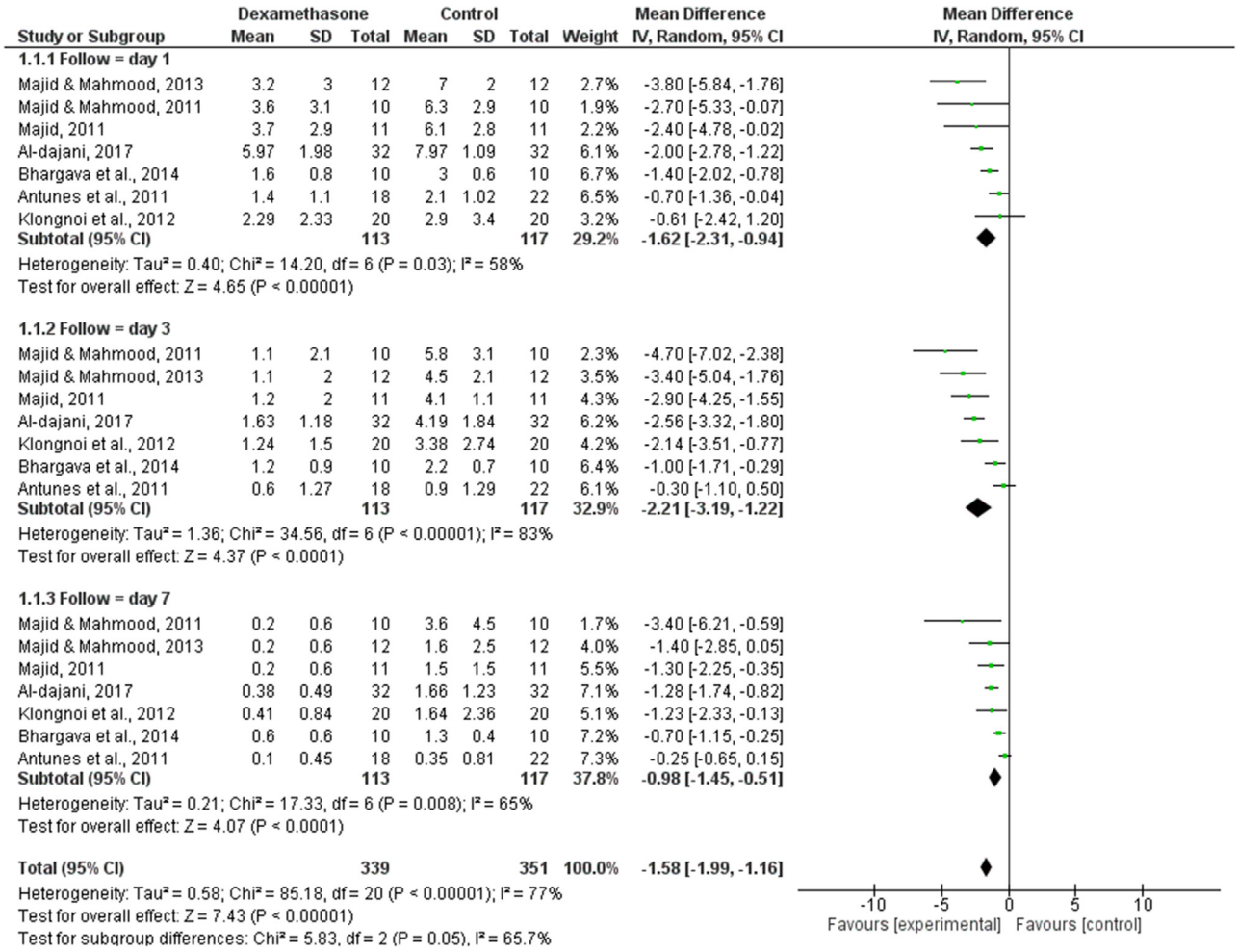

Fig. 3. Forest plots comparing the IM dexamethasone group with the control group regarding postoperative pain, as measured by VAS (in centimetres).

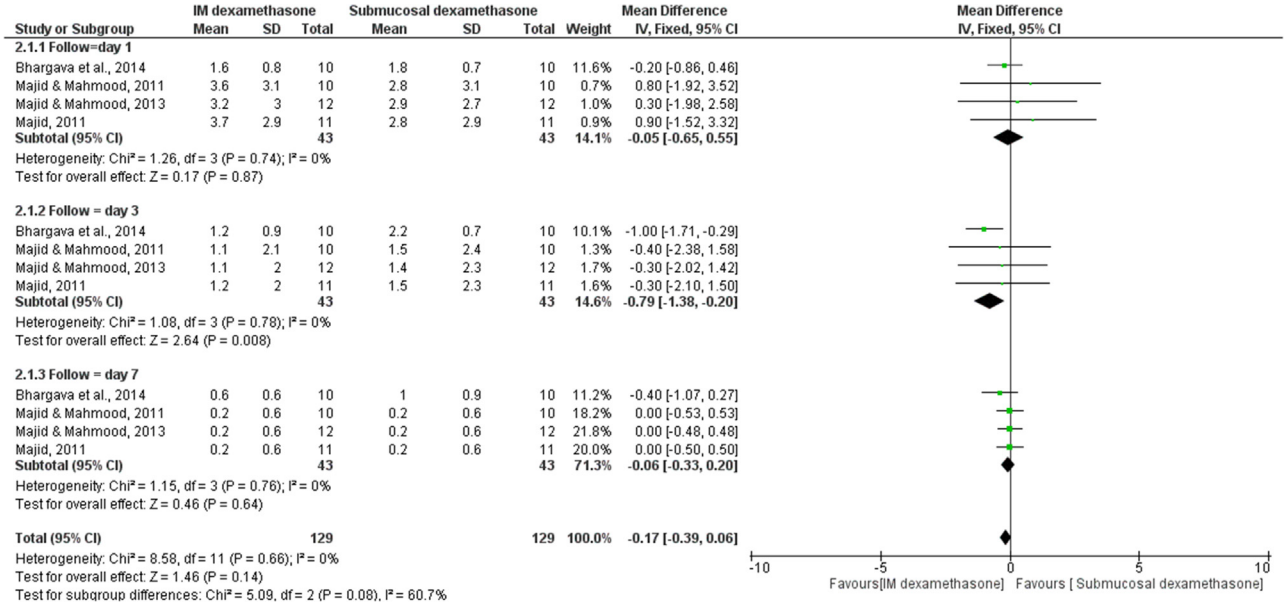

Fig. 4. Forest plots comparing the IM dexamethasone group with the submucosal dexamethasone group regarding postoperative pain, as measured by VAS (in centimetres).

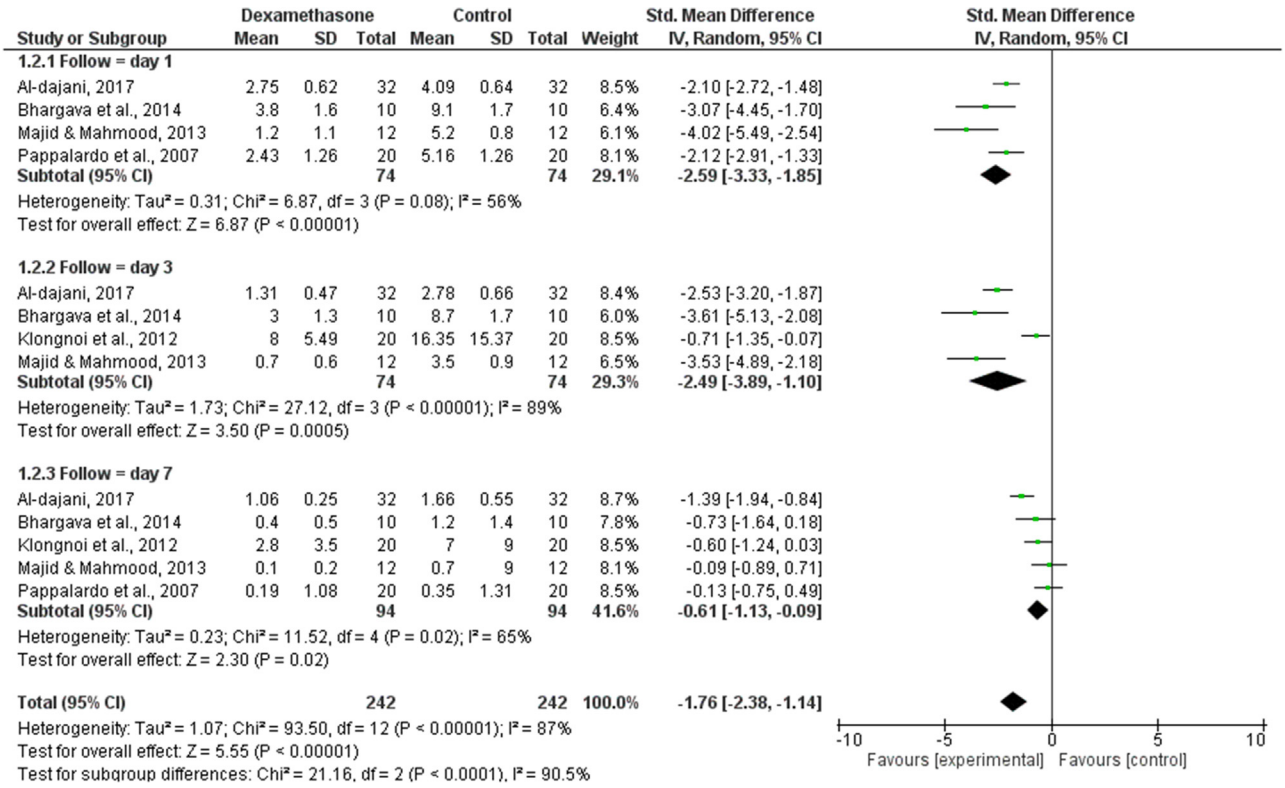

Fig. 5. Forest plots comparing the IM dexamethasone group with the control group regarding postoperative oedema.

occur from the first to the third postoperative day[25]. Thus, it would be expected that the level of pain on the seventh day postoperative would be greatly reduced, regardless of the treatment protocol applied. We suggest more clinical trials with effective randomization to better assess the pain variable.

The meta-analysis showed that the IM dexamethasone group had less oedema when compared to the control group (non-corticosteroid treatment). This can be explained by the fact that dexamethasone alters protein production, which inhibits leukocyte infiltration during the inflammatory process, resulting in dysfunction of the inflammatory mediators, a decrease in the humoral immune response, and thus the oedema[28]. Despite differences found in the methodologies

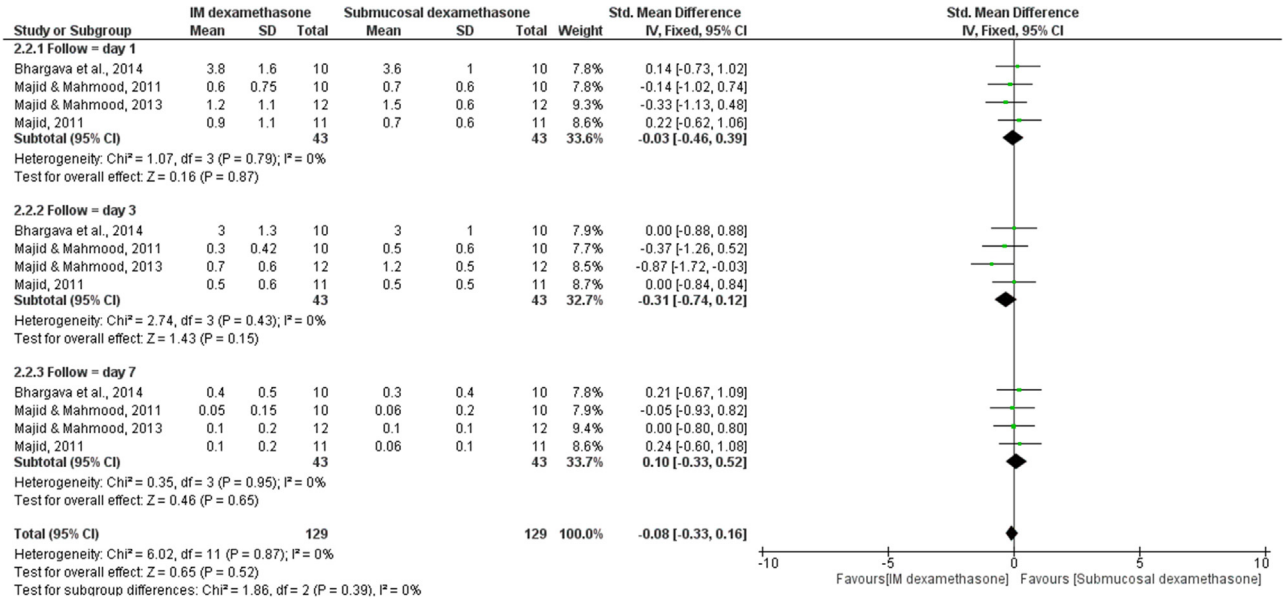

Fig. 6. Forest plots comparing the IM dexamethasone group with the submucosal dexamethasone group regarding postoperative oedema.

used to measure this variable, five articles were included in the statistical analysis. When the IM group was compared to the submucosal group, there was no statistically significant difference at any follow-up point or overall. A standardized methodology to measure oedema may be a solution to assess the real efficiency of the different routes of dexamethasone administration in a quantitative analysis, since only four studies were included in this meta-analysis.

When trismus was assessed in the selected studies, it was not possible to compare the statistical data among them. Some studies showed the sum of maximum mouth opening values, without calculating the difference between each follow-up value and the baseline value[6,16]. Another article used a Likert scale to measure trismus[9]. Furthermore, another article did not report the mean and standard deviation values for this variable[21]. It is suggested that future studies follow a standard method of measurement for trismus and publish them. In order to evaluate the efficacy of IM dexamethasone for trismus after third molar surgery, the values of each follow-up measurement have to be compared to those found at baseline, and the mean and standard deviation values have to be reported. Moreover, when evaluating IM injection of dexamethasone or any other medications into the masseter and pterygoid muscles, the researchers should pay special attention when evaluating trismus, since injection into these muscles may itself cause difficulty in mouth opening.

The ideal dose of dexamethasone to be injected IM is still controversial. The suggested dose ranges from 4 mg[7,13–15,17,18,21,22] to 8 mg[6,11,12,16,19,20], and one study used the 0.1 mg/kg protocol[9]. The lack of standardization of the dexamethasone dosage could be a source of bias when evaluating postoperative parameters in the comparison of different routes of anti-inflammatory administration.

A broad search strategy was used in this systematic review, without restriction on language or publication date. This approach was done to avoid publication bias and to find the maximum number of related studies to provide solid results. Despite the comprehensive nature of this review, great heterogeneity was found among the studies included. The studies varied in methods to measure oedema and trismus, with different ways of reporting the results. In addition, there was no standardized muscle into which dexamethasone was injected. Some studies applied it to the deltoid muscle[6,9,13,14,16], and others to the masseter[11,12,19,21,22] and pterygoid[18]. This may be a source of bias, since the rate of dexamethasone absorption is highly related to the blood flow in the muscle of administration[29], and each muscle has a particular relationship with the maxillofacial structures, such as the amount of blood vessels, accessibility, and proximity to the area of operation. Furthermore, no study did any sample size calculation, which could have compromised the validity of their results. Besides this, blinding of participants and personnel was the least contemplated domain in the quality assessment and this represents another source of bias. Other sources of bias were the lack of strict standardization of third molar position (Pell and Gregory classification)[9,18], lack of reporting of surgery difficulty (e.g., ostectomy and tooth sectioning)[9,21,22], and the variety of medications used as rescue therapy in each study; these could have modulated the inflammatory process and altered the patients' perceptions of the real efficacy of dexamethasone and the different application routes. Therefore, it is suggested that future clinical trials with greater methodological rigor should be undertaken to improve the scientific evidence regarding the different routes of dexamethasone administration and its influence on pain, swelling, and trismus after third molar surgery.

Finally, a domain was added to the quality assessment, in which the studies had to have reported the exclusion of specific patients from their research, such as those with systemic disorders and/or an inflammatory process. A great number of the included studies presented a high risk of bias for this criterion. This topic was taken into consideration because other sources of inflammatory mediators in an organism may compromise the results of research in which an anti-inflammatory effect is being tested. Another reason is that dexamethasone can elevate blood glucose, mainly in diabetic patients[30]. Thus, patients with diabetes mellitus should be excluded from this field of research.

In conclusion, the IM injection of dexamethasone may be an alternative route of administration in third molar surgery, since it is effective in reducing pain and oedema when compared to non-steroidal treatment and has similar results to the submucosal route. We suggest further studies with a standardized muscle for dexamethasone injection and a standardized dosage to confirm the real effectiveness of IM injection of dexamethasone after third molar surgery.

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Competing interests

There is no conflict of interest.

Ethical approval

Not required. The study did not involve animal or human subjects.

Patient consent

Not required.

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