ADA CE Program ARTICLE 3

Evidence-based recommendations for antibiotic usage to treat endodontic infections and pain

A systematic review of randomized controlled trials

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ABSTRACT

Background. The purpose of this investigation was to identify evidence-based scientific methodologies to aid dental clinicians in establishing the indications for prescribing antibiotics for endodontic infection or pain.

Methods. The authors prepared and registered a protocol on PROSPERO. They conducted electronic searches in MEDLINE, Scopus, Cochrane Library, and ClinicalTrials.gov. In addition, the authors hand searched the bibliographies of all relevant articles, the gray literature, and textbooks for randomized controlled clinical studies. The authors independently selected the relevant articles.

Results. The overall quality of the studies was fair with a low risk of bias, but 2 studies had a moderate risk of bias.

Conclusions. The best available clinical evidence signals no indications for prescribing antibiotics preoperatively or postoperatively to prevent endodontic infection or pain unless the spread of infection is systemic, the patient is febrile, or both. Generally, an accurate diagnosis coupled with effective endodontic treatment will decrease microbial flora enough for healing to occur.

Practical Implications. To help decrease the number of drug-resistant microbes, oral health care providers should not prescribe antibiotics when they are not indicated.

Key Words. Endodontics; antibiotics; pain; flare-ups; randomized controlled clinical trials.

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Multidrug-resistant (MDR) bacterial strains are a global health care problem.[1] The genetic changes of these drug-resistant microbes have been linked to excessive prescribing of antibiotics by health care providers.[2] This link also has occurred with antibiotics prescribed for orofacial infections, including endodontic infections.[3] Unfortunately, the environmental development of generations of antibiotic-resistant microbes has resulted from human application of antibiotics via underuse, overuse, and misuse across many years.[4] Therefore, every dental clinician needs to be knowledgeable about exactly which clinical conditions warrant the prescription of antibiotics.

The authors of a systematic review published in 2015 reported the presence of antimicrobial-resistant genes in the oral cavity, especially those resistant to tetracycline and beta-lactam antibiotic agents in saliva, supragingival biofilm, and acute endodontic infections.[5] Indiscriminate administration of antibiotics in situations for which there is no evidence to support their use could result in an MDR strain that is resistant to more than 1 agent in 3 or more categories of antibiotics.[6]

In keeping with using evidence-based principles in clinical practice, we explored the scientific evidence for prescribing antibiotics to treat endodontic infections or pain using randomized controlled clinical studies, which are considered the criterion standard with the highest level of evidence.[7,8] We used the PICO (population [P], intervention [I], comparison [C], and outcome [O]) format to frame the following clinical question: In patients undergoing root canal treatment for an infected root canal system, does antibiotic treatment result in the reduction of pain and flare-ups?[9] Therefore, the purpose of our study was to discuss the latest indications for prescribing antibiotics for endodontic infections and pain reduction.

This article has an accompanying online continuing education activity available at: http://jada.ada.org/ce/home.

METHODS

We prepared and registered the protocol on PROSPERO (registration number CRD42015026945). We conducted electronic searches in MEDLINE, Scopus, Cochrane Library, and ClinicalTrials.gov, and we used strict inclusion and exclusion criteria. We also searched the gray literature for randomized controlled clinical studies. We excluded non–English-language articles that did not have English-language abstracts.

Key search terms included "endodontics," "root canal treatments," "antibiotics," "randomized-controlled-clinical studies," and "pain and/or flare-ups." In addition, we manually searched the bibliographies of all relevant articles, the gray literature, and textbooks for randomized controlled clinical studies. Two reviewers (A.A., J.C.K.) independently selected the relevant articles. In cases of disagreement, we discussed the divergence and then agreed on the final outcome.

The inclusion criteria for this review were as follows:

- articles whose authors described randomized controlled clinical trials and reported reduction of pain, flare-ups, or both, published in peer-reviewed English-language journals from January 1990 through September 2015;
- in vivo human studies;
- articles whose authors used pain and increased or reduced severity of the infection as measurements to compare patients undergoing endodontic therapy with antibiotics with patients undergoing endodontic therapy without antibiotics;
- articles whose authors provided the sample size of the study;
- articles whose authors measured the effect of pain reduction, flare-ups, or both, as a primary objective.

Exclusion criteria consisted of studies that did not meet the previously listed inclusion criteria, as well as animal studies and laboratory studies.

We used a data extraction sheet based on the Cochrane Consumers and Communication Review Groups data extraction template.[10] We used the AMSTAR checklist,[11] the Oxford Systematic Review Appraisal Sheet,[7,8] Critical Appraisal Skills Programme,[12] and the Grading of Recommendations Assessment, Development and Evaluation system[13] for grading evidence to ensure the accuracy of this data analysis in this systematic review. We used the Cochrane Collaboration's tool for assessing risk of bias to assess the methodological quality of the included studies.[14]

RESULTS

Owing to the variety of research methodologies, diagnoses, and antibiotic regimens we evaluated in our investigation, it was not possible to standardize the research data and to apply meta-analysis. The figure presents a flowchart of the systematic review process according to the Preferred Reporting Items for Systematic Reviews and Meta-analyses.[9]

Our review focused on 2 primary clinical situations involving the use of systemic antibiotics: the administration of antibiotics preoperatively and the administration of antibiotics postoperatively to prevent pulpal and periapical pain or flare-ups after endodontic treatment (Table 1[7,8,15-19]).

Administration of antibiotics to prevent pulpal and periapical pain or flare-ups before and after treatment. ***Preoperative administration.*** An endodontic flare-up is defined as "an acute exacerbation of an asymptomatic pulpal or periradicular pathosis after the initiation or continuation of root canal treatment."[20] We found only 2 prospective, cohort, randomized, double-masked, placebo-controlled clinical studies in which researchers addressed this topic.[17,19] The authors of these studies reported that the preoperative administration of antibiotics was ineffective in alleviating pain in pulpal tissue, periapical tissue, or both.[17,19]

Pickenpaugh and colleagues[19] examined the effect of administration of prophylactic amoxicillin on the occurrence of endodontic flare-ups in patients with necrotic pulps with asymptomatic periapical periodontitis. The authors randomly divided 70 participants into 2 double-masked treatment groups who had a diagnosis of necrotic pulp with asymptomatic periapical periodontitis. One group received 3 grams of amoxicillin orally 1 hour before endodontic treatment and the other received 3 g of placebo orally during the same time. The authors reported that prophylactic administration of antibiotics was ineffective and unrelated to the incidence of an endodontic flare-up ($P = .80$).

In a prospective, randomized, double-masked study, Nagle and colleagues[17] explored the effect of oral administration of penicillin on pain in patients with untreated teeth with a diagnosis of symptomatic irreversible pulpitis. The investigators randomly divided 40 participants with a diagnosis of irreversible pulpitis into 2 groups, 1 receiving a 7-day oral dose of penicillin V potassium (500 milligrams, 4 times per day) or receiving a 7-day dose of placebo. The participants also were instructed to initially take 1 600-mg tablet of ibuprofen every 4 to 6 hours as needed for pain and to take 30 mg of acetaminophen with codeine (2 tablets every 4 to 6 hours) only if the ibuprofen did not relieve their pain. Each participant received a 7-day diary to record symptoms and the number and type of pain medication taken. The investigators performed the administration in a double-masked manner, and the participants did not receive endodontic treatment. The investigators

ABBREVIATION KEY. **AB:** Attrition bias. **DM:** Double-masked. **MDR:** Multidrug-resistant. **RSG:** Random sequence generation. **SR:** Selective reporting.