Emergency Management of Acute Apical Abscesses in the Permanent Dentition: A Systematic Review of the Literature

• **Debora C. Matthews,** DDS, Dip Perio, MSc •
• **Susan Sutherland,** DDS, MSc •
• **Bettina Basrani,** DDS, Dip Endo, PhD •

Abstract

Objective: *To perform a systematic literature review and meta-analysis on the effectiveness of interventions used in the management of acute apical abscess in the permanent dentition.*

Methods: *Electronic databases were searched from their inception to March 2002. These searches, combined with manual searching, yielded 85 citations, of which 35 were relevant. Independent application of inclusion criteria by 3 reviewers yielded 8 eligible randomized controlled studies. Data on population, interventions, outcomes (reduction of pain or swelling or both, as reported by patients or clinicians) and methodological quality were determined by independent triplicate review. Disagreements were resolved by consensus.*

Results: *All papers included in the meta-analysis compared an antibiotic with an active control, a placebo or no pharmacotherapy as an adjunct for patients who had received concomitant therapy (i.e., incision and drainage, endodontic therapy or extraction). The 8 trials were randomized; in 3 of these, the method of randomization was described and appropriate. Five studies were double-blinded, and 2 of these described the method of blinding. Four trials described withdrawals, but none included an intention-to-treat analysis. Six studies compared 2 antibiotics. For the outcomes "absence of infection" and "absence of pain" the pooled odds ratios (ORs) were not statistically significant; for the outcome "absence of pain and infection," 3 studies showed an equivalent treatment effect in both treatment and control groups. One open-label study (with a quality score of 2) showed a result favouring azithromycin over co-amoxiclav in terms of reduction of pain alone (OR 0.58, 95% confidence interval 0.35–0.96). Two studies compared adjunctive antibiotic therapy with placebo; no benefit to patients was demonstrated with this intervention.*

Conclusions: *In the management of localized acute apical abscess in the permanent dentition, the abscess should be drained through a pulpectomy or incision and drainage. This analysis indicated that antibiotics are of no additional benefit. In the event of systemic complications (e.g., fever, lymphadenopathy or cellulitis), or for an immunocompromised patient, antibiotics may be prescribed in addition to drainage of the tooth.*

MeSH Key Words: *acute disease; emergency treatment; periapical abscess/therapy; root canal therapy*

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Acute apical abscess (AAA), also known as acute periapical abscess, acute dentoalveolar abscess or acute periradicular abscess, is a highly symptomatic inflammatory response of the periapical connective tissues.[1] It originates when the pulpal tissues initiate an inflammatory response to trauma or caries and may eventually lead to pulpal necrosis.

Clear clinical and radiographic signs are usually evident in a patient with AAA, although there is a continuum. Pain often occurs rapidly, the severity ranging from slight tenderness to intense, throbbing pain. The source of the pain is easy to determine, as the affected tooth becomes increasingly tender to percussion and chewing. In the late stages of abscess formation, the patient can usually

tolerate the discomfort if the tooth is not touched. Resorption of the overlying cortical bone and localization of the suppurative mass beneath the alveolar mucosa produces a palpable, fluctuant swelling. Frequently, a localized sense of fullness accompanies the pain. Radiographically, the appearance of the periodontal ligament space ranges from within normal limits, to slightly thickened,[2] to a large periapical radiolucency.

Because AAA is due to pulpal necrosis and localized infection, the recommended treatment is removal of the necrotic tissue. This is generally accomplished by drainage of the infection via trephination through the tooth and extirpation of the necrotic pulp (i.e., pulpectomy), incision of the soft-tissue swelling and drainage (as short-term relief), or extraction of the offending tooth.[2] Other therapies, including systemic or local medicaments, such as corticosteroids, analgesics and antibiotics, have been used on their own or in conjunction with pulpectomy. If untreated, AAA may progress to a more widespread infection and even cellulitis. There is a risk of dissemination of organisms from a periapical abscess into the bloodstream, resulting in systemic complications. The signs of systemic involvement are pyrexia, lymphadenopathy and malaise.[3] This risk is reduced in periapical infections that can drain freely.

If adequate drainage cannot be established through pulpectomy, incision and drainage, or extraction, antibiotics are commonly prescribed to prevent systemic complications. Although the incidence of such complications is unreported, it would seem logical to use antibiotics as an adjunct in immunocompromised patients.[4] Although the pain associated with AAA is the result of an infectious process, the infection is usually localized; thus, for most patients, the use of antibiotics as a sole or concomitant therapy is questionable. Nonetheless, up to 75% of patients with painful abscesses and no systemic symptoms may be treated with antibiotic therapy.[5–7]

The prevalence of AAA has been reported to range from 5% to 46%.[8,9] The condition can have a significant social impact[10] in terms of days of work missed and diminished quality of life. In terms of cost, emergency dental treatment accounts for 2% to 6% of the costs of all dental therapy, an amount similar to all periodontal treatment costs.[11,12] In view of the prevalence of this condition in everyday practice and the evidence of practice variation, a systematic review was warranted. The objective of this review was to determine the effectiveness of the various interventions used in the management of AAA in the permanent dentition.

Prior Reviews

Before this review was initiated, the MEDLINE database, DARE (Database of Abstracts of Reviews of Effects) and the Cochrane Library were searched for the period January 1991 to November 2001. The terms "apical periodontitis," "apical abscess," "pulpitis," "toothache" and "emergency care," with limitations of human studies published in English and application of "review articles" as a publication-type limit, were used to locate systematic reviews related to the topic. No other reviews were identified.

Methods

Study Identification

To identify relevant clinical trials, MEDLINE and the Controlled Trials Register of the Cochrane Library were searched from their inception to March 2002. A search of the Specialized Register of Clinical Trials of the Cochrane Oral Health Group was also performed. The search strategy for identifying articles about systemic antibiotics in the management of AAA is outlined in **Appendix 1**. This search was repeated for all reasonable interventions. Pharmacotherapeutics included systemic therapy with antibiotics, corticosteroids, and nonsteroidal anti-inflammatory drugs or analgesics. Surgical measures encompassed the establishment of drainage either through the tooth (pulpectomy, open or closed) or bone (trephination) and extraction. "Watchful waiting" was also considered. For the latter 2 interventions either no evidence was available for analysis, the outcomes did not fit the eligibility criteria, or the data were not suitable for analysis.

Article titles and available abstracts were examined by 2 reviewers (D.M., S.S.), and all papers deemed relevant or possibly relevant by either reviewer were obtained. The reference lists of all retrieved articles, review papers and relevant book chapters were scanned, and pertinent citations identified in this manner were also obtained. After the study selection process described below, endodontic experts and published authors were contacted and asked to provide further references that the search might have missed. To assess the proportion and possible impact of non-English citations, no citations were excluded from the list of relevant papers on the basis of language. However, the full text was obtained only for papers published in English and French. Throughout the project, an ongoing literature search was carried out. Unpublished studies were not sought.

Study Selection

The following criteria were used to determine the eligibility of studies for inclusion in the review.

Target Population: Patients presenting with AAA resulting from nonvital pulp in the permanent dentition. This condition is characterized by pulp necrosis, with pain on biting pressure with or without swelling, and soft-tissue edema with or without redness.

Table 1 **Quality assessment scale (adapted from Jadad and others[14])**

Question	Answer[a]	Points
1. Was the study described as randomized (this includes use of words such as "randomly," "random," and "randomization")?	**No**	0
	Yes	1
	Yes, and the method to generate the sequence of randomization was **described and it was appropriate** (table of random numbers, computer generated, etc.)	2
	Yes, and the method to generate the sequence of randomization was **described and it was inappropriate** (patients were allocated alternately or according to date of birth, hospital number, etc.)	0
2. Was the study described as double-blind?	**No**	0
	Yes	1
	Yes, and the method of double-blinding was **described and appropriate** (identical placebo, active placebo, dummy, sham)	2
Or, if double-blinding was not appropriate to the nature of the study, was the study described as blinded?	**No**	0
	Yes	1
	Yes, and the person evaluating the outcome was blinded to the **treatment allocation of the patient**	2
3. Was there a description of withdrawals and dropouts?	**No**	0
	Yes	1
Total possible score		**5**

[a]*For each question, pick only the best answer and circle the points for that answer.*

Interventions: Systemic and local pharmacotherapeutics, local surgical measures (pulpectomy with or without incision and drainage), watchful waiting, extraction.

Outcome Measures: The effect on patient outcomes in terms of local and systemic symptom relief as measured by patients or clinicians.

Types of Studies: All controlled clinical trials that met the eligibility criteria.

Three reviewers (D.M., S.S., B.B.) then independently and explicitly applied the criteria to the studies retrieved. Any disagreements were resolved by consensus.

Assessment of Methodological Quality

The 3 reviewers used a checklist to independently assess the methodological quality of the selected studies. The checklist addressed whether the population, intervention(s), outcomes and study design were described clearly. All studies that met the inclusion criteria were then evaluated according to a modification[13] of validated criteria proposed by Jadad and others[14] for determining the quality of controlled trials, as described in **Table 1**. The maximum possible score on the scale was 5.

Data Extraction

Pertinent information was extracted from each study, including study design and sample size, population (including the study setting), patient characteristics and eligibility criteria, interventions and comparisons used (including dose, schedule and route of drugs, or specifics of the technique and any co-interventions that were allowed), outcome measures and results. For papers published within the past 10 years for which data were missing or unclear, the authors were contacted and asked to provide detailed information.

There was considerable variation among the studies in the schedules for patient evaluation, which made it impossible to extract data for the same time frame for each study. Instead, the most comparable time frames were chosen, taking into consideration the pharmacokinetics of the particular drug and the timing of local anesthetic, if used.

Data Analysis

Potential sources of variability among the included studies in terms of the population, exposures, outcomes and methods were identified. Within each category of intervention, trials that were not too clinically different (i.e., not too heterogeneous) were pooled and evaluated statistically by means of meta-analytic techniques. RevMan 4.1 for Windows (Cochrane Collaboration, Oxford, UK) was used to perform the meta-analysis.

Meta-analysis

The outcomes of interest were relief of pain and swelling, and reduction in the systemic symptoms of AAA after emergency treatment, as assessed by patients or clinicians. The data were summarized for all studies for which they were available. For outcomes reported as binary data, the individual odds ratio (OR) of response to treatment (test versus control) and associated 95% confidence interval were calculated for each trial. For outcomes reported as continuous data, the individual weighted mean difference (WMD) was calculated for each study. When calculating the combined mean effect of treatment from several studies, this method gives greater weight to studies

Table 2 **Features of 8 included trials**

Study	No. of patients	Setting	Baseline patient characteristics	Intervention	Comparison	Concomitant treatment allowed	Additional therapy	Follow-up period (days)
Adriaenssen[20]	292	Private practice	Acute abscess	Azithromycin 500 mg daily for 3 days	Co-amoxiclav[a] 625 mg tid for 5–10 days	Not stated	None	4
Gilmore and others[21]	55	University dental clinic	Acute abscess with systemic involvement	Clindamycin 150 mg qid for 7 days	Pen V 250 mg qid for 7 days	Not stated	I&D, extraction or pulpectomy	7
Hood[18]	37	Not stated	Acute abscess with systemic involvement	Metronidazole 200 mg q8h for 3 days	Pen G 600 mg IM, followed by Pen V 250 mg qid for 5 days	Not stated	I&D	3–5
Ingham and others[19]	25	Dental hospital	Acute abscess	Pen G 600 mg + procaine penicillin 600 mg IM	Metronidazole 200 mg q8h for 3 days	Not stated	Surgery if indicated	3
Lewis and others[4]	60	Hospital dental clinic	Acute abscess	Amoxacillin 3.0 g post-op and 3.0 g 8 h later	Pen V 250 mg q6h for 5 days	Not stated	I&D, extraction or pulpectomy	2
Lewis and others[22]	78	Hospital dental clinic	Acute abscess	Amoxacillin 250 mg + clavulanic acid 125 mg q8h for 5 days	Pen V 250 mg q6h for 5 days	Not stated	I&D, extraction or pulpectomy	5
Fouad and others[24]	30	University dental clinic	Localized acute apical abscess	Pen VK 1 g post-op and 500 mg qid for 7 days	Placebo or no treatment	Ibuprofen	Pulpectomy; I&D if indicated	3
Henry and others[23]	41	University dental clinic	Symptomatic necrotic tooth with spontaneous pain[b,c]	Pen VK 500 mg q6h for 7 days	Placebo	Ibuprofen; acetaminophen with 30 mg codeine	Pulpectomy	7

I&D = incision and drainage.
[a]*Amoxycillin + clavulanic acid.*
[b]*Fifty-four percent of the patients had self-rated swelling (mild = mild puffiness of the face, not bothersome; moderate = bothersome facial distortion; severe = very bothersome, serious facial distortion).*
[c]*All affected teeth demonstrated radiographic periapical radiolucency.*

with larger sample sizes. Where different numeric scales were used in different studies, the data were transformed to a common percentage scale, by means of the method described by Eisenberg and others[15] according to the following formula: (reported value of scale) / (scale maximum value – scale minimum value) × 100 = value (%). A pooled interval estimate of the population OR or WMD was also calculated. Heterogeneity was assessed with the chi-square test. Significance for this test was set liberally at $p \leq 0.1$, because, in practice, the test often lacks the power to detect interstudy differences of treatment effect.[16] The DerSimonian and Laird[17] Random Effects Model of pooling was used, on the assumption of the presence of interstudy variability, to provide a more conservative estimate of the true effect.

Several sources of heterogeneity were anticipated. To explore the relationship between treatment effect and study features, several a priori hypotheses regarding heterogeneity were developed and subgroup analyses planned. A separate analysis was proposed for each intervention, if there were sufficient studies (more than one) for pooling within each category. A sensitivity analysis was planned to evaluate the influence of methodological quality (score ≥ 3 versus score < 3).

Table 3 **Quality scores (based on Jadad and others[14])[a]**

Study	Randomized			Double-blinded		Description of patient withdrawals[b] (1)	Total score (maximum 5)
	Yes, but method not described (1)	Yes and method appropriate (2)	Yes, but method not appropriate (0)	Yes, but method not described (1)	Yes and method described (2)		
Adriaenssen[20] [c]	X					X	2
Gilmore and others[21]		X			X	X	5
Hood[13]		X					2
Ingham and others[19]	X						1
Lewis and others[4]		X		X			3
Lewis and others[22]	X			X		X	3
Fouad and others[24]	X			X		X	3
Henry and others[23]	X				X		3

[a]*Parenthetical number below each heading indicates the number of points for the study characteristic.*
[b]*None of the studies did an intention-to-treat analysis.*
[c]*Randomized, open-label, comparative study.*

Table 4 **Odds ratios for 6 studies presenting binary data on the outcome "absence of pain and infection"**

Outcome[a]	No. of studies	References	No. of patients	Test for heterogeneity	Odds ratio	95% CI
Absence of infection AND absence of pain	4	Adriaenssen[20] Hood[18] [b] Lewis and others[4] [b] Lewis and others[22] [b]	460	NA	0.58	0.35–0.96
Absence of infection	3	Adriaenssen[20] Gilmore and others[21] Lewis and others[4] [b]	413	Chi-square = 0.23 df = 1 $p = 0.63$[c]	0.73	0.32–1.69[c]
Absence of pain	4	Adriaenssen[20] Gilmore and others[21] Ingham and others[19] [b] Lewis and others[4]	437	Chi-square = 2.40 df = 2 $p = 0.3$[c]	1.21	0.59–2.51[c]

NA = not applicable, CI = confidence interval.
[a]*Follow-up period varied.*
[b]*Odds ratios could not be estimated: equivalent treatment effect in treatment and control groups.*
[c]*Not statistically significant.*

Results

Study Identification and Selection

Seventy-two English-language studies but no French-language studies were identified by the database search. Eighteen reports in languages other than English and French were identified but were not reviewed because of lack of resources for translation. An additional 13 papers were identified through searching of bibliographies. Thirty-five of the 85 papers met the broad screening criteria and were retrieved and reviewed. Upon closer scrutiny by the 2 reviewers, a further 25 studies were eliminated because they did not meet the inclusion criteria.

For the remaining 10 papers, 2 authors were contacted for clarification or verification of the population, intervention or outcome. Neither responded, which resulted in the exclusion of 2 additional papers. References for the 27 excluded studies are listed in **Appendix 2**.

Trial Characteristics

Eight papers,[4,18–24] all controlled clinical trials, met all of the eligibility criteria. A total of 531 patients were included in these studies. There were 2 distinct groups of studies: those that compared 2 antibiotics (total of 460 patients) and those that compared an antibiotic with placebo or no antibiotic treatment (total of 71 patients). The salient features of the trials are presented in **Table 2**.

Methodological Quality

The median quality score[13] was 3 (range 1–5). Agreement concerning the quality of the studies was moderate (kappa = 0.51). Disagreements were related both

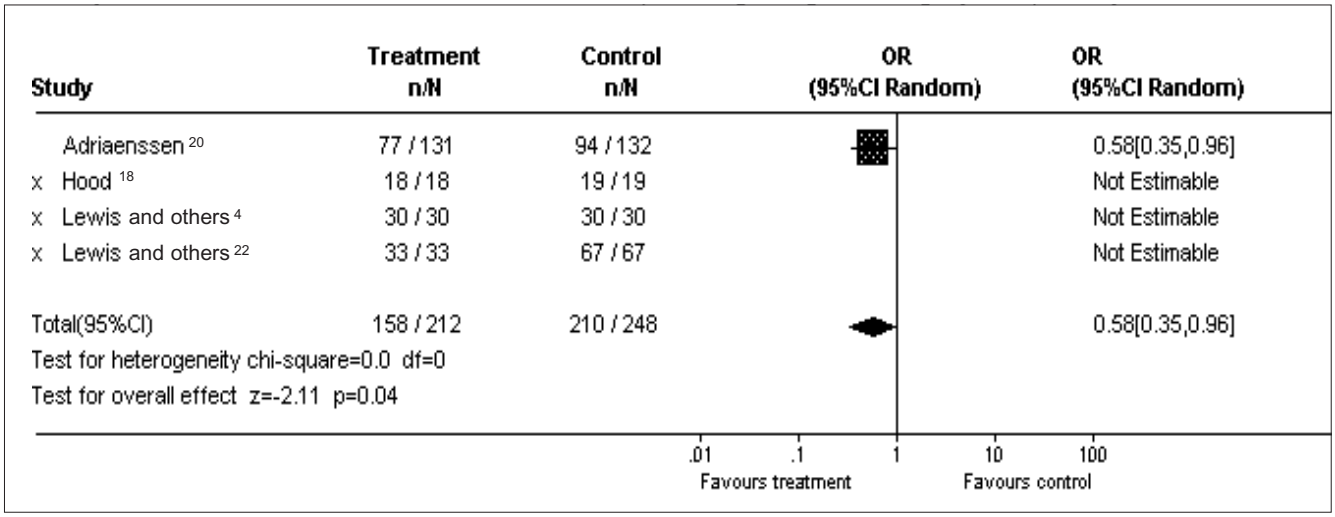

Figure 1: *Results of the meta-analysis for the outcome absence of pain and infection at the end of the follow-up period (Forrest plot).* n *= number of patients showing outcome of interest,* N *= number of patients in treatment or control group, OR = odds ratio, CI = confidence interval, df = degrees of freedom.*

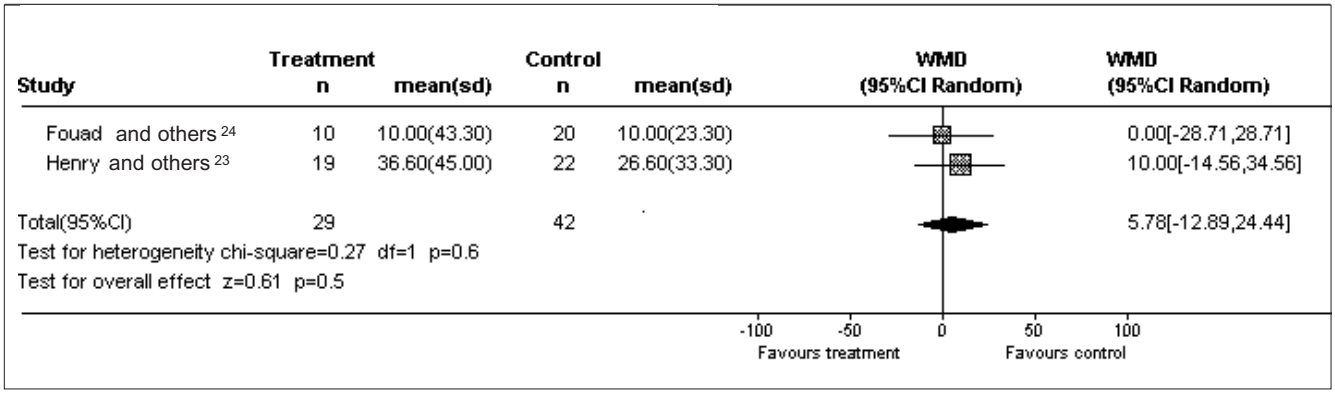

Figure 2: *Results of the meta-analysis for the outcome mean pain at 3 days follow-up (Forrest plot). SD = standard deviation, WMD = weighted mean difference, CI = confidence interval, df = degrees of freedom.*

Understanding meta-analysis graphs (Figs. 1 and 2)

For each individual study, the box represents the study result or point estimate (weighted mean difference for continuous data, odds ratio for dichotomous data), which is the best estimate of the true value for the population from which the sample of patients was taken. The horizontal bars on either side of the point estimate represent the 95% confidence interval, which is the uncertainty due to chance associated with the estimate; the true result may lie anywhere within that interval. Wide confidence intervals indicate a large amount of uncertainty about the estimate. Narrow confidence intervals lead to greater confidence that the estimate is close to the true result — there is greater precision associated with the result. The vertical line is the line of equivalence, where there is no difference between the effect of the treatment and the effect of the control. A point estimate that lies on the "favours treatment" side of the vertical line indicates that the intervention may be beneficial; one that lies on the "favours control" side indicates that the control or placebo may actually be more beneficial than the treatment being studied. However, if the confidence interval for the estimate crosses the vertical line, one of the possible values for the true estimate is zero. In this situation, the result is deemed to be not statistically significant. The diamond at the lower end of the graph represents the combined results of all studies and the associated 95% confidence interval.

to oversights and to subjective interpretation of unclear reports. The final scores (**Table 3**) represent consensus among the 3 reviewers.

Meta-analysis

Studies Comparing 2 Antibiotics

Six trials provided relevant binary data on the outcome of absence of pain and infection (proportions of patients in the treatment and control groups experiencing absence of pain and/or swelling after administration of the intervention or comparison/control) (**Table 4**). Four of these studies[4,20–22] measured absence of pain alone (437 patients) (OR 1.21, 95% confidence interval [CI] 0.59–2.51). Three [4,20,21] measured absence of infection (swelling with or without systemic symptoms) alone (413 patients)

(OR 0.73, 95% CI 0.32–1.69). For both of these outcomes, none of the study results was statistically significant.

Four studies[4,18,20,22] measured a combined absence of pain and swelling or infection at the end of the follow-up period (460 patients). In 3 of these studies[4,18,22] (accounting for 197 patients), there was an equivalent treatment effect in the treatment and control groups. The remaining study,[20] an open-label comparison of azithromycin and co-amoxiclav (263 patients), showed a statistically significant result favouring azithromycin (OR 0.58, 95% CI 0.35–0.96). These results are displayed in a Forrest, or funnel, plot in **Fig. 1**.

Studies Comparing Antibiotics with Placebo or no Treatment

The 2 studies in this group[23,24] provided continuous data for postoperative pain ratings at day 3 (**Fig. 2**). Neither study showed any treatment benefit related to administration of antibiotics (combined WMD 5.78, 95% CI –12.89 to 24.44).

Discussion

In this overview, a systematic review[25] was used to assemble and synthesize evidence from the international literature on interventions used in the management of AAA and to evaluate the effectiveness of those interventions. Comprehensive search methods were used to help minimize bias. Potential sources of bias include publication bias (unpublished studies were not sought) and language bias. Resources did not permit the costly translation of studies published in languages other than English or French. However, a recent study of a number of disease areas has shown that language-restricted and language-inclusive meta-analyses do not differ with respect to the estimate of benefit of an intervention.[26]

The goal of this research was to compare the various interventions in clinical use for the management of AAA. Of the 8 eligible trials, 6 compared antibiotics as an adjunct to relief of swelling.[4,18–22] Four of these 6 studies tested alternatives of penicillin.[4,20,22,24] Given that neither of the studies comparing antibiotics with placebo or with no active treatment[18,19] demonstrated a benefit of antibiotics, a comparison of active treatments (antibiotics) for this condition may not be warranted. These 2 studies were small and therefore may have been underpowered to detect a true effect. Clearly, larger studies are needed to evaluate the use of adjunctive antibiotics for emergency treatment of AAA.

Although the overall quality scores, based on the modified Jadad scoring system, were good, examination of some key methodological features of these studies is informative. All of the 8 trials stated that they were randomized, but only 3 described the method of randomization. It has been demonstrated empirically that inadequate allocation concealment can exaggerate the estimate of treatment effect by 41% and that when the concealment methods are unclear the estimate of effect is exaggerated, on average, by 30%.[27] Four of the 8 papers did not mention or describe withdrawals or dropouts, and none stated a planned intention-to-treat analysis. This technique analyzes patients within the group to which they were originally randomly assigned and hence preserves the powerful function of randomization. The only study showing a significant difference between the treatment and control groups was an open-label comparative study.[20] Because this was a drug trial, there was no reason that a double-blinded placebo-controlled trial could not have been done. Overall, given some of the design and statistical problems, all of the trials in this review had some risk of bias.

None of the studies reported a power-based sample-size calculation. Furthermore, the poor quality of reporting and the inability to obtain vital information (particularly related to outcome data) from some authors led to the omission of studies that otherwise might have been included. This problem was compounded by inconsistencies in research designs, mixed populations (e.g., all odontogenic infections, including AAA) and the reporting of multiple outcome measures. In some studies, the rationale for including patients was unclear. For example, where the outcome measure was related to pain relief, patients were included who had no pain or only mild pain at baseline. A few studies used teeth, rather than patients, as the unit of analysis. For measurement of a patient outcome such as pain, this is clearly inappropriate.[28] All studies reported multiple outcome measures, mostly with unadjusted p values. Many of the outcomes used in some trials were not reported in others, which rendered pooling of studies difficult. None of the trials stated a priori the primary outcome or efficacy measure upon which the overall conclusion of the study would be based. Using endpoints in this manner is suitable for exploratory rather than definitive research.[29]

Recommendations for Research

These combined findings related to design, quality and reporting of trials studying interventions for the management of AAA suggest the need for an organized, methodical research agenda in endodontics. If journal editors were to require the reporting of trials in a manner consistent with the CONSORT statement[30] research reports would be more rigorous and consistent. Future research should clearly state appropriate eligibility criteria for various types of trials. More consistent and clinically relevant outcome measures, with patients as the unit of analysis, are important if efficacy is to be compared among therapies. Much of the pain research that has been published to date uses continuous scales such as the 100-mm Visual Analog Scale (VAS) to measure pain. Use of binary or dichotomous

outcomes (for example, proportion of patients who achieve 50% pain relief or total pain relief by a certain time point) would make the output of subsequent meta-analyses more intuitively understandable.

Assembling and synthesizing the evidence on the emergency management of AAA has made it apparent that more endodontic research is needed in several areas:

- the effect of nonsurgical endodontic therapy alone or combined with antibiotic therapy,
- appropriateness of endodontic therapy versus incision and drainage as an emergency treatment, and
- the most appropriate and effective drugs, routes, dosages and timing of analgesics and anti-inflammatory drugs.

In planning such trials, appropriate inclusion criteria with a clear definition of the disease or condition in question, attention to rigorous design and statistical issues, consistent use of validated measurement tools and choice of clinically relevant primary outcome measures are essential.

Recommendations for Practice

On the basis of the evidence gathered in this analysis, and within the study limitations, the following recommendations for practice are made. The strength of each recommendation has been graded based on the system of the U.S. Agency for Health Care Policy and Research[31] and the initial grading system of Sackett,[32] as outlined in **Appendix 3**.

For adult patients with AAA:

- There is some evidence to support the establishment of drainage to relieve pain and swelling (grade C).
- The use of antibiotics in the management of *localized* AAA, over and above establishing drainage of the abscess, is *not* recommended (grade B).
- There is no evidence to recommend one antibiotic over another in the management of AAA with systemic complications (grade A). ➧

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Dr. Matthews *is head, division of periodontics, Dalhousie University, Halifax, Nova Scotia.*

Dr. Sutherland *is active staff, department of dentistry, Sunnybrook and Women's College Health Sciences Centre, Toronto, Ontario.*

Dr. Basrani *is assistant professor, division of endodontics, Dalhousie University, Halifax, Nova Scotia.*

Correspondence to: *Dr. Debora C. Matthews, Division of Periodontics, Dalhousie University, Halifax, NS B3H 3J5. E-mail: dmatthew@dal.ca.*

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Appendix 1 Search strategy for articles about systemic antibiotics in treatment of acute apical abscess[a]

- Search was done through MEDLINE, as available on OVID — Database: MEDLINE <1966 to present>
- Each search included the disorder, one of the interventions and the limits.

1. The disorder

- Periapical abscess/ OR ((apical or apex or periradicular or peri-radicular or dentoalveolar) and abscess:).mp. OR (apical periodontitis and suppurative).mp. OR (((dental or tooth) and abscess:) not periodontal).mp.

2. Interventions

a. exp Antibiotics/
b. exp Analgesics/
c. exp Anti-inflammatory agents, steroidal/
d. exp Endodontics/ OR (endodontic$ or pulpectomy or pulpotomy or root canal therap$).mp.
e. exp Drainage/ OR drain$.mp.
f. exp Cresols/ OR exp Anti-infective agents/ OR Eugenol/ OR Calcium hydroxide/ OR Methenamine/ OR Silver/ OR Titanium/ OR Ketorolac tromethamine/ OR exp Chlorophenols/ OR Tolmetin/ OR Sodium hypochlorite/ OR Zinc oxide-eugenol cement
g. Trephining/ OR trephin$.mp. OR Decompression, surgical/ OR Punctures
h. Occlusal adjustment/ OR (adjust$ adj5 (bite or occlus$ or tooth)).mp.
i. Tooth extraction/
j. (no$1 adj treat$).mp. OR untreated.mp. OR "watchful waiting".mp.

3. Limits

a. human
b. (clinical trial or clinical trial, phase i or clinical trial, phase ii or clinical trial, phase iii or clinical trial, phase iv or consensus development conference or consensus development conference, nih or controlled clinical trial or meta analysis or multicenter study or practice guideline or randomized controlled trial or review, academic)
c. english language
d. Double-blind method/ OR random allocation/ OR exp clinical trials/ OR placeb$.mp. OR (double$ adj blind$).mp. OR (meta-anal$ or metaanal$).mp. OR ((quantitativ$ or qualitativ$ or systematic$ or methodologic$) and review$).mp.OR ((quantitativ$ or qualitativ$ or systematic$ or methodologic$) and overview$).mp.

exp = explode (MEDLINE term for a method that uses a subject heading as an umbrella term to capture more specific headings on the same subject), mp. = keyword, $ = wild card symbol, adj = adjective.

[a]*The same search strategy was applied for all reasonable interventions.*

Appendix 2 Studies excluded from analysis

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Appendix 3 Grading of evidence[32]

Level or grade[a]	
Evidence	**Definition**
Ia	Evidence obtained from meta-analysis of randomized controlled trials
Ib	Evidence obtained from at least one randomized controlled trial
IIa	Evidence obtained from at least one well-designed controlled study without randomization[b]
IIb	Evidence obtained from at least one other type of well-designed quasi-experimental study
III	Evidence obtained from well-designed nonexperimental descriptive studies, such as comparative studies, correlation studies and case studies
IV	Evidence obtained from expert committee reports or opinions and/or clinical experiences of respected authorities
Recommendations	
A	Based on at least one randomized controlled trial as part of a body of literature of overall good quality and consistency addressing the specific recommendation (evidence levels Ia, Ib)
B	Based on well-conducted clinical studies but no randomized clinical trials on the topic of recommendation (evidence levels IIa, IIb, III); alternatively, small randomized trials with uncertain results (and moderate to high risk of error)
C	Based on evidence obtained from expert committee reports or opinions and/or clinical experiences of respected authorities; absence of directly applicable clinical studies of good quality (evidence level IV)

[a] *"Level" applies to categories of evidence; "grade" applies to categories of recommendations.*
[b] *Randomized controlled trials are considered to represent level IIa evidence if the method of randomization is not clear.*