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Antibiotics to reduce post-tonsillectomy morbidity (Review)

Dhiwakar M, Clement WA, Supriya M, McKerrow W

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TABLE OF CONTENTS

[Intervention Review]

Antibiotics to reduce post-tonsillectomy morbidity

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ABSTRACT

Background

This is an update of a Cochrane Review first published in *The Cochrane Library* in Issue 2, 2008 and previously updated in 2010.

Tonsillectomy continues to be one of the most common surgical procedures performed in children and adults. Despite improvements in surgical and anaesthetic techniques, postoperative morbidity, mainly in the form of pain, remains a significant clinical problem. Postoperative bacterial infection of the tonsillar fossa has been proposed as an important factor causing pain and associated morbidity, and some studies have found a reduction in morbid outcomes following the administration of perioperative antibiotics.

Objectives

To determine whether perioperative antibiotics reduce pain and other morbid outcomes following tonsillectomy.

Search methods

We searched the Cochrane Ear, Nose and Throat Disorders Group Trials Register; the Cochrane Central Register of Controlled Trials (CENTRAL); PubMed; EMBASE; CINAHL; Web of Science; BIOSIS Previews; Cambridge Scientific Abstracts; ICTRP and additional sources for published and unpublished trials. The date of the most recent search was 20 March 2012.

Selection criteria

All randomised controlled trials examining the impact of perioperative administration of systemic antibiotics on post-tonsillectomy morbidity in children or adults.

Data collection and analysis

Two authors independently collected data. Primary outcomes were pain, consumption of analgesia and secondary haemorrhage (defined as significant if patient re-admitted, transfused blood products or returned to theatre, and total (any documented) haemorrhage). Secondary outcomes were fever, time taken to resume normal diet and activities and adverse events. Where possible, we generated summary measures using random-effects models.

Main results

Ten trials, comprising a pooled total of 1035 participants, met the eligibility criteria. Most did not find a significant reduction in pain with antibiotics. Similarly, antibiotics were mostly not shown to be effective in reducing the need for analgesics. Antibiotics were not associated with a reduction in significant secondary haemorrhage rates (risk ratio (RR) 0.49, 95% CI 0.08 to 3.11, P = 0.45) or total secondary haemorrhage rates (RR 0.90, 95% CI 0.56 to 1.44, P = 0.66). With regard to secondary outcomes, antibiotics reduced the proportion of patients with fever (RR 0.63, 95% CI 0.46 to 0.85, P = 0.002).

Authors' conclusions

The present systematic review, including meta-analyses for select outcomes, suggests that although individual studies vary in their findings, there is no evidence to support a consistent, clinically important impact of antibiotics in reducing the main morbid outcomes following tonsillectomy (i.e. pain, need for analgesia and secondary haemorrhage rates). The limited benefit apparent with antibiotics may be a result of positive bias introduced by several important methodological shortcomings in the included trials. Based on existing evidence, therefore, we would advocate against the routine prescription of antibiotics to patients undergoing tonsillectomy. Whether a subgroup of patients who might benefit from selective administration of antibiotics exists is unknown and needs to be explored in future trials.

PLAIN LANGUAGE SUMMARY

Antibiotics to reduce pain and improve recovery following tonsillectomy

Tonsillectomy is a commonly performed operation in children and adults. Following the operation nearly all patients experience significant pain, need regular painkillers and are unable to resume normal diet and activities for several hours. Rarer but more dangerous complications, such as bleeding from the operated area, also occur. Antibiotics are commonly prescribed to reduce some or all of these undesirable consequences of tonsillectomy.

The present review, however, suggests that antibiotics do not reduce pain, the need for painkillers or bleeding. They do, however, appear to reduce fever. This relatively minor benefit is more likely to be due to weaknesses in the studies themselves than any direct antibiotic effect. The risk of adverse events, such as skin rash and diarrhoea, is also slightly higher in patients who were prescribed antibiotics. Therefore, in the absence of clear-cut and significant benefit, and with the potential for harm, we advocate against prescribing antibiotics routinely for patients undergoing tonsillectomy.

BACKGROUND

This is an update of a Cochrane Review first published in *The Cochrane Library* in Issue 2, 2008 and previously updated in 2010.

Tonsillectomy continues to be one of the most common surgical procedures performed in children and adults. Despite improvements in surgical and anaesthetic techniques, postoperative morbidity remains a significant clinical problem. The most common problems encountered in the postoperative period include pain, which is almost universal, and the consequent need for analgesics, as well as the inability to resume normal diet and activity for a few hours to several days. Post-tonsillectomy pain has been estimated to last well beyond the first week in the majority of patients, and the resultant economic and social costs are considerable (Salonen 2002). Furthermore, the incidence of postoperative haemorrhage in various studies ranges from 2% to 40% depending on the definition of haemorrhage (Evans 2003; Lowe 2004; Wei 2000) and this may incur additional morbidity in the form of readmission, blood transfusion and return to theatre for haemostasis. Several adjuvant techniques such as administration of potent systemic analgesics, local infiltration with anaesthetic and topical analgesic sprays have all been studied, but their efficacy remains to be proven (Dhiwakar 2005; Hollis 1999).

After tonsillectomy the tonsillar bed heals by secondary intention and is contaminated by bacteria normally present as commensals in the oropharyngeal mucosa (Telian 1986). Several authors argue that this predisposes the patient to an inflammatory reaction and infection and contributes to postoperative morbidity. They therefore recommend prophylactic antibiotics to reduce the morbidity (Colreavy 1999; Grandis 1992; Telian 1986); their routine perioperative administration is frequent and has been well established for decades in otolaryngology practice (Kay 2003; Krishna 2004). However, there is considerable variation in practice worldwide: a recent study from the UK showed that only 12% of otolaryngologists routinely prescribe antibiotics (Dhiwakar 2005), while another study showed a figure of 79% among American otolaryngologists (Krishna 2004). Those who favour routine administration of antibiotics cite decreased pain, decreased inflammation and faster healing as the most common reasons (Krishna 2004). Other authors, however, do not favour routine antibiotic administration, citing a lack of evidence to support a direct causal link between infection and postoperative morbidity (Cannon 1996; O'Reilly 2003), hence the subject remains contentious. Furthermore, while traditionally secondary haemorrhage is attributed to infection and in such patients antibiotics are prescribed (Pavelic 1960), it is unclear if a causal relationship exists and whether or not antibiotics reduce the risk.

Due to the high potential for contamination by commensals, culture results of the tonsillar bed are difficult to interpret. Hence the definition and incidence of post-tonsillectomy infection are unclear. Clinically worsening pain, continuing inability to resume diet and raised temperature are considered features of infection and these patients are typically administered antibiotics (Murthy 1998). However, it is unclear whether infection contributes to postoperative morbidity in all or a majority of patients, what the risk factors for infection are and whether they are different for adults and children. The role of routine antibiotics therefore remains unclear. For transurethral resection of the prostate, which is analogous to tonsillectomy in that tissue resection leaves denuded mucosa to heal by secondary intention in a bacterial milieu, a recent systematic review suggests that antibiotic prophylaxis improves some outcomes such as high fever and bacteraemia (Qiang 2005). A systematic review is similarly required to evaluate the effectiveness of antibiotics in reducing post-tonsillectomy morbidity. Furthermore, while individual trials might not be sufficiently large, a meta-analysis would potentially have sufficient power to determine whether antibiotics reduce rarer complications such as secondary haemorrhage.

OBJECTIVES

To determine whether perioperative antibiotics reduce pain, associated morbidity and complications following tonsillectomy.

METHODS

Criteria for considering studies for this review

Types of studies

Only randomised controlled trials (blinded and unblinded).

Types of participants

Patients undergoing tonsillectomy or adenotonsillectomy. Where explicitly stated we excluded patients undergoing the following procedures: unilateral tonsillectomy, tonsillar biopsy, tonsillectomy for known carcinoma, tonsillectomy in conjunction with palatal surgery and 'hot' tonsillectomy for peritonsillar abscess.

Types of interventions

We included trials in which an antibiotic was administered as a study medication intraoperatively and/or postoperatively in patients undergoing tonsillectomy or adenotonsillectomy. We also considered for inclusion trials in which an antibiotic was administered within the 48-hour preoperative period. We excluded trials in which the antibiotic was administered topically, or where explicitly stated more than 48 hours before surgery, from the review.

Patients in whom an antibiotic was administered as a study medication (cases) were compared to patients not given an antibiotic (controls).

Types of outcome measures

Primary outcomes

1. Pain.
2. Consumption of analgesia.
3. Secondary haemorrhage using two parameters: significant haemorrhage (i.e. warranting re-admission, blood transfusion or return to theatre for haemostasis) and total (any documented) haemorrhage.

Secondary outcomes

1. Fever.
2. Time taken to resume normal diet and activities.
3. Adverse events such as rash, anaphylaxis, candidiasis and diarrhoea.

Where possible we used standardised and validated scales (such as visual analogue for pain) for outcome analysis. Although typically pain is reported to resolve spontaneously beyond the first week (Murthy 1998), we investigated whether antibiotics significantly shortened this duration or that of other morbid outcomes. We classified haemorrhage occurring within 24 hours of surgery as primary, and any haemorrhage occurring beyond this time period as secondary.

Search methods for identification of studies

We conducted systematic searches for randomised controlled trials. There were no language, publication year or publication status restrictions. The date of the last search was 20 March 2012 following previous searches in 2010, 2007 and 2005.

Electronic searches

We searched the following databases from their inception for published, unpublished and ongoing trials: the Cochrane Ear, Nose and Throat Disorders Group Trials Register; the Cochrane Central Register of Controlled Trials (CENTRAL, *The Cochrane Library*, 2012, Issue 3); PubMed; EMBASE; CINAHL; LILACS; KoreaMed; IndMed; PakMediNet; CAB Abstracts; Web of Science; BIOSIS Previews; ISRCTN; ClinicalTrials.gov; ICTRP; Google Scholar and Google.

We modelled subject strategies for databases on the search strategy designed for CENTRAL. Where appropriate, we combined subject strategies with adaptations of the highly sensitive search strategy designed by the Cochrane Collaboration for identifying randomised controlled trials and controlled clinical trials (as described in the *Cochrane Handbook for Systematic Reviews of Interventions* Version 5.1.0, Box 6.4.b. (Handbook 2011)). Search strategies for the major databases including CENTRAL are provided in Appendix 1.

Searching other resources

We scanned reference lists of identified studies for further trials. We searched PubMed, TRIPdatabase, The Cochrane Library, and Google to retrieve existing systematic reviews possibly relevant to this systematic review, in order to search their reference lists for additional trials.

Data collection and analysis

Study selection

From all identified studies, two authors (MD and MS) independently selected trials for possible inclusion. We initially assessed all trials examining the impact of systemic antibiotics on post-tonsillectomy morbidity and randomised controlled trials were included in the review. The senior author (WM) resolved any disagreement in study selection.

Quality assessment

Two authors (MD and AC) independently assessed studies included in the review for quality. We assessed four components of quality.

1. Adequacy of randomisation (randomisation sequence generation, allocation concealment and implementation)

Trials were scored as follows.
Grade A: all three sub-components adequately fulfilled.
Grade B: adequate allocation concealment, but one or both of the other sub-components unsatisfactory.
Grade C: unclear allocation concealment.
Grade D: clearly inadequate concealment.
(Grade A, B = high quality).

2. Blinding

Trials were scored as follows.
Grade A: participant and care provider and outcome assessor blinded.
Grade B: outcome assessor blinded.
Grade C: unclear.
Grade D: no blinding of outcome assessor.
(Grade A = high quality).

3. Reporting of participants by allocated group (intention-to-treat analysis)

Trials were scored as follows.
Grade A: the progress of all randomised patients in each group described.
Grade B: unclear or no mention of withdrawals or drop-outs.
Grade C: the progress of all randomised patients in each group clearly not described.
(Grade A = high quality).

4. Follow-up

Trials were scored as follows.
Grade A: outcomes measured in > 90%.
Grade B: outcomes measured in 80% to 90%.
Grade C: unclear.
Grade D: outcomes measured in < 80%.
(Grade A = high quality).

We then gave studies an overall quality grading:

A: Minimisation of bias (i.e. high quality) in all four components above.
B: Less than high quality (but not lowest quality) in one or more of the components above.
C: Lowest quality in one or more of the components above.

Where necessary, we contacted the principal author of the relevant trial for additional information regarding methodology and/or results. The senior author (WM) resolved any disagreement.

We examined any actual or potential conflicts of interest in the included trials (such as whether sponsored by a drug company). We also noted whether surgical and anaesthetic techniques were controlled and exclusion criteria explicitly applied, but this did not necessarily serve to include/exclude trials.

Data extraction

Two authors independently extracted data (MD and AC) and separately entered these into a specific, pre-designed pro forma. One author (MD) then entered data into RevMan (RevMan 2011) for analysis.

Data analysis

For continuous outcomes, we extracted mean and standard deviation (SD) values to facilitate meta-analysis. If mean and/or SD values were not explicitly stated, we used raw data, t values, P values and/or graphs to generate mean/SD values. For

dichotomous outcomes, we converted percentage values to the nearest number for meta-analysis.

If insufficient data were available, we considered children and adults together for outcome analysis. If an eligible trial did not evaluate or report any of the outcomes detailed above, we excluded that trial from the analysis of that particular outcome. We attempted intention-to-treat analysis, wherein all participants randomised into a trial, irrespective of which (or how much) treatment they actually received and regardless of other protocol irregularities such as ineligibility, were included for analysis.

Statistics

We calculated summary measures where possible for combinable data. Given the expected variability in participants, interventions, outcomes studied and trial design and quality, we used DerSimonian and Laird random-effects models to generate summary measures. For rarer outcomes, such as secondary haemorrhage and adverse events, if sufficient numbers of patients were not available, we calculated number needed to treat or number needed to harm as appropriate. We used RevMan version 5.1 (RevMan 2011) for the analysis.

RESULTS

Description of studies

Of the 120 abstracts retrieved from our original searches in 2007 and update searches in 2009, we excluded 98 as these were incomplete trials, did not examine post-tonsillectomy morbidity, did not include patients undergoing tonsillectomy, studied topical antibiotics, studied 'hot' tonsillectomy for peritonsillar abscess, compared one systemic versus another systemic antibiotic, or did not have a control group. Seven further studies (Al-Tamimi 2000; Aslam 1998; Lackmann 1992; Lee 1996; Minet 1978; Szmeja 1997; Udaipurwala 2002) were excluded after review as they were non-randomised trials. We excluded two further trials (Akbas 2004; Inci 2009) as they compared systemic versus topical antibiotics. We excluded three further studies due to failure to complete study (Browning 1995) or unavailability of complete study copies (Novais 2003; Udaipurwala 2004).

We again updated the searches in March 2012. In total the searches retrieved 104 references; this number dropped to 85 once duplicates were removed. We screened the titles and abstracts of the 85 references and looked at five potentially relevant references in detail, however none were eligible for inclusion in the review. One had already been excluded at a previous update of the review (Inci 2009); we excluded Zagolski 2012 because tonsillotomy with incision of the tonsil was performed instead of tonsillectomy; Dawar 2011 was excluded as it was a non-randomised trial and Miura 2009 was excluded as it assessed the efficacy of a topical antibiotic. Details of Khalil 2004 are awaited from the authors (see Characteristics of ongoing studies).

The summaries of all excluded studies are shown in the table Characteristics of excluded studies.

Ten randomised controlled trials examining the impact of systemic antibiotics on post-tonsillectomy morbidity fulfilled the eligibility criteria and were included for analysis. The characteristics of these trials are set out in the table Characteristics of included studies. All studies compared a short course of systemic antibiotics versus placebo. Many trials included children with no explicit information about the age range, or reported children and adults together with no means to extract data separately. Hence all participants, irrespective of age, were included in the analyses.

Data extraction

No study explicitly stated standard deviation (SD) values for any continuous outcome measure. Raw data were available from bar graphs for the outcomes reported by Cannon 1996. For the rest, the following indirect data were derived to facilitate meta-analyses, if appropriate.

Pain

Mann 1999 reported mean pain scores for each of five days as a bar graph on a scale of 0 to 100 with standard error (SE) bars. O'Reilly 2003 used a visual analogue scale of 1 to 5 over 10 days and expressed the results as a line graph. Similarly, Grandis 1992 used a scale of 1 to 10 over seven days and expressed the results as a line graph. Colreavy 1999 similarly provided mean pain scores on a scale of 1 to 10 for seven days. Ramos gave mean pain scores on a scale of 0 to 3 (duration unclear). Guerra 2008 used a pain scale of 1 to 5 for each of the first seven postoperative days. Given the variability of parameters used in these studies and the paucity of important values such as SD, meta-analysis for pain was not possible.

Consumption of analgesics

Linden 1990 expressed subjective rating of consumption of pain medicine as a bar chart which was converted to mean scores for comparison.

Time taken to return to diet and activities

In the trial by Telian 1986, for time taken to resume normal diet and activity, pooled SDs were estimable from published mean differences, t and P values. Guerra 2008 published mean number of days (with SD) taken to resume normal diet and activities. However, Khan 1994 reported only the mean and range of the number of days taken to resume activity and oral intake, whereas Colreavy 1999 reported only the mean values of the time taken to resume normal diet. Grandis 1992 expressed the results as line graphs, from which accurate data could not be extracted. Therefore, given the variability of parameters used and paucity of important values such as SD, meta-analysis of the time taken to resume diet and activities was not possible.

Fever

Telian 1986 reported the percentage of patients manifesting fever, which was converted to the nearest number for meta-analysis.

Secondary haemorrhage

Telian 1986 excluded from analysis patients who were non-compliant or suffered complications. However details of secondary haemorrhage were available for the excluded patients. Hence we performed an intention-to-treat analysis for the meta-analysis of secondary haemorrhage, imputing an equal number of treatment and control group patients (N = 50 each).

Risk of bias in included studies

Of the 10 included trials, none attained quality grading A. One (Telian 1986) attained quality grading B. In this trial, all components

attained the highest quality except for randomisation, wherein allocation concealment was unclear. The rest attained a quality grading of C. However, the trial by O'Reilly 2003 attained the highest quality grading in all components, except for follow-up, wherein the drop-out rate was high at 52%.

Effects of interventions

Pain

Of the six studies that assessed pain using linear pain scores (Colreavy 1999; Grandis 1992; Guerra 2008; Mann 1999; O'Reilly 2003; Ramos 2000), only one (Colreavy 1999) found a significant reduction with antibiotics. Khan 1994 calculated the mean number of days with sore throat (10.3 in antibiotic group versus 11 in control group) and otalgia (8.1 versus 7.8), and found no significant difference. However, Guerra 2008, while assessing pain each day during the first postoperative week, found a significant reduction with antibiotics on day four, with no benefit on the other days. Telian 1986 found the mean number of days with continuous subjective pain to be improved with antibiotics (3.3 versus 4.4, P < 0.05). For the reasons previously mentioned, we could not perform meta-analysis for pain as an outcome.

Need for analgesia

Six studies assessed for the need for analgesics (Colreavy 1999; Grandis 1992; Guerra 2008; Khan 1994; Linden 1990; O'Reilly 2003). Four did not find a significant reduction with antibiotic use, one (Colreavy 1999) found a significant reduction, while in the last (Linden 1990) the result was indeterminate. O'Reilly 2003 reported a mean of 43% and 46% patients in the antibiotic and placebo groups, respectively, needing to consume additional analgesics. A respective mean of 63% and 51% contacted primary care physicians for analgesia. Grandis 1992 found no difference between the antibiotic and placebo groups in the mean number of days wherein more than five doses of pain medicine was taken (1.8 versus 2.4 respectively), or in the mean number of doses of pain medication (19.45 versus 19.23). Guerra 2008 reported that 79% and 88% patients in the antibiotic and control groups respectively required analgesic medication with no statistical difference between the groups. Similarly Khan 1994 calculated the number of days taken until no analgesia was needed and found no significant difference (8.2 versus 8.5). However Colreavy 1999 found a significant reduction in analgesic consumption with antibiotics. The antibiotic group consumed on average 112 mg/kg of paracetamol in 24 hours as opposed to the control group which used on average 200 mg/kg in the same period (P = 0.038). Given the variability in the parameters used, we could not perform meta-analysis for analgesic consumption.

Postoperative haemorrhage

Seven studies evaluated postoperative haemorrhage and reported incidence rates (Colreavy 1999; Grandis 1992; Guerra 2008; Khan 1994; Mann 1999; O'Reilly 2003; Telian 1986). Where not clear, correspondence with the first author of the relevant trials clarified the distinction between significant and insignificant but documented haemorrhage. Cannon 1996 reported that the rate of postoperative haemorrhage was the same in both groups, but did not give the exact incidence rates. We therefore excluded this trial from the meta-analyses for haemorrhage. There was only one primary haemorrhage reported among all seven trials (in the control group in the trial Khan 1994). No fatality occurred and no bleeding event re-occurred in the same patient.

Among a total of 567 participants, 14 (2.5%) significant and 70 (12.3%) total secondary haemorrhages occurred. This is comparable to rates cited in the literature (Krishna 2001; Lowe 2004).

Total secondary haemorrhage

We combined data from the seven studies in a meta-analysis for total secondary haemorrhage. We deemed pooling appropriate because the outcome parameters used fulfilled the predefined criteria, precise incidence rates were available and there was excellent overlap of confidence intervals in the forest plot. Meta-analysis confirmed that antibiotics did not reduce the total secondary haemorrhage rate (risk ratio (RR) 0.90, 95% confidence interval (CI) 0.56 to 1.44, P = 0.66) (Analysis 1.1). The I^2 statistic revealed minimal heterogeneity.

Significant secondary haemorrhage

With regard to significant secondary haemorrhage, the incidence rate was lower; in fact it was zero in several studies. Confidence intervals were therefore wider and could be derived only for a limited set of data. Nevertheless, the outcome parameter used fulfilled the predefined criteria, which were more rigid than for total haemorrhage, precise outcome data were available and there was good overlap of confidence intervals in the forest plot. Therefore, despite moderate heterogeneity demonstrated by the I^2 statistic (54%), we combined data in a meta-analysis. This confirmed that antibiotics did not reduce significant secondary haemorrhage rates (RR 0.49, 95% CI 0.08 to 3.11, P = 0.45) (Analysis 2.1). However, unlike for total secondary haemorrhage, the data for significant secondary haemorrhage may be underpowered to detect any difference.

Fever

Two studies (Grandis 1992; Telian 1986) used the same parameter (temperature > 99.9 °F) to define fever. Both measured the outcome for the first seven days following surgery. We therefore combined these data in a meta-analysis, which revealed antibiotics to reduce the number of patients manifesting fever (RR with antibiotics 0.63, 95% CI 0.46 to 0.85, P = 0.002) (Analysis 3.1). There was no heterogeneity (I^2 statistic = 0%), excellent overlap of the confidence intervals and unidirectional outcomes. Telian 1986 also reported a significant reduction in the mean number of oral temperature recordings more than 100 °F (1.5 versus 2.9, P < 0.05) and more than 101.5 °F (0.02 versus 0.23, P < 0.05), with use of antibiotics. Similarly, Cannon 1996 reported a significant reduction in the number of patients with fever (> 99 °F, 6 versus 16, P = 0.003). Grandis 1992 reported reduction in the mean number of days with fever (> 99.9 °F) (0.35 versus 0.51, P > 0.05). On the contrary, Guerra 2008 reported no difference in the percentage of patients in the antibiotic and control groups having fever (48% versus 49%); Ramos 2000 reported mean of subjective intensity of fever on a scale of 0 to 3, and found no difference (0 versus 0.2); and Mann 1999 reported no significant difference in postoperative fever (no data available).

Time taken to resume diet

Seven studies analysed the time taken to resume normal or soft diet (Cannon 1996; Colreavy 1999; Grandis 1992; Guerra 2008; Khan 1994; Mann 1999; Telian 1986). Three found a significant reduction

with antibiotics. Colreavy 1999 reported a mean reduction of 2.4 days (P = 0.007) and Telian 1986 reported a mean reduction of one day (P < 0.01), while Grandis 1992 did not quantify the reduction in time. However the other four studies (Cannon 1996; Guerra 2008; Khan 1994; Mann 1999) reported no significant benefit with antibiotics. Given the variability in the parameters used, we could not perform meta-analysis for time taken to resume diet.

Time taken to resume normal activity

Six studies analysed the time taken to resume normal activity (Cannon 1996; Grandis 1992; Guerra 2008; Khan 1994; Mann 1999; Telian 1986). Two studies reported earlier return to activity with antibiotics. Telian 1986 reported a mean reduction of one day (P < 0.05), while Grandis 1992 did not quantify the reduction in time (P = 0.045). However, the other four trials (Cannon 1996; Guerra 2008; Khan 1994; Mann 1999) reported no significant benefit with antibiotics. Given the variability in the parameters used, we could not perform meta-analysis for time taken to resume normal activity.

Adverse effects

There was no major adverse event reported in either group. With regard to minor adverse events, in the antibiotic group there were four cases manifesting a rash (in the trials by Colreavy 1999; Grandis 1992; Mann 1999 and Telian 1986), one developed oropharyngeal candidiasis (Telian 1986) and four developed diarrhoea (three in the trial by Grandis 1992 and one in the trial by Colreavy 1999). In comparison, in the control group one patient developed a rash and two others had diarrhoea (all in the trial by Grandis 1992). The RR of adverse effects with antibiotic use was 2.06 (95% CI 0.68 to 6.27, P = 0.20) (Analysis 4.1). The number needed to treat to harm for antibiotics was 26.

DISCUSSION

The present systematic review suggests that although individual studies vary in their findings, there is no evidence to support a consistent, clinically important impact of antibiotics in reducing the main morbid outcomes following tonsillectomy (i.e. pain, need for analgesia and secondary haemorrhage rates). There is some evidence to suggest that antibiotics may reduce fever. With regard to other secondary outcomes, such as time taken to resume normal diet and activity, there is no clear evidence that antibiotics are beneficial.

These results challenge the widely held rationale for the routine prescription of antibiotics. A causal relationship between bacterial inflammation of the tonsillar fossa and postoperative morbidity, such as pain, need for analgesia and secondary haemorrhage, has not been proven. The difficulty of establishing such a correlation is complicated by the variety of commensals harboured in the oropharyngeal mucosa. This renders bacterial culture results of the postoperative tonsillar fossa as reported in a few studies (Colreavy 1999; Grandis 1992; Telian 1986) difficult to interpret. While some studies show that antibiotics reduce the bacterial count in the postoperative tonsillar fossa (Colreavy 1999; Grandis 1992), a clinical correlation in terms of reduction in morbidity is lacking. This suggests that other proposed mechanisms, such as surgical trauma to the peritonsillar tissues (Parsons 2006; Stoker 2004), ensuing inflammatory response to tissue damage (Akbas 2004), loss of pharyngeal mucosa with exposed muscle and nerve endings (D'Eredita 2004), and ensuing nerve irritation and spasm of the pharyngeal muscles (Akbas 2004) account for postoperative pain and morbidity, with minimal or nil additional morbidity conferred by bacterial inflammation.

Similarly, secondary haemorrhage is widely assumed to be caused by bacterial infection (Pai 2005; Timms 2002) and is commonly treated with antibiotics, despite scant evidence to support an infective aetiology (Pai 2005). Kumar found that of 24 patients with secondary post-tonsillectomy haemorrhage who were not on antibiotics, only four had a positive culture on throat swab (Kumar 1984). The current review similarly fails to show that antibiotics protect against secondary haemorrhage and therefore bacterial infection as an aetiology is questionable. A more plausible explanation is that sloughing of the primary eschar, which usually occurs between day five and day 10 in the postoperative period, manifests as secondary haemorrhage (Krishna 2001). Further support for this theory comes from the large prospective audit of tonsillectomies conducted in England, in which diathermy dissection was found to increase the risk of secondary haemorrhage. The authors conclude that compared to traditional cold steel, diathermy dissection causes more tissue damage and hence a larger eschar formation, thus conferring a higher risk of secondary haemorrhage (Lowe 2004).

Reduction of fever apparent with antibiotic therapy is likely due to the amelioration of bacteraemia, which is recognised to occur during and immediately after tonsillectomy (Soldado 1998). However, given the varying parameters used, no quantification of the reduction in fever is possible and the overall clinical benefit derived is unclear.

The potential for adverse events needs to be considered while prescribing antibiotics. Antibiotic allergy is unpredictable and not dose dependent (Gruchalla 2000), therefore it is difficult to quantify the risk of allergy in an individual patient precisely (Robinson 2002). The overall frequency of allergy to beta-lactam antibiotics such as penicillin is cited as 2% per course (Saxon 1987). However, a history of allergy to penicillin is elicited in 5% to 20% of the population (Adkinson 1998). In this population, the risk of allergy is as high as 60% on re-exposure to beta-lactams (Green 1977) and 13% on exposure to a different antibiotic (Moseley 1991). Further, although no major adverse event has been reported in the included trials in this review, anaphylaxis is estimated to occur in 0.01% to 0.05% of all penicillin courses (Greenberger 2002). Given the frequency and volume of tonsillectomy as a surgical procedure, this small risk of minor and major allergic events may translate into significant harm when balanced against the lack of evidence to support a consistent, clinically important impact of antibiotics. However non-allergic adverse events such as toxicity, side effects and drug interactions may be minimised by reducing the dose or length of treatment, i.e. single perioperative administration (Gruchalla 2000).

Limitations

The main limitation of this review is the weak methodology of the included trials. First, allocation concealment, the most important criterion in the randomisation process, was adequate in only one trial (O'Reilly 2003). Studies with inadequate allocation concealment may overestimate treatment effect by 37% (Moher 1998). Second, only five out of the 10 included trials had adequate double-blinding. Unblinded trials are well known to produce bias favouring treatment (Noseworthy 1994; Schulz 2002), particularly so when subjective outcomes such as pain are assessed (Schulz 2002). Third, intention-to-treat analysis was possible in only two

trials (O'Reilly 2003; Telian 1986). There is some evidence to suggest that meta-analyses of trials which do not report all participants by allocated group (i.e. inadequate intention-to-treat analysis) produce results favouring the treatment (Tierney 2004). It is likely that all these shortcomings have aggregated to produce significant bias favouring antibiotics. Finally, the overall drop-out rate was high. This leaves a large potential for attrition bias, despite a comparable number being lost to follow-up, within each trial, between the study and control groups.

There is also considerable heterogeneity between studies in terms of methodological quality, participants, interventions (type, dose, method and duration of administration of antibiotics) and outcome assessment. This is, however, unlikely to have significantly impacted on the results of this review, as results from individual trials broadly conform to one another, and to the results of meta-analyses, where done. It is, however, not known if the dosage and antibacterial spectrum of antibiotics used in the trials have been adequate or if there exists a dose-response effect. Further, it was not possible to analyse data stratified on the basis of indications for tonsillectomy (i.e. sleep apnoea, recurrent tonsillitis, etc.). Hence it is not clear whether a subgroup of patients exists (i.e. severe recurrent tonsillitis or peritonsillar abscess) in whom antibiotics might reduce morbidity.

Conclusion

The present review including meta-analyses for select outcomes suggests that there is no evidence to support a consistent, clinically important impact of antibiotics in reducing the main morbid outcomes following tonsillectomy (i.e. pain, need for analgesia and secondary haemorrhage rates). Any limited benefit apparent with antibiotics may be a result of positive bias introduced by several important methodological shortcomings in the included trials. Any putative benefit of antibiotics also needs to be carefully weighed against the risk of adverse events and other negative consequences that are more difficult to evaluate and quantify, such as the possible emergence of resistant bacteria and fungal colonisation and infection.

Based on this review, therefore, we advocate against prescribing antibiotics routinely to all patients undergoing tonsillectomy. Whether a subgroup of patients who might benefit from selective administration of antibiotics exists is unknown and needs to be explored in future trials. Further well-designed trials are recommended to confirm and expand our findings. In future studies, continuous outcome values need to be explicitly stated with mean and SD in order to facilitate meta-analyses.

AUTHORS' CONCLUSIONS

Implications for practice

Antibiotics should not be routinely administered to reduce postoperative morbidity in patients undergoing tonsillectomy.

Implications for research

Whether a subgroup of patients who might benefit from selective administration of antibiotics exists is unknown and needs to be explored in future trials. Further well-designed trials are recommended to confirm and expand our findings. In future studies, continuous outcome values need to be explicitly stated with mean and standard deviation in order to facilitate meta-analyses.

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CHARACTERISTICS OF STUDIES

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

Cannon 1996

Methods	Randomised, double-blind, placebo-controlled study conducted in USA; number of centres involved in study unclear

Cannon 1996 *(Continued)*

	Grading of quality: Randomisation = C Blinding = A Intention-to-treat analysis = C Follow-up = A Overall quality grading = C
Participants	50 children and adults (age range 13 to 40 years) undergoing tonsillectomy primarily for recurrent tonsillitis. Study and control groups were well matched in terms of age, sex and number of episodes of tonsillitis prior to surgery. Exclusion criteria: antibiotic administered within 1 week preoperatively, medical condition requiring perioperative antibiotic therapy, or allergy to antibiotic studied
Interventions	Cefonicid, IV 1 g before initiation of surgery
Outcomes	Primary outcome: consumption of analgesics (number of doses of Tylenol with codeine) Secondary outcomes: fever (number of patients with fever, defined as temperature > 99 °F) and number of days required to resume soft diet and activities Period of observation: 7 days
Notes	Anaesthetic technique was not mentioned as controlled. Surgical technique was controlled, with all patients undergoing dissection and snare of the tonsils with electrocautery for haemostasis. Follow-up: 46 (92%) patients (24 in antibiotic and 22 in control groups) completed follow-up

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment (selection bias)	Unclear risk	B - Unclear

Colreavy 1999

Methods	Single-centre, randomised controlled trial conducted in Ireland Grading of quality: Randomisation = C Blinding = D Intention-to-treat analysis = C Follow-up = D Overall quality grading = C
Participants	78 children (2 to 12 years, mean 6.2 years) undergoing tonsillectomy with or without other lesser surgical procedures (indication not specified). Study and control groups well matched in terms of age and sex. Exclusion criteria: antibiotic administered within 1 week preoperatively, medical condition requiring perioperative antibiotic therapy, or allergy to antibiotic studied
Interventions	1ne week of oral amoxicillin + clavulanic acid, dosage according to the British National Formulary (1996 edition)

Colreavy 1999 *(Continued)*

Outcomes	Primary outcomes: pain (visual analogue score (0 = little or no pain, 10 = unbearable pain)) and analgesic consumption Secondary outcomes: number of days to resume normal diet Period of observation: 7 days
Notes	Anaesthetic technique mentioned as controlled, but no details given. Similarly, surgical technique was controlled, with all patients undergoing bipolar diathermy extracapsular dissection and haemostasis with bismuth subgallate and bipolar diathermy. Follow-up: 54 (69%) patients completed follow-up

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment (selection bias)	Unclear risk	B - Unclear

Grandis 1992

Methods	Single-centre, randomised, double-blind, placebo-controlled study conducted in USA Grading of quality: Randomisation = C Blinding = A Intention-to-treat analysis =C Follow-up = D Overall quality grading = C
Participants	198 adults and children aged 12 to 48 (mean 21.7) years undergoing tonsillectomy or adenotonsillectomy (indication not specified). Study and control groups were well matched with regard to age, sex and adenoidectomy (18 versus 14 respectively). Exclusion criteria: antibiotic administered within 1 week preoperatively, medical condition requiring perioperative antibiotic therapy, or allergy to antibiotic studied
Interventions	Ticarcillin + clavulanic acid, IV 3.1 g at completion of surgery, 6 and 12 hours after surgery; followed by amoxicillin + clavulanic acid 250 mg tds oral for 7 days
Outcomes	Primary outcomes: pain (scale of 1 to 10, 10 being most severe) and consumption of analgesics Secondary outcomes: fever (temperature > 99.9 °F) and return to regular diet (scale of 1 to 3; 1 = regular, 2 = soft, 3 = liquid) and activities (1 = normal, 2 = moderate, 3 = bed rest) Period of observation: 7 days
Notes	Anaesthetic and surgical techniques not mentioned as being controlled Follow-up: only 101 (51%) patients (51 in antibiotic and 50 in control groups) completed follow-up

Risk of bias

Bias	Authors' judgement	Support for judgement

Grandis 1992 *(Continued)*

Allocation concealment (selection bias)	Unclear risk	B - Unclear

Guerra 2008

Methods	Randomised, controlled, single-centre study conducted in Brazil Grading of quality: Randomisation = C Blinding = C Intention-to-treat analysis = B Follow-up = D Overall quality grading = C
Participants	120 children aged 14 years or less undergoing adenotonsillectomy. Study and control groups were well matched in terms of age and sex.
Interventions	Postoperative amoxicillin 50 mg/kg/day for 7 days
Outcomes	Primary outcomes: pain, analgesic consumption and secondary haemorrhage Secondary outcomes: fever and time taken to resume normal diet and activities Period of observation: 7 days
Notes	Exclusion criteria: allergy to amoxicillin or haematological disorder. Surgical technique was controlled: all patients underwent dissection, with no use of electrocautery, anaesthetic technique not mentioned as controlled. Follow-up: 95 (%) patients (43 in the antibiotic group and 52 in the control group) completed follow-up

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment (selection bias)	Unclear risk	B - Unclear

Khan 1994

Methods	Single-centre, randomised controlled trial conducted in UK Grading of quality: Randomisation = C Blinding = D Intention-to-treat analysis = C Follow-up = B Overall quality grading = C
Participants	90 children and adults, age range 6 to 36 years, undergoing tonsillectomy for recurrent tonsillitis. Study and control groups well matched with regard to age, sex, episodes of tonsillitis within previous 6 months and history of quinsy.

Khan 1994 *(Continued)*

	Exclusion criteria: poor general medical condition, history of adverse drug reactions including penicillin allergy or presence of concomitant ear nose throat pathology
Interventions	One IV dose of amoxicillin (appropriate to age and body weight) at the time of induction, and 2 further oral postoperative doses at 6 and 12 hours (age 6 to 10 years: 125 mg; 10 to 16: 250 mg; over 16: 500 mg)
Outcomes	Primary outcomes: pain (number of days until no sore throat and otalgia), analgesia (number of days until no analgesia) and haemorrhage Secondary outcomes: time taken to resume normal activities and intake Period of observation: 14 days
Notes	Anaesthetic technique not mentioned as controlled. Surgical technique was controlled, with all patients undergoing dissection with ties for haemostasis. Follow-up: 80 (89%) patients (40 each in antibiotic and control groups) completed follow-up

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment (selection bias)	Unclear risk	B - Unclear

Linden 1990

Methods	Randomised controlled trial conducted in USA, number of centres unclear; patients initially divided into 4 groups based on surgical technique, and then further subdivided based on whether received antibiotics or not, to attain a total of 8 subgroups; study remained open until sufficient numbers were recruited and questionnaires returned Grading of quality: Randomisation = C Blinding = D Intention-to-treat analysis = C Follow-up = C Overall quality grading = C
Participants	80 children (age range 13 months to 17 years (mean: 5 years)) undergoing tonsillectomy (indication not specified). Whether children undergoing adenotonsillectomy were included was not clear. Study and control group demographics and other characters not mentioned. Exclusion criteria: not specified
Interventions	No detail regarding the type of antibiotic or the method of administration given
Outcomes	Primary outcome: analgesic consumption (mean subjective rating on a scale of 1 to 3) Period of observation: 5 days
Notes	Anaesthetic technique not mentioned as controlled. Surgical technique was quasi-controlled: 4 different surgical and haemostatic techniques in equal numbers (electrocautery + electrocautery, dissection + electrocautery, dissection + ligature, laser + laser) were used between the study and control groups. Follow-up: follow-up rate of the 40 patients recruited in each of the antibiotic and control groups unclear

Linden 1990 *(Continued)*

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment (selection bias)	Unclear risk	B - Unclear

Mann 1999

Methods	Single-centre, randomised, double-blind, placebo-controlled study conducted in USA Grading of quality: Randomisation = C Blinding = A (author correspondence confirmed dispensation of placebo as a capsule, but could not confirm if it was exactly identical to amoxicillin capsule; we believe this was adequate double-blinding) Intention-to-treat analysis = C Follow-up = D Overall quality grading = C
Participants	51 adults 18 years and above undergoing tonsillectomy for tonsillitis, peritonsillar abscess or tonsillithiasis were enrolled and randomised into 4 arms: systemic antibiotic, placebo and 2 different topical antibiotics. The 2 arms that studied topical antibiotics were unsuitable for analysis and therefore excluded, leaving 18 patients in the first 2 arms (8 in antibiotic and 10 in control arms) who completed the study. Study and control groups well-matched with regard to age and sex. Exclusion criteria: significant medical conditions (i.e. diabetes, chronic lung disease, bleeding disorders), antibiotic administered within 1 week preoperatively, medical condition requiring perioperative antibiotic therapy, or allergy to antibiotic studied
Interventions	Amoxicillin tds oral for 7 days
Outcomes	Primary outcome: pain (scale 1 to 100; 0 = no pain, 100 = severe pain) Period of observation: 5 days
Notes	Anaesthetic technique not mentioned as controlled. Surgical technique was quasi-controlled: the tonsillectomy technique is not mentioned, and instead only the haemostatic method (electrocautery) is mentioned. Follow-up: 36 (71%) of 51 patients in the whole study completed follow-up. Authors stated that the numbers lost to follow-up were evenly distributed in the 4 arms, but exact follow-up rates in the systemic antibiotic and placebo arms not available.

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment (selection bias)	Unclear risk	B - Unclear

O'Reilly 2003

Methods	Randomised, double-blind, placebo-controlled study conducted in UK; number of centres involved in study unclear

O'Reilly 2003 *(Continued)*

	Grading of quality: Randomisation = A (author correspondence confirmed adequacy of the randomisation process) Blinding = A Intention-to-treat analysis = A Follow-up = D Overall quality grading = C
Participants	200 adults aged 16 to 53 years undergoing tonsillectomy for non-malignant disease. Study and control groups had similar age distribution and sex ratios. Exclusion criteria: not described
Interventions	Amoxicillin IV 250 mg at induction, followed by 250 mg tds oral for 7 days
Outcomes	Primary outcomes: pain (scale of 1 to 5), additional analgesic consumption and haemorrhage Period of observation: 10 days
Notes	Anaesthetic technique not mentioned as controlled. Surgical technique was quasi-controlled, i.e. mostly electro-dissection for tonsillectomy was used. Follow-up: only 95 (48%) of 200 patients (46 in antibiotic and 49 in placebo groups) completed follow-up

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment (selection bias)	Low risk	A - Adequate

Ramos 2000

Methods	Single-centre, randomised controlled, physician-blinded trial conducted in Brazil Grading of quality: Randomisation = C Blinding = B Intention-to-treat analysis = C Follow-up = C Overall quality grading = C
Participants	58 children (age range not given) undergoing tonsillectomy (indication not specified) randomised to 29 each in the antibiotic and control groups. Study and control groups well matched with regard to age. Exclusion criteria: not specified
Interventions	Amoxicillin + clavulanic acid during and after the operative period, with dosage calculated according to weight, for 7 days. Route of administration in the perioperative period not specified.
Outcomes	Primary outcomes: pain (scale of 0 to 3; 0 = no, 1 = mild, 2 = moderate and 3 = intense) Secondary outcomes: fever (subjective intensity on a scale of 0 to 3) Period of observation: unclear

Ramos 2000 *(Continued)*

Notes	Anaesthetic technique mentioned as controlled, but no details given. Surgical technique also appears to have been controlled - the authors mention Sluder's technique as being employed in all children, but no other details are given. All surgeries were performed by a single surgeon. Follow-up: details not given

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment (selection bias)	Unclear risk	B - Unclear

Telian 1986

Methods	Single-centre, randomised, double-blind, placebo-controlled study conducted in USA Grading of quality: Randomisation = C Blinding = A Intention-to-treat analysis = A Follow-up = A Overall quality grading = B
Participants	100 children (age range not reported) undergoing tonsillectomy or adenotonsillectomy. The number of children who underwent adenoidectomy was not specified. Most underwent surgery for obstructive sleep apnoea. Study and control groups were well matched with regard to age, sex, number of infections in the past 12 months and indications for surgery. Exclusion criteria: antibiotic administered within 1 week preoperatively, medical condition requiring perioperative antibiotic therapy, or allergy to antibiotic studied
Interventions	At completion of surgery, amoxicillin IV 1 g for children weighing >= 20 kg and 500 mg for children weighing < 20 kg was administered; this was followed by equivalent doses at 6-hour intervals until discharge (usually 24 hours). After discharge oral amoxicillin was given tds for 7 days, at 250 mg tds in children weighing >= 20 kg and 125 mg for children weighing < 20 kg.
Outcomes	Primary outcomes: pain (number of days with continuous subjective pain) Secondary outcomes: fever (temperature > 99.9 °F), time taken to resume soft or usual diet and activities Period of observation: 7 to 14 days
Notes	Anaesthetic technique not mentioned as controlled. Surgical technique was controlled, with all patients undergoing dissection and snare of the tonsils with electrocautery for haemostasis. Follow-up: all patients completed follow-up and were available for analysis

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment (selection bias)	Unclear risk	B - Unclear

IV = intravenous; tds = three times a day

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

Study	Reason for exclusion
Akbas 2004	ALLOCATION: Randomised PARTICIPANTS: 60 children aged between 4 and 14 years undergoing tonsillectomy or adenotonsillectomy INTERVENTION: Compared systemic with topical antibiotic
Al-Tamimi 2000	ALLOCATION: Non-randomised
Aslam 1998	ALLOCATION: Study described as randomised, but alternate allocation was used
Browning 1995	Study not completed (registered in National Research Register (UK) in 1995)
Dawar 2011	ALLOCATION: Non-randomised
Inci 2009	ALLOCATION: Randomised PARTICIPANTS: 78 patients undergoing tonsillectomy for recurrent tonsillitis INTERVENTION: Compared systemic with topical antibiotic regimes
Lackmann 1992	ALLOCATION: Non-randomised
Lee 1996	ALLOCATION: Non-randomised
Minet 1978	ALLOCATION: Non-randomised
Miura 2009	ALLOCATION: Randomised PARTICIPANTS: 82 children aged between four and 12 years of age undergoing adenotonsillectomy INTERVENTION: Assessed the efficacy of a topical antibiotic
Novais 2003	Unable to obtain full paper
Szmeja 1997	ALLOCATION: Non-randomised; included patients undergoing otolaryngological procedures other than tonsillectomy

Study	Reason for exclusion
Udaipurwala 2002	ALLOCATION: Non-randomised
Udaipurwala 2004	Unable to obtain full paper
Zagolski 2012	ALLOCATION: Randomised PARTICIPANTS: 124 children aged 5 to 7 years with obstructive symptoms INTERVENTION: Tonsillotomy with incision of the tonsil was performed instead of tonsillectomy

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

Khalil 2004

Trial name or title	Peri-operative antibiotics in tonsillectomy patients
Methods	Randomised, placebo-controlled, parallel-group trial
Participants	Adult patients listed for tonsillectomy
Interventions	Group 1: to receive 3 doses of peri- and postoperative cefuroxime Group 2: to receive normal saline in a similar fashion
Outcomes	Visual analogue scale for pain at 24 hours, 1 week and 2 weeks Analgesia requirements at the end of 2 weeks
Starting date	1 March 2004
Contact information	Mr H Khalil, ENT Department, North Bristol NHS Trust, Southmead Hospital, Bristol, BS10 5NB
Notes	ISRCTN52345875

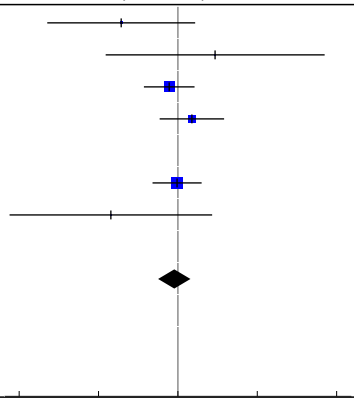
DATA AND ANALYSES

Comparison 1. Total secondary haemorrhage

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Number of patients with total secondary haemorrhage	7	567	Risk Ratio (M-H, Random, 95% CI)	0.90 [0.56, 1.44]

Analysis 1.1. Comparison 1 Total secondary haemorrhage, Outcome 1 Number of patients with total secondary haemorrhage.

Study or subgroup	Treatment n/N	Control n/N	Risk Ratio M-H, Random, 95% CI	Weight	Risk Ratio M-H, Random, 95% CI
Colreavy 1999	1/44	4/34		4.65%	0.19[0.02,1.65]
Grandis 1992	1/51	0/50		2.15%	2.94[0.12,70.56]
Guerra 2008	9/43	14/52		33.47%	0.78[0.37,1.62]
Khan 1994	9/40	6/40		22.11%	1.5[0.59,3.82]
Mann 1999	0/8	0/10			Not estimable
O'Reilly 2003	11/46	12/49		35.1%	0.98[0.48,1.99]
Telian 1986	0/50	3/50		2.51%	0.14[0.01,2.7]
Total (95% CI)	**282**	**285**		**100%**	**0.9[0.56,1.44]**
Total events: 31 (Treatment), 39 (Control)					
Heterogeneity: Tau^2=0.03; Chi^2=5.45, df=5(P=0.36); I^2=8.23%					
Test for overall effect: Z=0.44(P=0.66)					

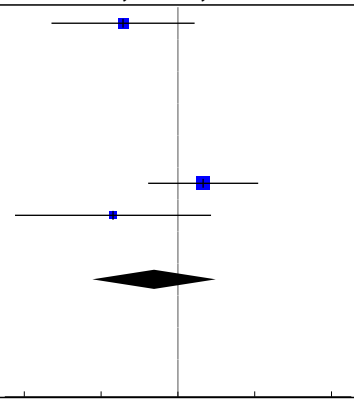


Comparison 2. Significant secondary haemorrhage

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Number of patients with significant secondary haemorrhage	7	567	Risk Ratio (M-H, Random, 95% CI)	0.49 [0.08, 3.11]

Analysis 2.1. Comparison 2 Significant secondary haemorrhage, Outcome 1 Number of patients with significant secondary haemorrhage.

Study or subgroup	Treatment n/N	Control n/N	Risk Ratio M-H, Random, 95% CI	Weight	Risk Ratio M-H, Random, 95% CI
Colreavy 1999	1/44	4/34		33.97%	0.19[0.02,1.65]
Grandis 1992	0/51	0/50			Not estimable
Guerra 2008	0/43	0/52			Not estimable
Khan 1994	0/40	0/40			Not estimable
Mann 1999	0/8	0/10			Not estimable
O'Reilly 2003	4/46	2/49		41.77%	2.13[0.41,11.08]
Telian 1986	0/50	3/50		24.27%	0.14[0.01,2.7]
Total (95% CI)	**282**	**285**		**100%**	**0.49[0.08,3.11]**
Total events: 5 (Treatment), 9 (Control)					
Heterogeneity: Tau^2=1.43; Chi^2=4.31, df=2(P=0.12); I^2=53.59%					
Test for overall effect: Z=0.76(P=0.45)					

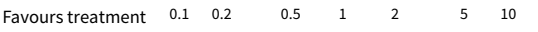


Comparison 3. Fever

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Number of patients with fever	2	186	Risk Ratio (M-H, Random, 95% CI)	0.63 [0.46, 0.85]

Analysis 3.1. Comparison 3 Fever, Outcome 1 Number of patients with fever.

Study or subgroup	Treatment n/N	Control n/N	Risk Ratio M-H, Random, 95% CI	Weight	Risk Ratio M-H, Random, 95% CI
Grandis 1992	8/51	14/50		14.92%	0.56[0.26,1.22]
Telian 1986	23/45	32/40		85.08%	0.64[0.46,0.88]
Total (95% CI)	**96**	**90**		**100%**	**0.63[0.46,0.85]**
Total events: 31 (Treatment), 46 (Control)					
Heterogeneity: Tau^2=0; Chi^2=0.11, df=1(P=0.74); I^2=0%					
Test for overall effect: Z=3.06(P=0)					

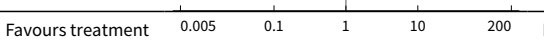


Comparison 4. Adverse events

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Number of patients with adverse events or side effects	4	282	Risk Ratio (M-H, Random, 95% CI)	2.06 [0.68, 6.27]

Analysis 4.1. Comparison 4 Adverse events, Outcome 1 Number of patients with adverse events or side effects.

Study or subgroup	Treatment n/N	Control n/N	Risk Ratio M-H, Random, 95% CI	Weight	Risk Ratio M-H, Random, 95% CI
Colreavy 1999	2/44	0/34		13.75%	3.89[0.19,78.43]
Grandis 1992	4/51	3/50		59.42%	1.31[0.31,5.55]
Mann 1999	1/8	0/10		13.11%	3.67[0.17,79.54]
Telian 1986	2/45	0/40		13.72%	4.46[0.22,90.14]
Total (95% CI)	**148**	**134**		**100%**	**2.06[0.68,6.27]**
Total events: 9 (Treatment), 3 (Control)					
Heterogeneity: Tau^2=0; Chi^2=0.96, df=3(P=0.81); I^2=0%					
Test for overall effect: Z=1.27(P=0.2)					



APPENDICES

Appendix 1. Search strategies

CENTRAL	PubMed	EMBASE
#1 TONSILLECTOMY single term (MeSH) #2 TONSIL [su] single term (MeSH) #3 tonsillectom* OR tonsilectom* #4 adenotonsillectom* OR adenotonsilectom* #5 #1 OR #2 OR #3 OR #4 #6 TONSILLITIS explode all trees (MeSH) #7 TONSIL single term (MeSH) #8 tonsil* OR peritonsil* #9 adenotonsil* #10 #6 OR #7 OR #8 OR #9 #11 SURGERY single term (MeSH) #12 surg* OR excis* OR extract* OR remov* #13 DISSECTION explode all trees (MeSH) #14 dissect* OR electrodissect* OR coblat* OR ablat* OR ultrasonic* OR harmonic* OR guillotin* OR plasma OR ultracis* #15 ion* NEAR field* OR bipolar NEAR probe* #16 DIATHERMY explode all trees (MeSH) #17 CAUTERY explode all trees (MeSH) #18 ULTRASONICS explode all trees (MeSH) #19 ELECTROSURGERY single term (MeSH) #20 electr* NEAR coagulat* OR electrocoagulat* OR electrocauter* OR electr* NEAR cauter* #21 electrosurg* OR electr* NEAR surg* OR bovie OR elmed OR somnoplast* #22 diatherm* OR thermocauter* OR thermocoagul* OR galvanocaut* #23 RADIOSURGERY single term (MeSH) #24 CRYOSURGERY single term (MeSH) #25 radiosurg* OR radiofrequenc* OR cryosurg* #26 LASER SURGERY explode all trees (MeSH) #27 LASERS single term (MeSH) #28 laser* NEAR surg* #29 #11 OR #12 OR #13 OR #14 OR #15 OR #16 OR #17 OR #18 OR #19 OR #20 OR #21 OR #22 OR #23 OR #24 OR #25 OR #26 OR #27 OR #28 #30 #10 AND #29 #31 #5 OR #30 #32 ANTI BACTERIAL AGENTS explode all trees (MeSH)	(("Tonsillectomy"[Mesh]) OR ("Palatine TOnsil/surgery"[Mesh]) OR (Search tonsillectom*[tiab] OR tonsilectom*[tiab] OR tonsillot*[tiab] OR adenotonsillectom*[tiab] OR adenotonsilectom*[tiab]) OR (("Tonsillitis"[Mesh] OR "Palatine TOnsil"[Mesh] OR tonsil*[tiab] OR peritonsil*[tiab] OR adenotonsil*[tiab]) AND (("Surgical Procedures, Operative"[Mesh]) OR (surg*[tiab] OR excis*[tiab] OR extract*[tiab] OR remov*[tiab]) OR ("Dissection"[Mesh] OR dissect*[tiab] OR electrodissect*[tiab] OR coblat*[tiab] OR ablat*[tiab] OR ultrasonic*[tiab] OR harmonic*[tiab] OR guillotin*[tiab] OR plasma[tiab] OR ultracis*[tiab]) OR ("Diathermy"[Mesh] OR "Cautery"[Mesh] OR "Ultrasonics"[Mesh] OR "Electrosurgery"[Mesh] OR "Radiosurgery"[Mesh] OR "Cryosurgery"[Mesh] OR "Laser Surgery"[Mesh] OR "lasers"[Mesh]) OR ((ion*[tiab] AND field*[tiab]) OR (bipolar[tiab] AND probe*[tiab]) OR (electr*[tiab] AND coagulat*[tiab]) OR eletrocoagulat*[tiab] OR (electr*[tiab] AND cauter*[tiab]) OR electrosurg*[tiab] OR (electr*[tiab] AND surg*[tiab]) OR bovie[tiab] OR elmed[tiab] OR somnoplasty[tiab]) OR (diatherm*[tiab] OR thermocauter*[tiab] OR thermocoagul*[tiab] OR galvanocaut*[tiab] OR radiosurg*[tiab] OR radiofrequenc*[tiab] OR cryosurg*[tiab]))))) AND (("ANTI-BACTERIAL AGENTS"[Mesh] OR "ANTIBIOTIC PROPHYLAXIS"[Mesh] OR "LACTAMS"[Mesh] OR "QUINOLONES"[Mesh] OR "MACROLIDES"[Mesh]) OR (antibiot*[tiab] OR (anti[tiab] AND biot*[tiab]) OR antimicrobial*[tiab] OR (anti[tiab]	1. TONSILLECTOMY#.DE. 2. TONSIL-DISEASE-SU#.DE. 3. (tonsillectom$3 OR tonsilectom$3).TI,AB. 4. (adenotonsillectom$3 OR adenotonsilectom$3).TI,AB. 5. 1 OR 2 OR 3 OR 4 6. TONSILLITIS#.DE. 7. TONSIL#.DE. 8. (tonsil$3 OR peritonsil$3).TI,AB. 9. adenotonsil$3.TI,AB. 10. 6 OR 7 OR 8 OR 9 11. SURGERY#.DE. 12. (surg$6 OR excis$4 OR extract$4 OR remov$3).TI,AB. 13. SURGICAL-TECHNIQUE#.DE. 14. (dissect$4 OR electrodissect$4 OR coblat$3 OR ablat$3 OR ultrasonic$4 OR ultracis$4 OR harmonic$4 OR guillotin$3 OR plasma).TI,AB. 15. (ion$1 NEAR field$1 OR bipolar NEAR probe$1).TI,AB. 16. SCALPEL.DE. 17. ULTRASOUND.DE. 18. (electr$6 NEAR coagula$4 OR electrocoagula$4 OR electrocauter$7 OR electro NEAR cauter$7).TI,AB. 19. (electrosurg$6 OR electr$6 NEAR surg$6 OR bovie OR elmed OR somnoplasty).TI,AB. 20. (diatherm$4 OR thermocauter$7 OR thermocoagula$4 OR galvanocauter$7).TI,AB. 21. (radiosurg$6 OR radiofrequenc$3 OR cryosurg $6).TI,AB. 22. laser$1 NEAR surg $6.TI,AB. 23. 11 OR 12 OR 13 OR 14 OR 15 OR 16 OR 17 OR 18 OR 19 OR 20 OR 21 OR 22 24. 10 AND 23 25. 5 OR 24 26. ANTIBIOTIC-AGENT#.DE. 27. (antibiot$3 OR anti ADJ biot$3 OR antimicrobial$2 OR anti ADJ microbial$2 OR

(Continued)

#33 ANTIBIOTIC PROPHYLAXIS single term (MeSH)
#34 LACTAMS explode all trees (MeSH)
#35 QUINOLONES explode all trees (MeSH)
#36 MACROLIDES explode all trees (MeSH)
#37 antibiot* OR anti ADJ biot* OR antimicrobial* OR anti ADJ microbial* OR bacteriocid* OR antibacterial* OR anti ADJ bacterial*
#38 penicillin* OR amoxicillin OR ampicillin OR clavulanic acid OR amoxiclav OR augmentin OR ticarcillin OR timentin OR flucloxacillin OR fluampicil OR magnapen OR piperacillin
OR tazocin
#39 cephalosporin* OR cefaclor OR distaclor OR cefadroxil OR baxan OR cefalexin OR ceporex OR keflex OR cefamandole OR kefadol OR cefazolin OR kefzol OR cefixime OR
suprax OR cefotaxime OR claforan OR cefoxitin OR mefoxin OR cefpirome OR cefrom OR cefpodoxime OR orelox OR cefprozil OR cefzil OR cefradine OR velosel OR ceftazidime
OR fortum OR kefadim OR ceftriaxone OR rocephin OR cefuroxime OR zinacef OR zinnat OR cefonicid OR aztreonam OR azactam OR imipenem OR cilastatin OR primaxin OR
meropenem or meronem or tetracycline* or deteclo or demecleocyclin or ledermycin or doxycycline or vibramycin or minocycline or minocine or oxytetracycline or terramycin
#40 macrolide* OR erythromycin OR erymax OR erythrocin OR erythroped OR azithromycin OR zithromax OR clarithromycin OR klaricid OR telithromycin OR ketek OR trimoxazole OR
septrin OR trimethoprim OR monotrim OR trimopan OR metronidazole OR flagyl OR metrolyl
#41 quinolone* OR ciprofloxacin OR ciproxin
#42 #32 OR #33 OR #34 OR #35 OR #36 OR #37 OR #38 OR #39 OR #40 OR #41
#43 #31 AND #42

AND microbial*[tiab]) OR bacteriocid*[tiab] OR antibacterial*[tiab] OR (anti[tiab] AND bacterial*[tiab])) OR (penicillin*[tiab] OR amoxicillin[tiab] OR ampicillin[tiab] OR clavulanic acid[tiab] OR amoxiclav OR tiab OR augmentin[tiab] OR ticarcillin[tiab] OR timentin[tiab] OR flucloxacillin[tiab] OR fluampicil[tiab] OR magnapen[tiab] OR piperacillin[tiab] OR tazocin[tiab] OR cephalosporin*[tiab] OR cefaclor[tiab] OR distaclor[tiab] OR cefadroxil[tiab] OR baxan[tiab] OR cefalexin[tiab] OR ceporex[tiab] OR keflex[tiab] OR cefamandole[tiab] OR kefadol[tiab] OR cefazolin[tiab] OR kefzol[tiab] OR cefixime[tiab] OR suprax[tiab] OR cefotaxime[tiab] OR claforan[tiab] OR cefoxitin[tiab] OR mefoxin[tiab] OR cefpirome[tiab] OR cefrom[tiab] OR cefpodoxime[tiab] OR orelox[tiab] OR cefprozil[tiab] OR cefzil[tiab] OR cefradine[tiab] OR velosel[tiab] OR ceftazidime[tiab] OR fortum[tiab] OR kefadim[tiab] OR ceftriaxone[tiab] OR rocephin[tiab] OR cefuroxime[tiab] OR zinacef[tiab] OR zinnat[tiab] OR cefonicid[tiab] OR aztreonam[tiab] OR azactam[tiab] OR imipenem[tiab] OR cilastatin[tiab] OR primaxin[tiab] OR meropenem[tiab] OR meronem[tiab]) OR (tetracycline*[tiab] OR deteclo[tiab] OR demecleocyclin[tiab] OR ledermycin[tiab] OR doxycycline[tiab] OR vibramycin[tiab] OR minocycline[tiab] OR minocine[tiab] OR oxytetracycline[tiab] OR terramycin[tiab] OR macrolide*[tiab] OR erythromycin[tiab] OR erymax[tiab] OR erythrocin[tiab] OR erythroped[tiab] OR azithromycin[tiab] OR zithromax[tiab] OR clarithromycin[tiab] OR klaricid[tiab] OR telithromycin[tiab] OR ketek[tiab] OR trimoxazole[tiab] OR septrin[tiab] OR trimethoprim[tiab] OR monotrim[tiab] OR trimopan[tiab] OR

bacteriocid$2).TI,AB.
28. (antibacterial$2 OR anti ADJ bacterial$2 OR antimycobacterial$2 OR anti ADJ mycobacterial$2).TI,AB.
29. penicillin$1 OR amoxicillin OR ampicillin OR clavulanic ADJ acid OR amoxiclav OR augmentin OR ticarcillin OR timentin OR flucloxacillin OR fluampicil OR
magnapen OR piperacillin OR tazocin OR sulfisoxazole
30. cephalosporin$1 OR cefaclor OR distaclor OR cefadroxil OR baxan OR cefalexin
OR ceporex OR keflex OR cefamandole OR kefadol OR cefazolin OR kefzol OR
cefixime OR suprax OR cefotaxime OR claforan OR cefoxitin OR mefoxin
31. cefpirome OR cefrom OR cefpodoxime OR ORelox OR cefprozil OR cefzil OR
cefradine OR velosel OR ceftazidime OR fortum OR kefadim OR ceftriaxone OR
rocephin OR cefuroxime OR zinacef OR zinnat OR cefonicid OR aztreonam
32. azactam OR imipenem OR cilastatin OR primaxin OR meropenem OR meronem
OR tetracycline$1 OR deteclo OR demecleocyclin OR ledermycin OR doxycycline
OR vibramycin OR minocycline OR minocine OR oxytetracycline OR terramycin
33. macrolide$1 OR erythromycin OR erymax OR erythrocin OR erythroped OR
azithromycin OR zithromax OR clarithromycin OR klaricid OR telithromycin OR
ketek OR trimoxazole OR septrin OR trimethoprim OR monotrim OR trimopan OR
metronidazole OR flagyl OR metrolyl OR quinolone$1 OR ciprofloxacin OR
ciproxin
34. 26 OR 27 OR 28 OR 29 OR 30 OR 31 OR 32 OR 33
35. 25 AND 34

(Continued)

	metronidazole[tiab] OR flagyl[tiab] OR metrolyl[tiab] OR quinolone*[tiab] OR ciprofloxacin[tiab] OR ciproxin[tiab]))	
BIOSIS Previews	**CAB Abstracts**	**CINAHL**
1 exp tonsillectomy/ 2 [exp tonsil disease/su [Surgery]] 3 (tonsillectom* or tonsilectom* or tonsillot* or adenotonsillectom* or adenotonsilectom*).tw. 4 exp tonsillitis/ or exp tonsil/ 5 (tonsil* or peritonsil* or adenotonsil*).tw. 6 4 or 5 7 exp SURGERY/ or exp surgical technique/ or scalpel/ or ultrasound/ 8 (surg* or excis* or extract* or remov*).tw. 9 (dissect* or electrodissect* or coblat* or ablat* or ultrasonic* or harmonic* or guillotin* or plasma or ultracis* or (ion* and field*) or (bipolar and probe*) or (electr* and coagulat*) or eletrocoagulat* or (electr* and cauter*) or electrosurg* or (electr* and surg*) or bovie or elmed or somnoplasty or diatherm* or thermocauter* or thermocoagul* or galvanocaut* or radiosurg* or radiofrequenc* or cryosurg*).tw. 10 8 or 7 or 9 11 6 and 10 12 11 or 1 or 3 or 2 13 exp ANTIBIOTIC AGENT/ 14 (antibiot* or (anti and biot*) or antimicrobial* or (anti and microbial*) or bacteriocid* or antibacterial* or (anti and bacterial*)).tw. 15 (penicillin* or amoxicillin or ampicillin or clavulanic acid or amoxiclav or augmentin or ticarcillin or timentin or flucloxacillin or fluampicil or magnapen or piperacillin or tazocin or cephalosporin* or cefaclor or distaclor or cefadroxil or baxan or cefalexin or ceporex or keflex or cefamandole or kefadol or cefazolin or kefzol or cefixime or suprax or cefotaxime or claforan or cefoxitin or mefoxin or cefpirome or cefrom or cefpodoxime or orelox or cefprozil or cefzil or cefradine or velosel or ceftazidime or fortum or kefadim or ceftriaxone or rocephin or cefuroxime or zinacef or zinnat or cefonicid or aztreonam or azactam or imipenem or cilastatin or primaxin or meropenem or meronem).tw.	1 exp tonsillectomy/ 2 [exp tonsil disease/su [Surgery]] 3 (tonsillectom* or tonsilectom* or tonsillot* or adenotonsillectom* or adenotonsilectom*).tw. 4 exp tonsillitis/ or exp tonsil/ 5 (tonsil* or peritonsil* or adenotonsil*).tw. 6 4 or 5 7 exp SURGERY/ or exp surgical technique/ or scalpel/ or ultrasound/ 8 (surg* or excis* or extract* or remov*).tw. 9 (dissect* or electrodissect* or coblat* or ablat* or ultrasonic* or harmonic* or guillotin* or plasma or ultracis* or (ion* and field*) or (bipolar and probe*) or (electr* and coagulat*) or eletrocoagulat* or (electr* and cauter*) or electrosurg* or (electr* and surg*) or bovie or elmed or somnoplasty or diatherm* or thermocauter* or thermocoagul* or galvanocaut* or radiosurg* or radiofrequenc* or cryosurg*).tw. 10 8 or 7 or 9 11 6 and 10 12 11 or 1 or 3 or 2 13 exp ANTIBIOTIC AGENT/ 14 (antibiot* or (anti and biot*) or antimicrobial* or (anti and microbial*) or bacteriocid* or antibacterial* or (anti and bacterial*)).tw. 15 (penicillin* or amoxicillin or ampicillin or clavulanic acid or amoxiclav or augmentin or ticarcillin or timentin or flucloxacillin or fluampicil or magnapen or piperacillin or tazocin or cephalosporin* or cefaclor or distaclor or cefadroxil or baxan or cefalexin or ceporex or keflex or cefamandole or kefadol or cefazolin or kefzol or cefixime or	S1 (MH "Tonsillectomy") S2 TX tonsillectom* or tonsilectom* or tonsillot* or adenotonsillectom* or adenotonsilectom* S3 (MH "Tonsil") or (MH "Tonsillitis S4 TX tonsil* or peritonsil* or adenotonsil* S5 (MH "Surgery, Operative") S6 TX surg* or excis* or extract* or remov* S7 TX dissect* or electrodissect* or coblat* or ablat* or ultrasonic* or harmonic* or guillotin* or plasma or ultracis* or (ion* and field*) or (bipolar and probe*) or (electr* and coagulat*) or eletrocoagulat* or (electr* and cauter*) or electrosurg* or (electr* and surg*) or bovie or elmed or somnoplasty or diatherm* or thermocauter* or thermocoagul* or galvanocaut* or radiosurg* or radiofrequenc* or cryosurg* S8 S3 or S4 S9 S5 or S6 or S7 S10 S8 and S9 S11 S1 or S2 or S10 S12 (MH "Antibiotics") S13 (MH "Antibiotic Prophylaxis") S14 antibiot* or (anti and biot*) or antimicrobial* or (anti and microbial*) or bacteriocid* or antibacterial* or (anti and bacterial*) S15 TX penicillin* or amoxicillin or ampicillin or clavulanic acid or amoxiclav or augmentin or ticarcillin or timentin or flucloxacillin or fluampicil or magnapen or piperacillin or tazocin or cephalosporin* or cefaclor or distaclor or cefadroxil or baxan or cefalexin or ceporex or keflex or cefamandole or kefadol or cefazolin or kefzol or cefixime or suprax or cefo-

(Continued)

16 (tetracycline* or deteclo or demecleocyclin or ledermycin or doxycycline or vibramycin or minocycline or minocine or oxytetracycline or terramycin or macrolide* or erythromycin or erymax or erythrocin or erythroped or azithromycin or zithromax or clarithromycin or klaricid or telithromycin or ketek or trimoxazole or septrin or trimethoprim or monotrim or trimopan or metronidazole or flagyl or metrolyl or quinolone* or ciprofloxacin or ciproxin).tw.
17 16 or 13 or 15 or 14
18 17 and 12

suprax or cefotaxime or claforan or cefoxitin or mefoxin or cefpirome or cefrom or cefpodoxime or orelox or cefprozil or cefzil or cefradine or velosel or ceftazidime or fortum or kefadim or ceftriaxone or rocephin or cefuroxime or zinacef or zinnat or cefonicid or aztreonam or azactam or imipenem or cilastatin or primaxin or meropenem or meronem).tw.
16 (tetracycline* or deteclo or demecleocyclin or ledermycin or doxycycline or vibramycin or minocycline or minocine or oxytetracycline or terramycin or macrolide* or erythromycin or erymax or erythrocin or erythroped or azithromycin or zithromax or clarithromycin or klaricid or telithromycin or ketek or trimoxazole or septrin or trimethoprim or monotrim or trimopan or metronidazole or flagyl or metrolyl or quinolone* or ciprofloxacin or ciproxin).tw.

17 16 or 13 or 15 or 14
18 17 and 12

taxime or claforan or cefoxitin or mefoxin or cefpirome or cefrom or cefpodoxime or orelox or cefprozil or cefzil or cefradine or velosel or ceftazidime or fortum or kefadim or ceftriaxone or rocephin or cefuroxime or zinacef or zinnat or cefonicid or aztreonam or azactam or imipenem or cilastatin or primaxin or meropenem or meronemTX penicillin* or amoxicillin or ampicillin or clavulanic acid or amoxiclav or augmentin or ticarcillin or timentin or flucloxacillin or fluampicil or magnapen or piperacillin or tazocin or cephalosporin* or cefaclor or distaclor or cefadroxil or baxan or cefalexin or ceporex or keflex or cefamandole or kefadol or cefazolin or kefzol or cefixime or suprax or cefotaxime or claforan or cefoxitin or mefoxin or cefpirome or cefrom or cefpodoxime or orelox or cefprozil or cefzil or cefradine or velos ...
S16 TX tetracycline* or deteclo or demecleocyclin or ledermycin or doxycycline or vibramycin or minocycline or minocine or oxytetracycline or terramycin or macrolide* or erythromycin or erymax or erythrocin or erythroped or azithromycin or zithromax or clarithromycin or klaricid or telithromycin or ketek or trimoxazole or septrin or trimethoprim or monotrim or trimopan or metronidazole or flagyl or metrolyl or quinolone* or ciprofloxacin or ciproxin
S17 S12 or S13 or S14 or S15 or S16
S18 S11 and S17

Web of Science	***m*RCT**	**ClinicalTrials.gov**
# 1 TS=(tonsillectom* or tonsilectom* or tonsillot* or adenotonsillectom* or adenotonsilectom*) # 2 TS=(tonsil* or peritonsil* or adenotonsil*) # 3 TS=(surg* or excis* or extract* or remov*)	((tonsillectom% OR tonsilectom% OR adenotonsillectom% OR adenotonsilectom%) AND (antibiot% OR antimicrob% OR antibact% OR "anti bacterial" OR "anti microbial%" penicillin% OR amoxicillin OR ciprofloxacin))	((tonsillectomy OR tonsilectomy OR adenotonsillectomy) AND (antibiotic OR antimicrobial OR antibacterial OR penicillin OR amoxicillin OR ciprofloxacin))

(Continued)

4 TS=(dissect* or electrodissect* or coblat* or ablat* or ultrasonic* or harmonic* or guillotin* or plasma or ultracis* or (ion* and field*) or (bipolar and probe*) or (electr* and coagulat*) or eletrocoagulat* or (electr* and cauter*) or electrosurg* or (electr* and surg*) or bovie or elmed or somnoplasty or diatherm* or thermocauter* or thermocoagul* or galvanocaut* or radiosurg* or radiofrequenc* or cryosurg*)
5 #4 OR #3
6 #5 AND #2
7 #6 OR #1
8 TS=(antibiot* or (anti and biot*) or antimicrobial* or (anti and microbial*) or bacteriocid* or antibacterial* or (anti and bacterial*))
9 TS=(penicillin* or amoxicillin or ampicillin or clavulanic acid or amoxiclav or augmentin or ticarcillin or timentin or flucloxacillin or fluampicil or magnapen or piperacillin or tazocin or cephalosporin*)
10 TS=(cefaclor or distaclor or cefadroxil or baxan or cefalexin or ceporex or keflex or cefamandole or kefadol or cefazolin or kefzol or cefixime or suprax or cefotaxime or claforan or cefoxitin or mefoxin or cefpirome or cefrom or cefpodoxime or orelox or cefprozil or cefzil or cefradine or velosel or ceftazidime or fortum or kefadim or ceftriaxone or rocephin or cefuroxime or zinacef or zinnat or cefonicid or aztreonam or azactam or imipenem or cilastatin or primaxin or meropenem or meronem)
11 TS=(tetracycline* or deteclo or demecleocyclin or ledermycin or doxycycline or vibramycin or minocycline or minocine or oxytetracycline or terramycin or macrolide* or erythromycin or erymax or erythrocin or erythroped or azithromycin or zithromax or clarithromycin or klaricid or telithromycin or ketek or trimoxazole or septrin or trimethoprim or monotrim or trimopan or metronidazole or flagyl or metrolyl or quinolone* or ciprofloxacin or ciproxin)
12 #11 OR #10 OR #9 OR #8
13 #12 AND #7

WHAT'S NEW

Date	Event	Description
9 October 2012	New citation required but conclusions have not changed	We identified no new studies which were eligible for inclusion in the review. Three further studies are excluded and one has been identified as ongoing.
20 March 2012	New search has been performed	New searches run.

HISTORY

Protocol first published: Issue 1, 2006
Review first published: Issue 2, 2008

Date	Event	Description
15 March 2010	New citation required and conclusions have changed	One new study added (Guerra 2008), resulting in a change to the review conclusions.
30 October 2009	New search has been performed	Full new searches run 30 October 2009.
28 August 2008	Amended	Converted to new review format.

CONTRIBUTIONS OF AUTHORS

MD: drafting the protocol, searching for studies, selecting studies, quality assessment, data extraction, data analysis.
AC: selecting studies, quality assessment, data extraction.
MS: searching for studies, selecting studies, data analysis.
WM: drafting the protocol, selecting studies, quality assessment, data analysis.

DECLARATIONS OF INTEREST

None known.

SOURCES OF SUPPORT

Internal sources

- None, Not specified.

External sources

- None, Not specified.

INDEX TERMS

Medical Subject Headings (MeSH)

Analgesics [administration & dosage]; Anti-Bacterial Agents [adverse effects] [*therapeutic use]; Antibiotic Prophylaxis; Bacterial Infections [drug therapy]; Convalescence; Fever [drug therapy]; Pain, Postoperative [*drug therapy] [prevention & control]; Postoperative Hemorrhage [*drug therapy] [etiology]; Randomized Controlled Trials as Topic; Tonsillectomy [*adverse effects]

MeSH check words

Adult; Child; Humans