Post-Operative Pain from Lower Impacted Third Molar Surgery by Corticosteroids

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Abstract

Objective: There are many studies related to dexamethasone for prevention the postoperative sequelae of pain which is the most common complaint of the patient after mandibular third molar surgery. This objective was to study, analyze and justify the use of corticosteroids for post-operative pain from third molar surgery.

Methodology: A Science Direct, PubMed and Medline search in combination with a relevant journal and the systematic search strategy (PICOS: Population, Intervention, Comparison, Outcome, Study design strategy) were conducted by including randomized controlled trials published in English literature 20 years from 1998 to 2017.

Results: A total of 36 comparative cases were analyzed from 27 articles; 31 case studies of pain assessment were based on the comparison with a placebo control group, whereas the remaining 5 case studies were compared between steroids. Methylprednisolone and Dexamethasone were the most commonly used corticosteroids in all the study and found to provide effective reduction of pain after mandibular third molar surgery. The intramuscular injection showed invariably effective route for pain reduction as compared to others.

Conclusions: Corticosteroids can be used in combination with analgesic drugs to reduce inflammatory symptoms including pain. Methylprednisolone and Dexamethasone via intramuscular injections should be the suggested route of administration for effective pain reduction.

Keywords: Corticosteroid; The Corticosteroids; Mandibular Third Molar; Postoperative Pain; Surgical Removal

Introduction

Impacted lower third molars are routinely encountered by dental surgeons. Impaction usually occurs when a tooth does not fully erupt into functional occlusion. Surgical approach for extraction of impacted lower third molars is advocated in some cases to prevent further complications which could make the mandible more susceptible to diseases and pathologies [1-3]. The surgical removal of mandibular third molars is the most common procedure in oral surgery field [4] which accompanies by various postoperative sequelae [5,6]. Apart from severe complications such as paraesthesia, dysaesthesia, severe infection, fracture of mandible and dry socket; the inflammatory reaction and response following the surgical injury can present with complaints of pain, swelling and reduced mouth opening [7] which affects patient’s quality of life.

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Pain from lower third molar surgery

Post-operative pain following the extraction of impacted third molars may cause severe distress to the patient [8]. The prescribed analgesics, anti-inflammatory medication in support after surgery should relieve pain, reduce swelling and trismus to as minimum as possible and also improve healing without undesirable side-effects. Therefore, a medication incorporating both analgesic with anti-inflammatory properties such as corticosteroids should be used [9] that can provide effective management of postoperative discomfort.

The study of corticosteroids groups

Corticosteroids can be divided into two major groups; the glucocorticoids and the mineralocorticoids. Glucocorticoids has anti-inflammatory properties with either minimal or no influence on fluid and electrolyte balance; thus, this group that is studied in this article. Henceforth, “corticosteroids”, will be used to express the glucocorticoids [10] in this current presentation.

For the previous 20 years, various former studies supporting the practice of corticosteroids for pain reduction in lower third molar surgery have been highly debatable. The current shreds of evidence, support and questions, the benefits of corticosteroid therapy usage in lessening the risk of postoperative complication, especially pain.

This study intends to assemble and analyze the considerations regarding the efficacy of corticosteroids in pain management after mandibular third molar surgery. Therefore, this study aimed to review various scientific literature to investigate the efficiency of corticosteroids in postoperative pain management after mandibular third molar surgery and to obtain knowledge about more effective analgesic methods.

Materials and Methods

Trial selection

The search methodology was organized using the systematic search strategy (PICOS strategy) that can be viewed in table 1. Database was searched in Scopus, PubMed and Medline 20 years from 1998 to 2017. The keywords used to explore the database were: (“third molar” or “third molar surgery” or “impacted third molar”) and (steroid or steroids or corticosteroid) and (“pain” or “postoperative pain”).

<table>
<thead>
<tr>
<th>Variable Study</th>
<th>Code</th>
<th>Used Keywords</th>
</tr>
</thead>
<tbody>
<tr>
<td>Population</td>
<td>#1</td>
<td>(“third molar” or “third molar surgery” or “impacted third molar”)</td>
</tr>
<tr>
<td>Intervention</td>
<td>#2</td>
<td>(“steroid” or “steroids” or “corticosteroid”)</td>
</tr>
<tr>
<td>Comparison</td>
<td>#3</td>
<td>(“corticosteroid” or “placebo effect” or “analgesic”)</td>
</tr>
<tr>
<td>Outcome</td>
<td>#4</td>
<td>(“pain” or “postoperative pain”)</td>
</tr>
<tr>
<td>Study design</td>
<td>#5</td>
<td>Randomized controlled trials and controlled clinical trials</td>
</tr>
<tr>
<td>Search combination</td>
<td></td>
<td>#1 and #2 and #3 and #4 and #5</td>
</tr>
<tr>
<td>Database search</td>
<td></td>
<td>English</td>
</tr>
<tr>
<td>Electronic database</td>
<td></td>
<td>Scopus, PubMed and Medline</td>
</tr>
</tbody>
</table>

Table 1: PICOS strategy in this study.
Study criteria

The previous studies were included if all of the following eligibility criteria studies

1. Randomized Clinical Trial Studies (RCT) and Controlled Clinical Trials (CCT).
2. Involving the surgical removal of the impacted mandibular third molar.
3. Including corticosteroid as intervention.
4. Including outcomes that are described as postoperative pain by VAS assessment method.

Data extraction

As in table 1 [11-37] the data isolated from the involved studies are: authors, year of publication, study design, number of subjects, mean age, mean duration of surgery, group of subject, corticosteroid dosage, route of corticosteroid, time of using corticosteroid, time of measurement, method of assessment of pain, mean VAS and P-values.

Results

Ninty-nine studies pertaining to this topic were identified via search engine. After title screening, 36 studies were selected for abstract screening. Subsequently, 7 studies were excluded based on the following criteria: articles that

1. Comprise unclear data on the patient selection, treatment, route of administration, dose and surgical procedure.
2. Contributed improper evaluation of pain or inadequate information on pain outcomes.
3. Compared corticosteroids and others with other drugs.

Two articles were later excluded because they did not use the VAS for pain assessment. Finally, twenty-seven articles were chosen for this study.

Figure 1 illustrates flow chart of twenty-seven case studies were selected for this. Twenty-two of the previous article studied the effect of varying concentrations of corticosteroids versus the placebo control group. The other five previous articles studied a type of corticosteroid versus another type of corticosteroid in pain score of after the surgical removal of mandibular third molar showed in table 2.

These corticosteroids that were used Dexamethasone 64%, Methylprednisolone 19%, Betamethasone 6%, Prednisolone 8% an Placebo/ Dexamethasone 3%.

<table>
<thead>
<tr>
<th>Author</th>
<th>year</th>
<th>No of study</th>
<th>Type of Steroid and dose (mg)</th>
<th>Route</th>
<th>Time</th>
<th>Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ma’aita and Alwrikat [2]</td>
<td>2000</td>
<td>16</td>
<td>Dexamethasone (8) vs Methylprednisolone (40)</td>
<td>IV vs PO</td>
<td>pre-op</td>
<td>ND</td>
</tr>
<tr>
<td>Laureano Filho., et al. [4]</td>
<td>2008</td>
<td>10</td>
<td>Dexamethasone (8)</td>
<td>IM vs PO</td>
<td>post-op</td>
<td>ND</td>
</tr>
<tr>
<td>Majid [16]</td>
<td>2011</td>
<td>5</td>
<td>Methylprednisolone (40)</td>
<td>IM (masseter VS gluteal)</td>
<td>pre-op</td>
<td>ND</td>
</tr>
<tr>
<td>McCoy [1]</td>
<td>2012</td>
<td>100</td>
<td>Dexamethasone (4 VS 8)</td>
<td>IV vs PO</td>
<td>pre-op</td>
<td>ND</td>
</tr>
<tr>
<td>Simone [24]</td>
<td>2013</td>
<td>20</td>
<td>Methylprednisolone (1.5mg/kg VS 3mg/kg)</td>
<td>IV</td>
<td>pre-op</td>
<td>ND</td>
</tr>
</tbody>
</table>

Table 2: These previous studies compared of different types or doses of steroid.

Remark: vs: Versus; IM: Intramuscular; IV: Intravenous; PO: Per Oral; pre-op: Preoperation; post-op: Postoperation; ND: No Difference.

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This study showed a significant reduction in pain in cases that were given corticosteroids as opposed to the placebo control group. When methylprednisolone and dexamethasone were compared with each other, no significant difference in post-op pain was recorded as in table 2, these results suggest that all corticosteroids (glucocorticoids) offer the same efficiency in pain reduction following the surgical removal of lower third molars. This study also focused on the group that studied with no steroids treatment or placebo. There was 31 case study with 4 features (steroid, dose, route and time) as table 2.

We applied one hot methodology and spearman correlation to determine the important factor that contributed to pain reduction; the route of drug delivery (max of corr. = 0.3727) is the most important factor followed by type of steroid (max of corr. = 0.1667) and time (max of corr. = 0.1373) as shown in figure 2.

Figure 1: Number of articles that were exclude and include for this analysis from search engine.

Figure 2: Heat map shows spearman correlation of studies that base on no steroid use.

The different routes of administration of corticosteroids, this study found 100% reduction in pain in cases where the corticosteroid was injected via the IM route. 83.33% in IV and 50% in other routes (SM, PO and endo-alveolar powder).

The different types of corticosteroids and their efficiency in pain reduction after surgical removal of impacted mandibular molars. Methylprednisolone reduces pain by 75% (3 of 4), Dexamethasone 72.72% (16 of 22), Betamethasone 50% (1 of 2) and Prednisolone 33% (1 of 3).

The best administration time for corticosteroids is post-operative, with 77.77% (7 of 9) in pain reduction, followed by pre-operative, 70.58% (12 of 15) and 40% in intra-operative.

From figure 3 the decision flow chart shows 3 factors that influence the effectiveness of corticosteroids for reducing pain (Route, Steroid and Time), this study found IM to be extremely effective for reducing pain which aligns with the route factor from the prior results. This study also found 5 experiments that documented 100% efficiency of corticosteroids in pain reduction and 4 experiments that reported no effect in pain reduction.

**Figure 3:** Shows decision tree of 3 factor to effect on reducing pain (Route, Steroid and Time).

Remark: IM: Intramuscular; IV: Intravenous; SM: Submucosa; PO: Per Oral; pre-op: Preoperation; intra-op: Intraoperation; post-op: Post operation.

This current study showed that 100% effectiveness or no effect at all for reducing pain. However, one major limitation is the extremely small sample size in 6 studies in each case study. Although the case study with prednisolone by PO had 2 patients, the time at which the drug was delivered was not taken into consideration.

This study also conclusion about the effectiveness of corticosteroids for pain reduction, thus, they could not be part of the decision tree method. The case study that have 2 examples (ID#1, 2 and 3) has a 50% probability of effective reduction in pain. Dexamethasone by SM

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post-operation (ID#5) effectively reduces pain with a dose of 4 mg but Dexamethasone by SM pre-operation (ID#4) with the same dose produced no significant pain reduction.

Discussion

Patients are usually restrained from having their wisdom teeth removed due to the fear of pain. Post-operative pain could be managed by analgesics that reduce pain to a bearable level. Although the role of corticosteroids has been mainly for reducing post-operative swelling and limited mouth opening; corticosteroids also have additional analgesic properties if administered at the right time of procedure and through an ideal route of drug administration.

Corticosteroids acts by suppressing each phase of the initial inflammatory response, thereby decreasing cellular permeability and capillary dilatation by inhibiting the production of vasoactive substances and diminishing the amount of cytokines [38,39]. Furthermore, the generation of prostaglandin is also repressed by corticosteroids, resulting in an analgesic effect [40,41].

This article studied 27 previous articles (36 studies group) that were randomized clinical trials either involving corticosteroids versus the placebo control group (31 studies group) and the study between corticosteroids comparison (5 studies group). This study found dexamethasone and methylprednisolone to be the most used corticosteroids because of their pure glucocorticoid nature with no mineralocorticoid effect. These corticosteroids have been used widely in dento-alveolar surgery with the least adverse effects on leukocyte chemotaxis; the half-life is an intermediate duration (18 - 36 hr.) and are more potent than hydrocortisone [42].

There was no significant difference in post-operative pain scores while comparing corticosteroids with another type of corticosteroid. Chaudhary., et al. [11] found evidence that there would be a good control of pain with the use of dexamethasone in either oral or intravenous administration. This study also found that there is no significant difference in post-operative pain between 4mg of dexamethasone intravenous and 8mg consumption administration.

Meanwhile, Boonsiriseth and colleagues [14] revealed the visual analogue scale scores for pain assessment demonstrated no significant difference among 8 mg dexamethasone intramuscular injection and 8 mg oral dexamethasone following impacted third molar extraction.

A single dose preoperative intramuscular dexamethasone 8 mg on impacted mandibular third molar surgery was used in the study by Klongnoi., et al. which revealed no significant difference of dexamethasone versus the placebo in pain assessment by the visual analogue scale [13].

Moreover, the previous research of Alcântara., et al. [12] mentioned there is no statistically significant difference in pain scores within dexamethasone 8 mg IV versus methylprednisolone 40 mg PO following surgical third molar removal. The intrabuccal approach of massteric muscle injection and gluteal muscle injection of methylprednisolone in concerning pain in previous study of Selvaraj., et al. there is also the result of no statistically significant difference [26]. In the same time, the article of Üstün., et al. studied pain between the 2 groups of 1.5 mg/kg and 3 mg/kg of methylprednisolone in intravenous injection administration, showed no statistically significant difference [34].

Those articles studied post-operative pain within corticosteroids versus a placebo control group, this study found 21 cases from a total of 31 cases (67.74%) that showed post-operative pain relief and found that using corticosteroids via intramuscular injections can be the most effective drug delivery administration for post-operative pain control when compared to other routes administration.

A single dose of pre or post-operative intramuscular administration [13] can deliver stable plasma drug concentrations and extended anti-inflammatory activity. The masseter and deltoid muscle injection are the most effective in the previous study of the articles.
From this study, the corticosteroids intravenous injection before surgery provides better pain than intra-operation and post-operation intravenous injections. The pre-operative intravenous injection provides immediate therapeutic drug concentrations in the blood before actual surgical trauma [43]. Nonetheless, the distinct disadvantage of both intramuscular and intravenous injection is an additional discomfort or pain at injection site of the body.

The limitation of this study is each study is different operative technique and difficulty in surgery. Additionally, the post-operative pain measurements were done at different periods. The objective and subjective factors such as degree of surgical trauma, duration of surgery and experience of the surgeon as well as the anxiety, pain tolerance or pain expectation of patient can affect the outcome of pain evaluation following impacted third molar surgery [44]. The socio-cultural background may also affect the pain outcome, tolerance and expectations, which could differ among individuals from developed countries to those from underdeveloped nations.

However, this study found that many articles that mentioned pain reduction with corticosteroids, but the exact mechanism for this effect is not yet defined. The authors assume that corticosteroids work by reducing prostaglandin synthesis, which suppresses the vascular events that lead to the cardinal signs of inflammation, thereby reducing swelling, redness, heat and most importantly pain.

**Conclusion**

Thus, corticosteroids can be used in combination with analgesic drugs to reduce inflammatory symptoms including pain. Methylprednisolone and Dexamethasone are the suggested drugs of effectiveness in decrease pain after impacted lower third molar surgery. This study can also conclude that intramuscular or intravenous injection is the most effective route for pain reduction. The perfect time for injection to obtain maximum benefit from corticosteroids for pain reduction is pre-operative injection. That mean the drug administration prior to any surgical intervention is the best in using corticosteroids for pain reduction.

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**Conflicts of Interest**

The authors declare no conflict of interest.

**Ethic Approval**

This research protocol and informed consent didn’t require because of previous studies in the article.

**Bibliography**


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