Review Article

Efficacy of Corticosteroids on Postoperative Endodontic Pain: A Systematic Review and Meta-analysis

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Abstract

Introduction: The purpose of this systematic review and meta-analysis was to evaluate the effectiveness of corticosteroids on postoperative endodontic pain and to determine/adjust between-trial heterogeneity using meta-regression analysis. **Methods:** A systematic literature search was conducted to identify randomized clinical trials using corticosteroids to manage postoperative endodontic pain in adults. The outcome measure was pain intensity scores at 6, 12, and 24 hours postoperatively. Standardized mean differences (SMDs) with their 95% confidence intervals (CIs) were estimated using the random effect inverse variance method. The level of significance was set at $P < .05$. Meta-regression analysis was also performed to examine the associations between effect sizes and study-level covariates. **Results:** Eighteen randomized clinical trials, comprising 1088 patients, were included. Corticosteroids significantly reduced the incidence of postoperative pain in endodontic patients at 6 hours (SMD = −1.03; 95% CI, −1.55 to −0.51; $P = .000$), 12 hours (SMD = −1.089; 95% CI, −1.71 to −0.46; $P = .001$), and 24 hours (SMD = −0.957; 95% CI, −1.34 to −0.56; $P = .000$). Meta-regression analysis showed that the type and dose of drug, performing intention-to-treat analysis, and using rescue medication could significantly influence the effect size at different time points. **Conclusions:** Corticosteroids had a postoperative pain-reducing effect in endodontic patients, and the choice of drug regimens could be an important predictor of pain reduction. *(J Endod 2018;■:1–9)*

Key Words

Corticosteroids, endodontics, meta-analysis, meta-regression, postoperative pain, systematic review

Significance

For the first time, this meta-analysis has evaluated the efficacy of corticosteroids on postoperative endodontic pain. Based on the included individual studies (with low to moderate risk of bias), available evidences suggest that corticosteroids might reduce the incidence of postoperative pain up to 24 hours. The administration of prednisolone seems to result in greater pain reduction compared with other corticosteroids.

Postoperative pain is a common complication of endodontic procedures, with a reported incidence of 3%–58% after root canal treatments (1). Such pain can lead to dissatisfaction of both patients and dental clinicians. Thus, the management of postoperative pain is of the utmost importance in the field of endodontics.

The most probable factor contributing to postoperative endodontic pain includes periapical tissue irritation. It triggers a barrage of nociceptor activation and local inflammatory processes that lead to the release of chemical mediators, such as prostaglandins, bradykinin, and cytokines from damaged tissues. These inflammatory mediators may in turn activate and sensitize nociceptors, leading to peripheral sensitization (2).

Different pharmacologic strategies including nonsteroidal anti-inflammatory drugs (NSAIDs); acetaminophen and corticosteroids have been examined to manage postoperative endodontic pain (3). There is evidence that the use of NSAIDs and acetaminophen can effectively reduce postoperative endodontic pain (4). Corticosteroids are another efficient group of drugs that function via inhibiting phospholipase A2 and leukotrienes at the site of the tissue injury (5).

The dental literature presents several clinical studies assessing the administration of corticosteroids for the management of postoperative endodontic pain (6–8). A previous systematic review evaluated the effect of corticosteroids on postoperative endodontic pain and found a wide heterogeneity among selected studies. As a result, the researchers reported that performing a meta-analysis was not possible (9).

Systematic reviews with a meta-analysis often reveal high heterogeneity of results, which leads to a model that is not reliable in explaining the outcomes and the role of the involved variables. A mechanism to reduce the heterogeneity of a meta-analysis is to divide samples into subgroups according to a specific variable. However, this stratification procedure reduces the sample size of each analysis. In meta-regression analysis, data from different studies are pooled by accessing the effect magnitude of each variable included in the same analysis. In this way, the role of each variable could be isolated and adjusted to others. Meta-regression analysis is also appropriate for avoiding a stratified meta-analysis of each variable (10).

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The aim of the current study was to perform a meta-analysis in order to assess the efficacy of corticosteroids on postoperative endodontic pain. The study also included a coexisting object of determining/adjusting between trial heterogeneity using meta-regression analysis to examine the associations between effect sizes and study-level covariates.

Materials and Methods

The current study was performed in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses statement and the recommendation of the Cochrane Collaboration (11).

Selection Criteria

Studies were included if they were randomized controlled trials (RCTs) comparing the efficacy of corticosteroids with placebo in reducing postoperative endodontic pain. The target population was defined as adults (>15 years old) who had undergone primary root canal therapy. The intervention was defined as different types of corticosteroids delivered via any route. The primary outcome was postoperative pain intensity scores measured using the visual analog scale at 24 hours postoperatively. Studies were excluded if they had no placebo group or reported incomplete data.

Search Strategy

The electronic databases screened were PubMed, the Cochrane Central Register of Controlled Trials, Scopus, Web of Science, and Google Scholar. The searches were performed with no time and language restriction up to October 2017. The following key words were used: (root canal therapy OR endodontic) AND (postoperative pain) AND (corticosteroids). The reference lists of the retrieved articles were additionally looked up to identify any potential relevant article. Unpublished studies were found by electronically searching the ProQuest Dissertation and Theses database.

Two reviewers (A.S. and S.S.) independently screened titles and abstracts to identify potentially relevant articles. Next, the full text of eligible articles were screened to find whether they met the selection criteria. In case of disagreement, a third reviewer was consulted.

Data Extraction

Data from the included articles were extracted independently by 2 reviewers (A.S., and S.S.) using a customized data extraction form. Discrepancies between the 2 reviewers were resolved through a discussion with a third author. Data extracted were as follows:

1. Article identification information (authors and publication year)
2. Baseline demographic data (age, sex of participants, and preoperative pulpal status)
3. Study characteristics (sample size and number of visits)
4. Intervention feature (corticosteroid regimen)
5. Outcomes of interest (postoperative pain scores and *P* values)

If statistical variables were shown graphically without any description of the original data, Adobe Photoshop software (Adobe System Inc, San Jose, CA) was used to measure the values from the graphs.

Risk of Bias Assessment

The methodologic quality was examined using the Cochrane Collaboration's Risk of Bias Assessment Tool. Domains that were assessed are as follows:

1. Random sequence generation
2. Allocation concealment
3. Blinding of participants and personnel
4. Blinding of the outcome assessment
5. Incomplete outcome data
6. Selective reporting
7. Other sources of bias including group similarity, cointervention avoided, and loss to follow-ups

Each domain was rated as "low risk," "high risk," or "unclear." Any inconformity will be resolved by discussion.

Statistical Analysis

Meta-analysis was performed using Stata software version 12.0 (Stata Corporation, College Station, TX). Standardized mean differences (SMDs) were used as the measures of effect size. In trials that did not report standard deviation for the effect size calculation, we algebraically computed equivalent effect sizes from standard error, 95% confidence interval (CI), *t* statistics, or exact probability levels using approximation methods (12). In order to include as many appropriate studies in the meta-analysis as possible, SMDs were estimated based on the median, range, or sample size according to the following equation: $\mathrm{SMD} = \mathrm{t}\left(\frac{n1+n2}{n1n2}\right)^{1/2}$.

If eligible studies compared different types of corticosteroids, all types were included as separate comparisons (ie, 3-arm trials with 2 active interventions will generate 2 randomized comparisons with placebo). In this case, the numbers of participants in the placebo arms were divided by the number of active treatment arms, thus avoiding double counting of participants and yielding more conservative estimates.

The pooled effect was calculated using a random effect inverse variance model. Statistical heterogeneity was assessed using the Q statistic test. The level of significance was set at $P < .05$.

When there was significant heterogeneity in the pooled results, we performed random effects multivariable meta-regressions to explore whether our estimates of treatment effects had been influenced by explanatory covariates.

In the first model, different types of corticosteroids were fit by adjusting their dose to compare their efficacy at follow-ups. The second model was planned to investigate the following covariates on the treatment effect:

1. Intention-to-treat (ITT) analysis (explicitly reported vs not explicitly reported or unclear)
2. The use of a cointervention (given vs not given rescue medication)
3. Pulp status (irreversible pulpitis vs necrosis)
4. The number of appointments (single vs multiple)
5. The route
6. The time of drug administration.

All meta-regression analyses were performed using the restricted maximum likelihood estimate method, a recommended random effect approach that accounts for residual between-trial heterogeneity. The level of significance was set at $P < .05$.

Results

A search of the literature initially identified 205 publications. After deduplication, 80 articles remained. Titles and abstracts were reviewed, and 51 articles were identified as being potentially eligible at this stage. Thirty-three studies were excluded because they did not include a randomized double-blind study (13), did not provide appropriate treatment (14–17), did not mention corticosteroids (18), assessed the efficacy of corticosteroids on the depth of anesthesia (19–21), reported postoperative pain at the 7-day follow-up (22), had no full text available (23–25), or