

Frequency of Nonodontogenic Pain after Endodontic Therapy: A Systematic Review and Meta-Analysis

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Abstract

Introduction: Little is known about ill-defined pain that persists after endodontic procedures, including an estimate of the problem's magnitude. We conducted a systematic review of prospective studies that reported the frequency of nonodontogenic pain in patients who had undergone endodontic procedures. **Methods:** Nonodontogenic pain was defined as dentoalveolar pain present for 6 months or more after endodontic treatment without evidence of dental pathology. Endodontic procedures reviewed were nonsurgical root canal treatment, retreatment, and surgical root canal treatment. Studies were searched in four databases electronically, complemented by hand searching. A summary estimate of nonodontogenic tooth pain frequency was derived using random-effects meta-analysis. **Results:** Of 770 articles retrieved and reviewed, 10 met inclusion criteria, and nine had data on both odontogenic and nonodontogenic causes of pain. A total of 3,343 teeth were enrolled within the included studies and 1,125 had follow-up information regarding pain status. We identified 48 teeth with nonodontogenic pain and estimated a 3.4% (95% confidence interval, 1.4%-5.5%) frequency of occurrence. In nine articles containing data regarding both odontogenic and nonodontogenic causes of tooth pain, 56% (44/78) of all cases were thought to have a nonodontogenic cause. **Conclusions:** Nonodontogenic pain is not an uncommon outcome after root canal therapy and may represent half of all cases of persistent tooth pain. These findings have implications for the diagnosis and treatment of painful teeth that were previously root canal treated because therapy directed at the tooth in question would not be expected to resolve nonodontogenic pain. (*J Endod* 2010;36:1494-1498)

Key Words

Dentoalveolar, pain, root canal therapy, systematic review, tooth

Tooth pain, meaning pain of known pulpal or periradicular etiology, is not the only reason for pain perceived in the dentoalveolar regions (1). Nonodontogenic causes comprise varying etiologies, such as referred myofascial pain (2), headache (3), neuropathic disorders (4), and pain stemming from various pathological conditions (5). Quantifying the frequency of nonodontogenic pain after root canal therapy is important for dentists and patients, so patients can make educated decisions by knowing the risks and benefits associated with treatment. Determining the extent of this problem is the first step toward the long-term goal of reducing diagnostic errors that often lead to irreversible dental procedures in an attempt to alleviate the pain, such as root canal retreatments, surgical root canal treatments, and tooth extractions (6).

Several studies have investigated the component diagnoses, listed earlier, that comprise this group of nonodontogenic pain cases referred to tertiary care centers (5, 7, 8). Even though such pain is thought to be "rare" (9), the magnitude of this problem is not known to a degree that would allow for development of appropriate public health policy. Important subtypes of this pain are not quantified either, especially those pains thought to be neuropathic in nature. For patients and dentists alike, they represent a considerable challenge because they are known to respond less than favorably to treatment (10). Given the current situation (ie, multiple diagnoses comprising this group of nonodontogenic pain that have widely differing treatment needs), it is important to quantify this problem to inform clinicians so they can use this information in their daily practice. Therefore, we sought to estimate the frequency of nonodontogenic dentoalveolar pain present at 6 months or greater after root canal therapy by performing a meta-analysis, which is a robust method of synthesizing published information (11).

Materials and Methods

Inclusion Criteria

Eligible for inclusion in this review were endodontic procedure articles published in any language before June 5, 2009, that reported on postoperative tooth pain after at least a 6-month follow-up. Qualifying endodontic procedures included initial root canal treatment or retreatment, surgical or nonsurgical, but not pulpotomy, partial pulpectomy, or pulp capping. The unit of observation considered was a human permanent tooth *in vivo*; primary teeth were excluded. The study outcome was the presence of dentoalveolar pain that explicitly did not have an odontogenic etiology, such as a cracked tooth, missed canal, or periapical pathosis. Pain could be spontaneous or provoked by biting, palpation, or percussion.

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Another inclusion criterion for studies was that they reported baseline data of the population from which the follow-up sample was drawn. This requirement, allowing the frequency of occurrence to be calculated, limited study inclusion to case series, cohort, and clinical trial studies and excluded cross-sectional and case-control studies. Articles reporting randomized trials were included as a special type of prospective cohort study; however, the treatment arms were collapsed for our analysis. Unpublished research and studies reported only in abstract form were not considered.

Information Sources and Search Strategy

We conducted an initial search in MEDLINE via the PubMed interface, covering the period from 1949 to June 5, 2009, and using the search terms specified in Figure 1. This search was then adapted for use and run in the Cochrane Library, TRIP database, and Google Scholar. We also hand searched the references of prominent articles, literature reviews, and textbook chapters (source list available upon request). Our intent was to be broad in scope to ensure the inclusion of as much relevant existing data as reasonably possible. The training and reliability assessment of article selection, data abstraction of study variables, and the assessment of reported study quality have been previously reported (12).

Statistical Methods

We used random-effects meta-analysis (13) to determine a summary estimate of nonodontogenic pain frequency. In a sensitivity analysis, we examined whether the deletion of a single study substantially changed the meta-analysis summary estimate. To explore factors influencing the estimate, we performed a meta-regression to investigate differences between studies with the following characteristics: (1) surgical versus nonsurgical treatment, (2) a follow-up rate of recall less than 50% versus greater than or equal to 50%, (3) follow-up at 6 to 12 months versus more than 12 months, (4) initial treatment versus retreatment, and (5) above-median quality reporting score versus below-median score according to the STROBE criteria (12, 14). We also estimated the proportion of nonodontogenic tooth pain among the subset of cases that had information on both “all-cause” and nonodontogenic pain. All analyses were performed using the STATA software package (Stata Statistical Software: Release 10.1; StataCorp LP, College Station, TX: StataCorp LP) and the user-written metan and metareg commands.

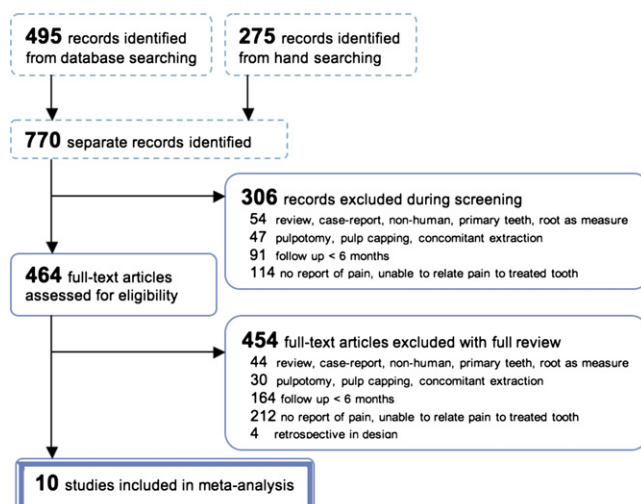


Figure 1. A flowchart of the systematic review process.

Results

Study Identification and Characteristics

We identified 770 articles (495 by electronic searching of databases and 275 by hand searching); the oldest was published in 1921. Twenty-eight were published in a language other than English (7 French; 6 Chinese; 5 Japanese; 2 each in Italian, Russian, and Spanish; and 1 each in Croatian, Danish, German, and Greek). Screening of titles and abstracts resulted in 306 articles being excluded. After full-text review, another 464 articles were excluded, so 10 articles were included in the meta-analysis (Fig. 1). All 10 articles were published in English, and 6 of them were identified by hand searching.

The 10 included studies varied in the types of endodontic treatments provided, numbers of teeth treated (6-276), duration of follow-up (1-6 years), and the percentage of teeth followed up (20%-100%) (Table 1). From 3,343 teeth enrolled in the 10 studies, 1,125 teeth were followed up for at least 6 months. Among them, 48 teeth (4.3%) in seven studies were reported to have pain without an identifiable odontogenic source. In these studies, teeth were determined to have tooth-related disease when the tooth was present and “not properly restored,” “fractured,” periapical radiolucency present (15, 16), sinus tract present (17), “root fracture associated with severe bone loss” (18), and “failure of coronal restoration” (19) could be identified with the root canal-treated teeth. Variation in the quality of reporting (STROBE criteria) was observed (interquartile range = 8.5-20.5, range = 5-20.5), with a median reporting quality score of 19.8 (possible scores ranging from 0 to 22). Furthermore, 9 studies contained details on both “all-cause” pain and nonodontogenic pain, making it possible to calculate the proportion of such pain outcomes.

Summary Estimate of Nonodontogenic Pain Frequency

The meta-analytic summary estimate of nonodontogenic pain frequency was 3.4% (95% confidence interval, 1.4%-5.5%, Fig. 2). “Moderate” heterogeneity (ie, inconsistency) (20) among study estimates was observed ($I^2 = 65%$, $p = 0.002$). When each study was eliminated in turn from the analysis and the meta-analysis was run with the nine remaining studies, the summary estimates ranged from 2.1% to 4.2%. Thus, individual studies did not unduly influence the summary estimate even though one study identified 21 of the 48 cases (44%) of nonodontogenic pain.

Exploration of Study Heterogeneity

In meta-regression analyses (Table 2), follow-up duration was the factor that differentiated pain frequency the most; the three studies with a follow-up of 6 to 12 months had a frequency of persistent nonodontogenic pain higher by 4.5 percentage points than in the seven studies with a follow-up greater than 12 months. The study reporting quality affected pain frequency the least; the five above-median STROBE criteria studies had a frequency of persistent nonodontogenic pain higher by 1.5 percentage points than in the five below-median studies. However, even when differences were substantial in magnitude, all were statistically nonsignificant because of small numbers of studies.

Proportion of “All-Cause” Pain That Is Nonodontogenic

Nine studies had data for “all-cause” tooth pain, as previously reported (12), as well as for nonodontogenic pain, thus allowing an estimation of the proportion of such pain outcomes in each study population. In these 9 studies, 44 nonodontogenic pain cases (56%) of the 78 “all-cause” pain cases were identified.

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