Antibiotic use for irreversible pulpitis (Review)

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[Intervention Review]

Antibiotic use for irreversible pulpitis

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ABSTRACT

Background

Irreversible pulpitis, which is characterised by acute and intense pain, is one of the most frequent reasons that patients attend for emergency dental care. Apart from removal of the tooth the customary way of relieving the pain of irreversible pulpitis is by drilling into the tooth, removing the inflamed pulp (nerve) and cleaning the root canal. However, a significant minority of dentists continue to prescribe antibiotics to stop the pain of irreversible pulpitis.

Objectives

To provide reliable evidence regarding the effects of prescribing systemic antibiotics for irreversible pulpitis by comparing clinical outcomes expressed as pain relief.

Search strategy

We searched the Cochrane Oral Health Group Trials Register (to 2nd February 2009); CENTRAL (*The Cochrane Library* 2009, Issue 1); MEDLINE (1966 to January 2009); and EMBASE (1980 to February 2009). There were no language restrictions.

Selection criteria

Randomised controlled trials which compared pain relief with systemic antibiotics and analgesics, against placebo and analgesics in the acute preoperative phase of irreversible pulpitis.

Data collection and analysis

Two review authors screened studies and extracted data independently. Pooling of data was not possible and a descriptive summary is presented.

Main results

One trial involving 40 participants was included. There was a close parallel distribution of the pain ratings in both the intervention and placebo groups over the 7-day study period. The between-group differences in sum pain intensity differences (SPID) for the penicillin group were (6.0±10.5), and for placebo (6.0±9.5) P = 0.776. The sum pain percussion intensity differences (SPPID) for the penicillin group were (3.5±7.5) and placebo (2.0±7.0) P = 0.290, with differences as assessed by the Mann-Whitney-Wilcoxon test considered to be statistically significant at P < 0.05. There was no significant difference in the mean total number of ibuprofen tablets (P = 0.839)

and Tylenol tablets (P = 0.325), in either group over the study period. The administration of penicillin over placebo did not appear to significantly reduce the quantity of analgesic medication taken (P > 0.05) for irreversible pulpitis.

Authors' conclusions

This review which was based on one methodologically sound but low powered small sample trial provides some evidence that there is no significant difference in pain relief for patients with untreated irreversible pulpitis who did or did not receive antibiotics in addition to analgesics.

PLAIN LANGUAGE SUMMARY

Antibiotic use for irreversible pulpitis

Antibiotics do not appear to significantly reduce toothache caused by irreversible pulpitis.

Irreversible pulpitis, where the dental pulp (nerve) has been damaged beyond repair is characterised by intense pain and considered to be one of the most frequent reasons that patients attend for emergency dental care.

This review, which included one trial (40 participants), found that there is a small amount of evidence to suggest that the administration of penicillin does not significantly reduce the pain perception, the percussion perception or the quantity of pain medication required by patients with irreversible pulpitis.

BACKGROUND

Dental emergencies are extremely common, in one survey in the USA 12% of the population had experienced toothache in the preceding 6 months (Lipton 1993). Although there are very little data available, irreversible pulpitis, which is characterised by acute and intense pain, is considered to be one of the most frequent reasons that patients attend for emergency dental care. Irreversible pulpitis is defined as an inflammatory process in which the dental pulp (nerve) has been damaged beyond repair and will eventually die (Bergenholtz 1990). Most commonly the inflammation of irreversible pulpitis in vital teeth occurs beneath deep caries (tooth decay) before the bacteria have even reached the pulp (Hahn 1991). Thus the involved tooth will usually have an extensive restoration (filling) and/or caries under which death of the pulp may occur quite quickly or which may take years to occur even if the irritant (dental caries) is removed (Tronstad 1991).

Description of the condition

The symptoms are a continuum and will vary with a history of spontaneous pain which may also include an exaggerated response to hot or cold that lingers after the stimulus is removed (Soames 1998). Any tooth may be affected by irreversible pulpitis, it is not restricted to particular age groups, it usually occurs as a direct result of dental caries, a cracked tooth or trauma and thus tends to occur more frequently in older patients. The involved tooth is usually not sensitive to percussion, and palpation tests do not produce an untoward reaction. The characteristics of irreversible pulpitis are a vital pulp which responds to cold and electric pulp testing, with responses to cold stimuli resulting in prolonged reaction. Not infrequently, cold may actually alleviate the pain of irreversible pulpitis and thus, can be used as a diagnostic test (Cecic 1983). A number of variations of irreversible pulpitis have been recognised (Cohen 2006). These include acute, subacute, chronic, partial or total, infected or sterile, however it is not possible to clearly differentiate these except by histopathological methods.

Description of the intervention

Apart from removal of the tooth the customary way of relieving the pain of irreversible pulpitis is by drilling into the tooth, removing the inflamed pulp (nerve and associated blood vessels) and cleaning the root canal (Oguntebi 1992). However, a significant minority of dentists continue to prescribe antibiotics to stop the pain of irreversible pulpitis (Yingling 2002).

Why it is important to do this review

The routine prescribing of systemic antibiotics for relieving pain in endodontic emergencies has received considerable attention (Fouad 1996). However there appears to be limited empirical evidence to support the generalisability and effectiveness of this approach and there have been questions raised about the safety of indiscriminate antibiotic prescription.

A study conducted in the USA on antibiotic use by members of the American Association of Endodontists (AAE) evaluated the practice of prescribing antibiotics for irreversible pulpitis among endodontists (Yingling 2002). This study which surveyed the prescribing habits of specialist endodontists reported that 16.76% of responders prescribed antibiotics for cases of irreversible pulpitis. Although very little data are available it maybe safe to assume that the number of general dental practitioners, who are the first point of contact for patients with irreversible pulpitis and who might prescribe antibiotics, could well exceed this figure.

The Centers for Disease Control estimates that about 100 million courses of antibiotics are prescribed by office-based physicians each year, and that approximately one half of those prescriptions appear to be unnecessary (Colgan 2001). The deaths in the USA of four children due to methicillin-resistant *Staphylococcus aureus* (MRSA) infections brought attention to the increase in drug-resistant infections seen in the general population (CDC 1999). Moreover there have been reports that 50% of *S. aureus* infections in the USA are methicillin-resistant and although the true prevalence of MRSA cannot be determined it is estimated that it has increased sharply over the last 20 years (CDC 2008). In the UK, the Department of Health Standing Medical Advisory Committee highlighted the problem of antibiotic resistance in clinical practice and recommended that improved education of prescribers would be a key element in reducing resistance (SMAC 1997). It is believed that the indiscriminate use of antibiotics may have contributed significantly to the increase in MRSA infections with concomitant staggering cost implications. Recent estimates in the USA have put the figure for treatment of resistant infections at more that US$7 billion, with up to US$4 billion used for the treatment of nosocomial infections due to antimicrobial resistant bacteria (John 1997). In 1995, the cost of containing an MRSA outbreak in a district general hospital in the UK was estimated to be greater than GB£400,000 (Cox 1995).

Dental caries is the result of bacterial attack on a tooth and is the precursor to irreversible pulpitis, considered to be an immune system mediated event which is most often not due to a bacterial infection of the pulp, but rather is a result of inflammatory mediators overcoming the host defences (Bergenholtz 1990). A number of studies appear to indicate that penicillin does not reduce pain, percussion sensitivity, or the amount of analgesics required in untreated teeth diagnosed with irreversible pulpitis (Nagle 2000). Nevertheless in a study of the prescribing habits of general dental practitioners in the UK it was found that there was evidence of overuse of antibiotics particularly for surgery whereas there was an encouragingly small proportion (< 6%) of the respondent practitioners who prescribed antibiotics before or after root canal therapy (Palmer 2000). There was a significantly higher number of practitioners prescribing antibiotics before root canal treatment (5.4%) than after (2.8%) but the study only focused on acute pulpitis with or without periapical abscess, and did not distinguish between the different classifications of pulpitis.

In addition to the possibility of contracting antibiotic-resistant infections there are other potential side effects to antibiotic use such as sensitization, skin rashes and on rare occasions anaphylactic shock and even death.

OBJECTIVES

The objective of this review was to provide reliable evidence regarding the effects of prescribing systemic antibiotics for irreversible pulpitis by comparing clinical outcomes expressed as pain relief.

The following null hypothesis was tested: for irreversible pulpitis there is no difference in pain relief between patients taking antibiotics and analgesics as compared to those who have received placebo or analgesics.

METHODS

Criteria for considering studies for this review

Types of studies

Only randomised controlled clinical trials (RCTs) were considered in this review.

Types of participants

Only studies which had recruited adult patients who were over the age of 18 and presented with a single tooth with a clinical diagnosis of irreversible pulpitis were included.

Types of interventions

Active interventions

Administration of any systemic antibiotic at any dosage and any analgesic at any dosage prescribed in the acute preoperative phase of irreversible pulpitis.

Control

Administration of placebo and any analgesic, at any dosage, prescribed in the acute preoperative phase of irreversible pulpitis.

Types of outcome measures

Primary outcomes

Patient reported pain (intensity/duration) and pain relief measured on a categorical scale in the preoperative phase of irreversible pulpitis.

Secondary outcomes

Type, dose and frequency of medication required for pain relief. We also reported on any adverse effects related to any clinically diagnosed hypersensitivity or other reactions to either the antibiotics or analgesics.

Search methods for identification of studies

Electronic searches

For the identification of studies included or considered for this review, detailed search strategies were developed for each database to be searched. These were based on the search strategy developed for MEDLINE but revised appropriately for each database. There were no language restrictions.
The following databases were searched:

- Cochrane Oral Health Group Trials Register (to 2nd February 2009)
- Cochrane Central Register of Controlled Trials (CENTRAL) (*The Cochrane Library* 2009, Issue 1)
- MEDLINE (1966 to January 2009)
- EMBASE (1980 to February 2009).

For the detailed search strategies applied to each of the databases *see* Appendix 1; Appendix 2; Appendix 3 and Appendix 4.

Searching other resources

No additional handsearching was carried out. Reference lists of relevant articles and clinical trials were searched in an attempt to identify any potential or additional studies.

Data collection and analysis

Selection of studies

The titles and abstracts of studies resulting from the searches were independently assessed by two review authors (Zbys Fedorowicz (ZF) and James Keenan (JVK)). All irrelevant records were excluded and only details of potential studies were noted. Full copies were obtained of all relevant and potentially relevant studies which appeared to meet the inclusion criteria, or where there were insufficient data in the title and abstract to make a clear decision. Studies not matching our inclusion criteria were excluded and their details and reasons for their exclusion were noted in the Characteristics of excluded studies table in Review Manager (RevMan) (RevMan 2008).

Data extraction and management

Study details were entered into the Characteristics of included studies table. Outcome data were collected using a predetermined from an entered into RevMan. The review authors only included data if there was an independently reached consensus. All disagreements were discussed and resolved by consulting with a third review author (Tim Newton (TN)).
The following details were extracted.

1. Study methods: method of allocation, masking of participants and outcomes.
2. Participants: country of origin, sample size, age, sex, inclusion and exclusion criteria.
3. Intervention: type of antibiotic.
4. Control: analgesic, placebo or nil.
5. Outcomes: primary and secondary outcomes as described in the Types of outcome measures section of this review.

Assessment of risk of bias in included studies

Each of the two review authors then graded the selected studies separately according to the domain-based evaluation described in the *Cochrane Handbook for Systematic Reviews of Interventions* 5.0.1 (updated September 2008) (Higgins 2008). The gradings were compared and any inconsistencies between the review authors were discussed and resolved.
The following domains were assessed as 'Yes' (i.e. low risk of bias, plausible bias unlikely to seriously alter the results), 'Unclear' (i.e. uncertain risk of bias, plausible risk of bias that raises some doubts about the results) or 'No' (i.e. high risk of bias, plausible bias that seriously weakens confidence in the results):

1. sequence generation;
2. allocation concealment;
3. blinding (of participants, personnel and outcomes assessors);
4. incomplete outcome data';

5. selective outcome reporting;
6. other sources of bias.

These assessments are reported for the included study in the Characteristics of included studies table.

Assessment of heterogeneity

There was only one single trial and therefore no assessments were made.

If further studies are included in future updates we will assess clinical heterogeneity by examining the characteristics of the studies, the similarity between the types of participants, the interventions and outcomes as specified in the criteria for included studies. Statistical heterogeneity will be assessed using a Chi^2 test and the I^2 statistic where I^2 values over 50% indicate moderate to high heterogenity (Higgins 2003).

Data synthesis

The single included study did not provide sufficient data to perform a statistical analysis and the only data presented are those which were published in the study. Unsuccessful attempts to obtain additional and individual level data from the trialists made it difficult to confirm the results presented in their study.

If further studies are included the following methods of data synthesis will apply. Data will be analysed using RevMan and reported according to Cochrane Collaboration criteria. Pooling of data will only occur if the included studies have similar interventions taken by similar participants. We will present risk ratios for outcomes and odds ratios for adverse effect outcomes. The risk ratio (relative risk) is the ratio of the risk of an event in the two groups whereas the odds ratio is the ratio of the odds of an adverse event in the intervention group to the odds of an event in the control group. Additionally any data obtained from visual analogue scales and any categorical outcomes will be transformed into dichotomous data prior to analysis if appropriate. Risk ratios, the number needed to treat and their 95% confidence intervals will be calculated for all dichotomous data.

Sensitivity analysis

We had expected to be able to conduct sensitivity analyses to assess the robustness of our review results by repeating the analysis with the following adjustments: exclusion of studies of lower methodological quality and unpublished studies. However as there was only a single trial that matched our inclusion criteria no sensitivity analyses were carried out.

RESULTS

Description of studies

See: Characteristics of included studies; Characteristics of excluded studies.

Results of the search

The search strategy identified 39 references of which all but four were excluded from further analysis. Full text copies of these four papers were obtained for further assessment. One paper was a systematic review (Matthews 2003) which included a potential trial (Henry 2001) which was subsequently excluded as it investigated the effect of antibiotics on postoperative endodontic pain. One trial (Fouad 1996) was excluded as it combined the interventions with operative endodontic treatment. We excluded Nusstein 2003 because it was a retrospective non-experimental study. Finally only one study (Nagle 2000) met the inclusion criteria and is included in the review.

Included studies

Methods

Nagle 2000 is a randomised double-blind placebo-controlled clinical trial conducted in the emergency department of a university dental college in the USA.

Participants and setting

Forty adult patients, 17 male, 23 female, with an age range of 30 to 34 years who had presented as an emergency with spontaneous moderate to severe pain associated with a tooth, participated in this study. All of the teeth were vital and responsive to an electric pulp tester (EPT) and to Endo Ice and displayed percussion sensitivity. The diagnosis of irreversible pulpitis was confirmed by a radiographically widened periodontal ligament space (*see* Additional Table 1).

Table 1. Baseline pain and percussion values for penicillin and placebo groups

	Penicillin	Placebo
Initial pain (median & interquartile range)	2.00+/- 0.00	2.00+/- 1.00

Table 1. Baseline pain and percussion values for penicillin and placebo groups (*Continued*)

Initial percussion pain (median & interquartile range)	2.00+/- 0.50	2.00+/- 1.00
Pain ratings: moderate	65%	80%
Pain ratings: severe	35%	20%
Percussion pain ratings: mild	20%	25%
Percussion pain ratings: moderate	50%	65%
Percussion pain ratings: severe	30%	10%

Intervention

Twenty participants were allocated to antibiotic and analgesic and 20 to placebo and analgesic. The participants received a 7-day oral dose (28 capsules each to be taken every 6 hours) of either penicillin (500 mg) or a placebo control in which the participants and trialists were double-blinded. They also received a supply of pain medication consisting of ibuprofen 600 mg; acetaminophen with codeine 30 mg (Tylenol). No operative endodontic treatment was performed during the course of the study.

Outcomes

The primary outcome for this review was pain relief in the preoperative phase of irreversible pulpitis. Participants in this study were requested to complete a 7-day diary in which they recorded pain, percussion pain, and the quantity and type of pain medication taken. Pain was assessed using a short ordinal numerical scale graded from 0 to 3: zero (0) indicating no pain; one (1) indicating mild pain, that is, pain that was recognizable but not discomforting; two (2) indicating moderate pain, or pain that was discomforting but bearable; three (3) indicating severe pain, or pain that caused considerable discomfort and was difficult to bear.

Additionally the patients were asked to use the same scale to rate pain to percussion which was achieved by tapping the affected tooth with a finger. The pain scale used in this trial had been used in previous pain studies which were referenced by the trialists of the included study. Furthermore in a personal communication the trialists indicated that they had more recently used a modified Heft-Parker visual analogue scale (Heft 1984) and that the two measures had shown a high degree of correlation although the results were as yet unpublished.

The secondary outcome for this review was the type and dose of pain medication required to achieve pain relief. The participants in the Nagle 2000 study were instructed to initially take one tablet of the ibuprofen every 4 to 6 hours as needed for pain and to take the Tylenol (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 their symptoms and the number and type of pain medication taken. No adverse effects to either the antibiotics or analgesics were reported in this trial.

Excluded studies

Three studies were excluded, please *see* Characteristics of excluded studies for further details.

Risk of bias in included studies

Allocation

In this study (Nagle 2000) the intervention (penicillin) and control (placebo) groups were assigned before the experiment by using 4-digit numbers from a random number table. To ensure adequate concealment only the random numbers were recorded on the data collection and postoperative diary sheets.

Blinding

The medications were blinded, randomised, and packaged by a pharmacy. Each 500 mg gelatin capsule of either penicillin or placebo was identical in form. The 500 mg tablets of penicillin VK were ground into a powder and placed into the clear, unlabelled

gelatin capsules. The white powder of the lactose placebo was indistinguishable from the white powder of the penicillin tablets when viewed through the capsule.

Incomplete outcome data

The trialists provided only group level data of the primary and secondary outcomes for every 1 of the 7 study days. In a personal communication they indicated that the pain intensity difference scores (PID) were derived by subtracting the pain intensity score at the given time interval from the patient's baseline pain intensity score. Additionally they confirmed that the sum of the pain intensity differences (SPID) comprised the total area under the time-effect curve over the first 7 days and was arrived at by summing the PID scores. Similarly the sum of percussion pain intensity difference (SPPID) was arrived at by totaling the percussion pain intensity difference scores (PPID) (Additional Table 2). The between-group differences in SPID and SPPID were then assessed by the Mann-Whitney-Wilcoxon test.

No individual level PID or PPID data were made available by the trialists and in the absence of more detailed individual level change data it was not possible to confirm the SPID or SPPID data. Moreover we noted that the reasoning for some of the statistical conclusions were not fully explained in the text.

We therefore only present the published group level outcomes data and a descriptive summary of results.

Table 2. Sum pain and percussion pain intensity differences

	Penicillin	Placebo	P value
Sum pain intensity difference (median and interquartile range)	6.0 +/- 10.5	6.0 +/- 9.5	.776
Sum percussion pain intensity difference (median and interquartile range)	3.5+/-7.5	2.0 +/- 7.0	.290

Selective reporting

There was no evidence of selective outcome reporting and the outcomes listed in the methods section were comparable to the reported results.

Other potential sources of bias

There was no evidence of other potential sources of bias in the report of the included trial.

Effects of interventions

Primary outcome: patient reported pain (intensity/duration) and pain relief

Baseline data indicated that all of the participants that entered the study had moderate to severe pain (Additional Table 1). After the first day of the study the average pain rating decreased and remained quite stable over the following 6 days. This initial decrease in pain may be considered to be due to the effect of the analgesics which was sustained by the gradual and progressive necrosis of the pulp. However, at the end of the study period and at the commencement of operative endodontic treatment it was found that 75% of the teeth in the penicillin group and 80% in the placebo were still vital.

There was a close parallel distribution of the pain ratings in both the intervention and placebo groups over the 7 days. The in between-group differences in sum pain intensity differences (SPID) for the penicillin group were (6.0±10.5), and for placebo (6.0±9.5) P = 0.776 . The sum pain percussion intensity differences (SPPID) for the penicillin group were (3.5±7.5) and placebo (2.0±7.0) P = 0.290 with differences as assessed by the Mann-Whitney-Wilcoxon test considered to be statistically significant at P < 0.05 (Additional Table 2).

Secondary outcome: type, dose and frequency of medication required for pain relief

The number, percentage and average use and non-use of ibuprofen and Tylenol are summarised in Additional Table 3.

On both day 1 and day 2 only 1 (5%) participant took neither medication. The number not taking any medication increased to 3 to 4 (15% to 20%) on day 3, and 2 to 6 (10% to 30%) on day 4. On the 5th to 7th days only 4 to 7 (20% to 35%) did not take any additional pain medication. At day 7, 20% of the penicillin group and 35% of the placebo group took no additional analgesics.

The trialists indicated that there was no significant difference in the mean total number of ibuprofen tablets (P = 0.839) and Tylenol tablets (P = 0.325), in either group over the study period (Additional Table 4). The administration of penicillin over placebo did not appear to significantly reduce the quantity of analgesic medication consumed (P > 0.05) for irreversible pulpitis.

Table 3. Use of pain medication for penicillin and placebo groups (n and quantity)

Day	n Ibuprofen	n Tylenol	Nil pain medication
DAY 1			
Penicillin	17 (85%)	10 (50%)	1 (5%)
No of tablets	33	21	0
Placebo	16 (80%)	8 (40%)	0
No of tablets	28	11	0
DAY 2			
Penicillin	17 (85%)	10 (50%)	0
No of tablets	30	28	0
Placebo	16 (80%)	9 (45%)	1 (5%)
No of tablets	31	18	0

Table 3. Use of pain medication for penicillin and placebo groups (n and quantity) (*Continued*)

DAY 3			
Penicillin	13 (65%)	9 (45%)	4 (20%)
No of tablets	27	20	0
Placebo	15 (75%)	8 (40%)	3 (15%)
No of tablets	28	14	0
DAY 4			
Penicillin	12 (60%)	9(45%)	6 (30%)
No of tablets	24	23	0
Placebo	17 (85%)	5 (25%)	2 (10%)
No of tablets	28	8	0
DAY 5			
Penicillin	12 (60%)	8 (40%)	7 (35%)
No of tablets	21	15	0
Placebo	16 (80%)	7 (35%)	3 (15%)
No of tablets	32	11	0
DAY 6			
Penicillin	13 (65%)	8 (40%)	5 (25%)
No of tablets	24	15	0
Placebo	13 (65%)	6 (30%)	6 (30%)
No of tablets	24	13	0
DAY 7			
Penicillin	14 (70%)	10 (50%)	4 (20%)
No of tablets	25	16	0
Placebo	11 (55%)	7 (35%)	7 (35%)
No of tablets	20	14	0

Table 4. Total number of Ibuprofen and Tylenol tabs

	Penicillin	Placebo	P value
Total number of Ibuprofen (mean & SD)	9.2 ± 6.02	9.6 ± 6.34	.839
Total number of Tylenol (mean & SD)	6.9 ± 6.87	4.45 ± 4.82	.325

SD = standard deviation

DISCUSSION

The results of this well constructed but underpowered trial of 20 participants in each study arm indicate that the administration of penicillin did not appear to significantly ($P > 0.05$) reduce either the pain perception, the percussion perception or the quantity of analgesic medication required by patients with irreversible pulpitis.

The significance of the relatively common occurrence of toothache, the prevalence of inappropriate prescribing of antibiotics with the potential for producing antibiotic resistance and patient sensitisation cannot be underestimated. It was somewhat disappointing to see the limited number of trials that matched our inclusion criteria. One of the excluded studies included operative endodontic treatment supplementary to the prescription of antibiotics and analgesics (Fouad 1996). Another one investigated the potential benefits of antibiotics for pain and swelling in post-operative endodontic treatment (Henry 2001).

There is an acceptance that changes in the dental pulp associated with irreversible pulpitis are a continuum and therefore it may not be possible to clearly differentiate either clinically or radiologically between the stages of pulp degeneration and necrosis to acute apical abscess formation. Our electronic searches did identify a systematic review (Matthews 2003) which offered strong confirmatory evidence that in the absence of systemic complications e.g. fever, lymphadenopathy, cellulitis or in immunocompromised patients, antibiotics alone have no place in the management of localised acute apical abscess. Furthermore they stated that although the pain from acute apical abscess is as a result of an infective process, the infection is localised and that even in this terminal stage of irreversible pulpitis the use of antibiotics as a sole or concomitant therapy remains questionable.

The indiscriminate prescribing of antibiotics was investigated in a study (Palmer 2000) commissioned by the National Health Service (NHS) in England which confirmed that there was evidence of overuse and inappropriate prescribing of antibiotics in NHS general dental practice and that antibiotics were not infrequently prescribed in clinical situations where there was limited evidence of benefit. This study noted that patient expectation (8%), pressure of time and workload (30%), and patient social history (8%) accounted for a large number of non-clinical factors responsible for antibiotic prescribing. This appeared to be supported by the American Association of Endodontists study (Yingling 2002) which indicated that some endodontists felt compelled to prescribe antibiotics for medico-legal reasons, to satisfy patient demand and expectation and to decrease the risk of losing referrals.

AUTHORS' CONCLUSIONS

Implications for practice

This review which was based on one methodologically sound but low powered small sample trial conducted in the USA provided some evidence that there is no significant difference in pain relief for patients with irreversible pulpitis who did or did not receive antibiotics in addition to analgesics.

There is a general awareness amongst dentists that antibiotics may not have a role to play in alleviating pain in irreversible pulpitis but it is apparent that the practice continues notwithstanding a lack of evidence of effectiveness and of potential risk.

The use of antibiotics in conjunction with cleaning and disinfection of the root canal or dental extraction should be considered when the spread of infection is systemic and the patient is febrile.

Therefore, careful evaluation of a patient's history, a thorough clinical examination and evaluation of each test is vital to establish the status of the pulp. Not infrequently symptomatic pulpitis may become symptomless as the degeneration of the pulp leading to pulpal necrosis may proceed gradually without the development of further symptoms, pulp tests may prove to be indecisive and the first indication may be a radiolucency visible at the periapex on a radiograph.

A clinical guide (Carrotte 2003) outlined five principal features of irreversible pulpitis which can be used to help determine the status of the dental pulp:

- a history of spontaneous bouts of pain which may last from a few seconds to several hours;
- hot and cold fluids exacerbating the pain. In the latter stages heat will be more significant cold will relieve the pain;
- pain radiating initially but once the periodontal ligament has become involved the pain will be more readily localised by the patient;
- the tooth may become tender to percussion once the inflammation has spread to the periodontal ligament;
- a radiographically visible widening of the periodontal ligament maybe seen.

Implications for research

The results of this systematic review confirm the necessity for further larger sample and methodologically sound trials that can assist in providing additional supportive evidence as to whether the prescription of antibiotics either therapeutically or prophylactically can adversely affect treatment outcomes for irreversible pulpitis. There is now a compelling urgency to investigate the teaching of the rationale for safe and effective antibiotic prescribing in endodontics and to advance the development of appropriate evidence-based clinical guidelines.

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* *Indicates the major publication for the study*

CHARACTERISTICS OF STUDIES

Characteristics of included studies *[ordered by study ID]*

Nagle 2000

Methods	Prospective randomised double-blind trial in the USA. Before the experiment, patient groups (penicillin or placebo) were assigned by using 4-digit numbers from a random number table. Only the random numbers were recorded on the data collection and postoperative diary sheets to blind the experiment. The medications were blinded, randomised, and packaged by a pharmacy.
Participants	Adults: (40) 17 male, 23 female. Mean age and standard deviation (SD) in the penicillin group 30 (9.8), placebo group 34 (11.6). 2 groups of 20: penicillin group 7 women and 13 men, placebo 16 women and 4 men. Inclusion criteria: • participants in "good health", • clinical diagnosis of irreversible pulpitis (spontaneous moderate/severe pain), • percussion sensitivity, • tooth vital to electric pulp tester (EPT) and painful response to Endo Ice, • radiographically widened periodontal ligament space. Exclusion criteria: • tooth not responsive to EPT, • participants taking antibiotics or in the preceding 30 days.
Interventions	Oral penicillin or placebo control (lactose) and all patients received analgesics. 7-day oral dose 500 mg 6 hourly; penicillin (Penicillin VK; Wyeth Laboratories, Philadelphia, Pa) or a placebo control (lactose). Analgesics: 600 mg ibuprofen (Motrin; HN Norton Co, Shreveport, La); acetaminophen with 30 mg of codeine (Tylenol No 3; McNeil Consumer Products, Fort Washington, Pa).
Outcomes	Primary outcomes: between-group differences in sum pain intensity differences (SPID), sum pain percussion intensity differences (SPPID) and quantity of pain medications taken.
Notes	There were no withdrawals or drop outs.

Risk of bias

Item	Authors' judgement	Description
Adequate sequence generation?	Yes	Quote: "Before the experiment, patient groups (penicillin or placebo) were assigned by using 4-digit numbers from a random number table". Comment: Probably done.

Nagle 2000 (*Continued*)

Allocation concealment?	Yes	Quote: "Only the random numbers were recorded on the data collection and post-operative diary sheets to blind the experiment". "The medications were blinded, randomized, and packaged by a pharmacy". Comment: Central randomisation, probably done.
Blinding? All outcomes	Yes	Participants/healthcare providers: Quote: "Each 500-mg gelatin capsule of either penicillin or placebo was identical in form. The 500-mg tablets of penicillin VK were ground into a powder and placed into the clear, unlabeled gelatin capsules. The white powder of the lactose placebo was indistinguishable from the white powder of the penicillin tablets when viewed through the capsule". Comment: Probably done. Outcomes assessors and data analysts: The outcomes were self assessed and as the caregivers were blinded, this was probably done.
Incomplete outcome data addressed? All outcomes	Yes	Outcome data were complete for all of the participants.
Free of selective reporting?	Yes	No evidence of selective choice of data for outcomes. Outcomes listed in the methods section comparable to the reported results.
Free of other bias?	Yes	Quote: "Supported by research funding from the Endodontic Graduate Student Research Fund and the Steve Goldberg Memorial Fund, The Ohio State University". Comment: Appears to be free of other bias.

Characteristics of excluded studies *[ordered by study ID]*

Fouad 1996	This study combined antibiotic or placebo or neither as an adjunct to operative endodontic treatment in resolving the acute apical abscess.
Henry 2001	This study combined antibiotic as an adjunct to endodontic treatment.
Nusstein 2003	This study was a retrospective non-experimental study.

DATA AND ANALYSES

This review has no analyses.

APPENDICES

Appendix 1. Cochrane Oral Health Group Trials Register search strategy

((anti-bacterial-agents OR penicillin* OR amoxicillin* OR erythromycin* OR antibiotic OR anti-biotic OR antibacterial* OR anti-bacterial*) AND (pulpectom*)))

Appendix 2. CENTRAL search strategy

1. ANTI-BACTERIAL AGENTS
2. PENICILLINS
3. antibiotic* OR anti-biotic*
4. (antibacterial agent* OR anti-bacterial agent*)
5. antibacterial* OR anti-bacterial*
6. (penicillin* or amoxicillin or erythromycin)
7. 1 OR 2 OR 3 OR 4 OR 5 OR 6
8. PULPECTOMY
9. pulpectom*
10. (#8 or #9)
11.(#7 and #10)

Appendix 3. MEDLINE (OVID) search strategy

1. Anti-Bacterial Agents/
2. PENICILLINS/
3. (antibiotic$ or anti-biotic$).mp. [mp=title, original title, abstract, name of substance word, subject heading word]
4. anti-bacterial-agent$.mp. [mp=title, original title, abstract, name of substance word, subject heading word]
5. antibacterial agent$.mp. [mp=title, original title, abstract, name of substance word, subject heading word]
6. (antibacterial$ or anti-bacterial$).mp. [mp=title, original title, abstract, name of substance word, subject heading word]
7. (penicillin$ or amoxicillin$ or erythromycin$).mp. [mp=title, original title, abstract, name of substance word, subject heading word]
8. or/1-7
9. PULPECTOMY/
10. pulpect$.mp. [mp=title, original title, abstract, name of substance word, subject heading word]
11. or/9-10
12. 8 and 11

Appendix 4. EMBASE (OVID) search strategy

1. Antibiotic Agent/
2. PENICILLIN DERIVATIVE/
3. (antibiotic$ or anti-biotic$).mp. [mp=title, abstract, subject headings, drug trade name, original title, device manufacturer, drug manufacturer name]
4. anti-bacterial-agent$.mp. [mp=title, abstract, subject headings, drug trade name, original title, device manufacturer, drug manufacturer name]
5. antibacterial agent$.mp. [mp=title, abstract, subject headings, drug trade name, original title, device manufacturer, drug manufacturer name]
6. (antibacterial$ or anti-bacterial$).mp. [mp=title, abstract, subject headings, drug trade name, original title, device manufacturer, drug manufacturer name]
7. (penicillin$ or amoxicillin$ or erythromycin$).mp. [mp=title, abstract, subject headings, drug trade name, original title, device manufacturer, drug manufacturer name]
8. or/1-7
9. pulpectom$.mp. [mp=title, abstract, subject headings, drug trade name, original title, device manufacturer, drug manufacturer name]
10. 8 and 9

WHAT'S NEW

Last assessed as up-to-date: 16 February 2009.

16 February 2009	New search has been performed	New searches: February 2009. New studies sought but none found. Text in 'Assessment of risk of bias in included studies' modified. Risk of bias table added.

HISTORY

Protocol first published: Issue 4, 2004

Review first published: Issue 2, 2005

8 August 2008	Amended	Converted to new review format.

CONTRIBUTIONS OF AUTHORS

James Keenan (JVK), Zbys Fedorowicz (ZF) and Tim Newton (TN) were responsible for: data collection for the review; screening search results; screening retrieved papers against inclusion criteria; appraising quality of papers; extracting data from papers; obtaining and screening data on unpublished studies; entering data into RevMan; analysis and interpretation of data; and writing the review.

ZF was responsible for: organising retrieval of papers; writing to authors of papers for additional information; and providing additional data about papers.

JVK and ZF were responsible for: designing and co-ordinating the review; data management for the review; and performing previous work that was the foundation of current study.

ZF conceived the idea for the review and will also be the guarantor for the review.

DECLARATIONS OF INTEREST

There are no financial conflicts of interest and the review authors declare that they do not have any associations with any parties who may have vested interests in the results of this review.

INDEX TERMS

Medical Subject Headings (MeSH)

Analgesics [therapeutic use]; Anti-Bacterial Agents [*therapeutic use]; Penicillins [therapeutic use]; Pulpitis [*drug therapy]; Randomized Controlled Trials as Topic; Toothache [drug therapy]

MeSH check words

Humans