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RESEARCH

Effect of systemic steroids on post-tonsillectomy bleeding and reinterventions: systematic review and meta-analysis of randomised controlled trials


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Abstract

Objective To evaluate the risk of postoperative bleeding and reintervention with the use of systemic steroids in patients undergoing tonsillectomy.

Design Systematic review and meta-analysis of randomised controlled trials.

Data sources Medline, Embase, Cochrane Library, Scopus, Web of Science, Intute, Biosis, OpenSIGLE, National Technical Information Service, and Google Scholar were searched. References from reviews identified in the search and from included studies were scanned.

Review methods Randomised controlled trials comparing the administration of systemic steroids during tonsillectomy with any other comparator were eligible. Primary outcome was postoperative bleeding. Secondary outcomes were the rate of admission for a bleeding episode, reintervention for a bleeding episode, blood transfusion, and mortality.

Results Of 1387 citations identified, 29 randomised controlled trials (n=2674) met all eligibility criteria. Seven studies presented a low risk of bias, but none was specifically designed to systematically identify postoperative bleeding. Administration of systemic steroids did not significantly increase the incidence of post-tonsillectomy bleeding (29 studies, n=2674 patients, odds ratio 0.96 (95% confidence interval 0.66 to 1.40), I^2=0%). We observed a significant increase in the incidence of operative reinterventions for bleeding episodes in patients who received systemic steroids (12, n=1178, 2.27 (1.03 to 4.99), I^2=0%). No deaths were reported. Sensitivity analyses were consistent with the findings.

Conclusions Although systemic steroids do not appear to increase bleeding events after tonsillectomy, their use is associated with a raised incidence of operative reinterventions for bleeding episodes, which may be related to increased severity of bleeding events. Systemic steroids should be used with caution, and the risks and benefits weighed, for the prevention of postoperative nausea and vomiting after tonsillectomy before further research is performed to clarify their condition of use.

Introduction

Tonsillectomy with or without adenoidectomy is one of the most commonly performed ear, nose, and throat surgeries worldwide.[1 2] After this intervention, many patients have nausea, vomiting, and pain.[3 4] Without prophylaxis, the reported incidence of postoperative vomiting in children undergoing tonsillectomy ranges from 40% to 73%.[5-8] Systemic steroids have been shown to be as efficient as 5-HT_3 antagonists and droperidol in reducing postoperative nausea and vomiting.[8] Their use is increasing and currently recommended in recent guidelines of the American Academy of Otolaryngology-Head and Neck Surgery Foundation for tonsillectomy in children.[9 10] Furthermore, some studies suggest that steroids could be associated with an earlier return to a regular diet after tonsillectomy.[2 11]

A recent randomised controlled trial comparing different doses of dexamethasone for preventing postoperative nausea and vomiting after tonsillectomy showed an increased incidence of

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Web appendix: Medline search strategy
Web figure: Funnel plot of post-tonsillectomy bleeding

postoperative bleeding and reoperation due to bleeding in the steroid group.[12] Previous observational studies have also reported this association.[13 14] A recent meta-analysis on dexamethasone and tonsillectomy bleeding found no increased risk of postoperative bleeding with the use of steroids.[15] However, this review was not exhaustive and did not evaluate clinically significant outcomes such as operative reinterventions.

Considering the frequent use and potential harm of systemic steroids to prevent postoperative nausea and vomiting after tonsillectomy, and the existence of effective alternatives such as 5-HT_3 antagonists,[10] we conducted a systematic review of randomised controlled trials to evaluate the risk of postoperative bleeding and of operative reinterventions after systemic steroids use in patients undergoing tonsillectomy.

Methods

Design and search strategy

We conducted a systematic review and meta-analysis of randomised controlled trials. A search strategy was developed for Medline (OVID, 1950-March 2011), Embase (OVID, 1947-March 2011), and the Cochrane Central Register of Controlled Trials (up to March 2011) (web appendix). We identified randomised controlled trials by incorporating validated filters for Medline[16] and Embase.[17] We also did a similar search of Scopus, the Web of Science, and Intute databases, as well as OpenSIGLE, Google Scholar, and the National Technical Information Service databases for the grey literature. Relevant abstracts and conference proceedings were identified using the Biosis database. References of pertinent reviews identified in the search were scanned to identify potentially relevant trials. Two reviewers (JP, LV) independently screened all studies for eligibility by titles and abstracts, and by full text publications if needed. A third reviewer (AFT) was consulted in instances when consensus could not be reached between the two reviewers. At the end of this selection process, Google Scholar was used to identify authors that cited any of the included studies. Additional studies identified by this method were then considered for eligibility.

Study eligibility

All randomised controlled trials of tonsillectomy (any indications) that compared the administration of any systemic steroids to any comparator (other intervention, placebo, or no intervention) were included, provided that bleeding or the absence of bleeding episodes (of any severity) were also reported or could be obtained from authors. We excluded studies including patients with bleeding disorders, patients on chronic steroid therapy, or patients in whom steroids were locally injected or sprayed on the tonsillar bed. Eligibility was not restricted by language, type of publication (for example, abstracts or full publications), or patients' age.

The primary outcome was the incidence of postoperative bleeding from the tonsillar fossa (any type of bleeding and of any severity). The secondary outcomes were the incidence of admission for bleeding episodes, operative reinterventions for bleeding episodes, red blood cells transfusion, and mortality. We defined an operative reintervention for a bleeding episode as any surgical procedure performed in the operating room or in the emergency department to stop bleeding from the surgical site. Patients requiring a reintervention in the operating room were considered being admitted to hospital after the procedure, and were included in the meta-analysis of admissions for bleeding episodes.

Data abstraction

We developed a data abstraction form to standardise the data collection process, which was pilot tested on a landmark publication.[12] For comparison purposes, all steroid doses were converted in dexamethasone equivalents. We converted fixed doses to mg/kg using the mean weight, when the data were provided. If weight was not provided, we used a standard weight of 60 kg for women and 70 kg for men in adults, and weight charts for children to estimate whether the mean dose was lower or greater than 0.5 mg/kg. Bleeding events that occurred on postoperative day zero, or within the first 24 hours, were considered as primary bleeding episodes. Episodes beyond that period of time were defined as secondary bleeding episodes. We contacted the corresponding authors of included studies if data were missing for bleeding episodes, admission, reintervention, red blood cells transfusion, or mortality, or if the methods required clarification. Two reviewers (JP, LV) performed the data collection process independently, and a third reviewer (AFT) resolved any discrepancies. A translator was consulted for studies published in languages other than English or French.

Risk of bias assessment

The risk of bias was assessed independently by two reviewers (JP, LV) using the Cochrane Collaboration's risk of bias tool.[16] Since the objective of the current review was to identify bleeding complications occurring in the acute and subacute perioperative period, studies with considerable numbers of patients lost to follow-up, as well as those with a short follow-up period (<24 h) were considered to have an increased risk of bias because of their potential for missed bleeding events.[16] For this reason, we assigned an "unclear" overall risk of bias to studies with a proportion of lost to follow-up greater than 10% (incomplete outcome data).

Data synthesis

Data were analysed using Cochrane Review Manager version 5.0 (Cochrane Collaboration) and summarised using Peto fixed effects models, appropriate for meta-analysis of rare events.[18] We applied a continuity correction of 0.5 to studies reporting no event in both groups. All data were dichotomous, and associations were presented using odds ratio with 95% confidence intervals. An odds ratio greater than 1 implies greater risk in the steroid group, and an odds ratio less than 1 implies greater risk in the control group. We assessed the presence of heterogeneity using the I^2 statistic, which estimates the percentage of variation between study results that is due to heterogeneity rather than sampling error.[19] We did sensitivity analyses, based on clinical (adults *v* children, cold or combined *v* hot dissection, high [>0.5 mg/kg] *v* low [≤0.5 mg/kg] dose steroids, non-steroidal anti-inflammatory drug administration, type of comparator, and timing of bleeding) and methodological (risk of bias, blinding, sample size, and short [≤24 h] *v* long [>24 h] follow-up) characteristics, to understand potential sources of heterogeneity and to evaluate the robustness of the results. Potential publication bias was assessed using funnel plot analyses.[20]

Quality of evidence

We graded the quality of evidence for the three main outcomes using the Grading of Recommendations Assessment, Development and Evaluation (GRADE) approach [21] with GRADEpro software (version 3.2 for Windows. Jan Brozek, Andrew Oxman, Holger Schünemann, 2008).

Results

Search results

We retrieved a total of 1387 citations (fig 1⇓). Fifty one studies were considered potentially eligible. Of these studies, 16 were excluded because they did not report bleeding episodes nor admission or reintervention, and this information could not be obtained despite attempts to contact the authors. The remaining excluded publications did not meet all inclusion criteria.[22-27] We included 29 studies in this systematic review,[12 28-55] representing 2674 patients (table 1⇓).

Study characteristics

Of the included studies, 24 were published in English, and one each in Turkish,[34] Korean,[39] Spanish,[54] Chinese,[29] and Hebrew.[38] Ten studies were conducted in North America,[30-33 35 40 47 53-55] 12 in Asia,[28 29 34 37-39 41 45 46 49-51] four in Europe,[12 42 43 52] two in Australia,[36 48] and one in Africa.[44] All studies were presented as full publications. In two studies, dexamethasone was provided by pharmaceutical companies,[12 32] and one of these studies specified that the funding organisation had no role in the design or conduct of the study.[12]

Nineteen studies were performed in children, six in adults only, and four included both children and adults. Twenty four studies compared the effects of systemic steroids with placebo[12 28-35 37 40 41 43 46-48 50 51 53-55] or no intervention (neither a placebo nor any intervention in the control group).[38 39 45] Six studies compared systemic steroids with other treatments (tropisetron, ondansetron, droperidol, piroxicam, bilateral glossopharyngeal nerve block with bupivacaine, or paracetamol).

Dexamethasone was used in 28 studies, while prednisolone was administered in the remaining study.[48] In 18 studies, the dexamethasone dose was calculated according to the patient's weight (mg/kg) and varied from 0.05 mg/kg [12] to 1.0 mg/kg. In the remaining studies, the steroid dose was fixed[29 31 40 42 43 50 52 55]; based on the patient's body surface (mg/m²)[32]; or either fixed or based on weight (mg/kg), according to patient's age.[48 49] Systemic steroids were administrated as a single dose, or repeated doses over a specific period of time: 16 h,[54] three days,[40] four days,[29] seven days,[48] or eight days.[52] In these studies, the total dose was taken into account.

In most studies, the main outcomes were the effect of steroids on pain,[12 28-33 35 37-45 47 48 50-55] nausea and vomiting,[12 28 30 33-39 41 43 45-53] and oral intake [12 28 30 32 35 37-39 41 43 45-48 50 51 53 55] after tonsillectomy. Other main outcome measures of included studies were the effect of steroids on oedema, fever, trismus, halitosis, and level of activity.

Twenty six studies reported data for post-tonsillectomy bleeding. Through private communications with authors, we obtained details pertaining to the severity of and to interventions related to the bleeding episodes for three of these studies,[40 42 53] and obtained unpublished data on bleeding episodes for three additional studies.[43 44 49] Eight studies reported no postoperative bleeding episodes or mentioned uneventful surgeries.[29 37 43 44 48 49 51 54] Among studies reporting bleeding episodes, 18 specified the timing of occurrence,[12 28 30-36 39 41 42 45-47 50 52 53] nine reported the need for admission due to bleeding,[12 28 30 31 35 46 47 50 53] and 12 reported data for reintervention.[12 30 32 34 39 40 42 46 47 50 52 55] No study reported transfusion of red blood cells or mortality.

A clear definition of post-tonsillectomy bleeding was presented in two of 29 studies.[12 42] Eight studies stated that bleeding episodes were going to be reported,[12 28 31-33 35 37 41] while six clearly questioned their patients about postoperative bleeding or provided instructions in the event of unexpected bleeding.[12 28 35 37 41 42] No study described a systematic method to evaluate postoperative bleeding.

Validity assessment

A low risk of bias was attributed to seven studies [33 35 36 40-42 50] (table 2⇓). Fifteen studies had an adequate sequence generation,[12 30 31 33 35-37 40-43 50-52 54] and 15 had an appropriate method of allocation concealment.[12 30 33 35 36 40-43 47 48 50 52 53 55] Six studies were not blinded,[28 38 39 45 46 49] and blinding was unclear in another study.[34] One study was terminated early because of an increased incidence of post-tonsillectomy bleeding in the intervention group.[12] Fourteen studies [12 31-33 36 38 40-43 47 52 53 55] reported losses to follow-up that varied from 2.7%[12] to 36.1%,[43] and losses to follow-up were unclear in four studies.[29 39 45 48] Eight studies had a follow-up period of 24 h or less.[30 34 37 44-46 49 51] Two studies reported performing an intention to treat analysis.[12 40] Five studies did not report all outcomes stated in their methods.[32 45 46 51 54]

Post-tonsillectomy bleeding episodes

The administration of steroids did not increase the incidence of bleeding events after tonsillectomy, based on pooled data from the 29 studies (n=2674, odds ratio 0.96, 95% confidence intervals 0.66 to 1.40, I^2=0%), of which eight did not observe any bleeding episodes[29 37 43 44 48 49 51 54] (fig 2⇓). Sensitivity analyses including trials with low risk of bias, observers blinded to the intervention, larger population, or longer follow-up periods yielded similar results (table 3⇓). Results were also comparable regardless of the population age, surgical technique, steroid dose, or concomitant administration of non-steroidal anti-inflammatory drugs. When we analysed primary and secondary bleeding events separately, we observed no increase in bleeding incident with the administration of steroids.

Hospital admission

Seventeen studies reported data for admission[12 28 30 31 35 46 47 50 53] or reinterventions[34 36 39 40 42 45 52 55] that required admission (fig 3⇓). The incidence of admission due to a bleeding episode did not increase in the steroid group (17 studies, n=1722 patients, odds ratio 1.16, 95% confidence interval 0.68 to 2.00, I^2=19%). All sensitivity analyses accorded with this finding (data not shown).

Reintervention for a bleeding episode

The incidence of operative reintervention for bleeding episodes was significantly increased in the steroid group (12 studies, n=1178; odds ratio 2.27, 95% confidence interval 1.03 to 4.99, I^2=0%; fig 4⇓). The average incidence of reintervention due to bleeding in patients receiving steroids was 3.0% versus 1.5% in controls. Sensitivity analyses were performed to evaluate the incidence of reintervention for bleeding episodes among different subgroups (table 4⇓). We observed a significant increase of reinterventions in children (eight studies[12 30 32 34 39 46 47 55]; 3.43, 1.29 to 9.13, I^2=0%) but not in adults (four[40 42 50 52]; 1.07, 0.29 to 4.03, I^2=0%). A dose effect was not observed. We found an increased incidence of reinterventions among patients receiving non-steroidal anti-inflammatory drugs (three[12 39 52]; 4.10, 0.99 to 16.97, I^2=0%). No significant association was seen among double blinded studies (nine[12 30 32 40 42 47 50 52 55]; 2.22, 0.95 to 5.18, I^2=0%) and those with longer follow-up periods (nine[12 32 39 40 42 47 50 52 55]; 2.16, 0.92 to 5.06, I^2=0%). In each case, the incidence of reinterventions for bleeding episodes was increased in the steroid

group compared with the control group without reaching significance (P=0.07 for double blinding, P=0.08 for longer follow-up periods), although the results suggested a strong trend. Studies with low risk of bias showed no clear association between steroids use and the incidence of operative reintervention (three studies[40 42 50]; 0.91, 0.22 to 3.68, I^2=0%).

Allogenic transfusion and mortality

None of the included studies reported transfusion of red blood cells or mortality.

Publication bias and quality of evidence

We evaluated the presence of potential publication bias using a funnel plot of intervention effect estimates versus the standard error for studies presenting data for bleeding episodes. Visual inspection of the funnel plot did not reveal evidence of publication bias (web figure). According to the GRADE methodology, the quality of the evidence for bleeding and admission outcomes after tonsillectomy was low; however, the association between post-tonsillectomy reintervention and systemic steroids was considered to be of high quality (table 5⇓).

Discussion

In this systematic review, we did not observe an increased incidence of postoperative bleeding events after perioperative administration of systemic steroids in patients undergoing tonsillectomy. However, we did observe a significant increase in the incidence of operative reinterventions needed to manage clinically significant bleeding episodes in patients who received systemic steroids. The quality of the evidence according to the GRADE approach was high for this specific outcome. This raised incidence of reinterventions was significantly increased in children.

Strengths and limitations if the study

An important limitation of our study concerned the data available within included publications. None of the included studies was designed to evaluate adverse complications of steroids use after tonsillectomy, and no study systematically screened for bleeding events after tonsillectomy. Therefore, the incidence of this complication could have been systematically underestimated. Moreover, only two studies presented a clear definition of post-tonsillectomy bleeding. Bleeding episodes of varying severity may not have received equal consideration across all studies, which could lead to an underestimation of overall bleeding episodes. This could explain why we did not observe a significant association between steroids use and bleeding events, while we did observe an association with reintervention for bleeding events.

On the other hand, the inclusion in meta-analyses of studies reporting no bleeding event in either group using a continuity correction could have underestimated the association. The majority of included studies were of limited methodological quality, and many studies had substantial numbers of patients who were lost to follow-up. These factors provide further concern that bleeding episodes may have been missed. A significant proportion of studies had a very limited follow-up period precluding the evaluation of the incidence of secondary bleeding episodes. Since bleeding episodes are relatively rare events, unreported episodes could greatly affect the study results.

Despite of known limitations, our systematic review had important strengths. Firstly, the extensive search strategy using different databases, including the grey literature and conference proceedings, allowed us to retrieve a comprehensive list of the studies performed on the topic. Importantly, the decision to evaluate the incidence of reinterventions for bleeding episodes, as opposed to only bleeding episodes, allowed us to summarise the effect of clinically significant bleeding events with greater fidelity. We believe that operative reintervention for bleeding episodes represents a more reliable and clinically meaningful endpoint than bleeding episodes. Severe enough bleeding events to require operative reintervention are less likely to have been overlooked and may therefore represent the optimal clinical outcome to understand the impact of systemic steroids in tonsillectomy.

Comparison with other studies

Overall, the mean incidence of post-tonsillectomy bleeding events observed in our systematic review was 4.4%, which is consistent with the current literature.[56-60] Our results on postoperative bleeding are in accordance with a recent systematic review.[15] However, this previous meta-analysis identified half the number of studies as compared with our study, and did not evaluate other clinically significant outcomes such as operative reinterventions for bleeding and hospital admission. The increased incidence of reintervention observed in a recent landmark study by Czarnetzki and colleagues[12] was also seen in our pooled analysis. But our systematic review did not confirm the higher incidence of bleeding episodes associated with perioperative steroids use in tonsillectomy procedures, as observed in this trial.

The increased incidence of reinterventions associated with steroids occurred in the absence of increased bleeding events, and thus probably represents an increased severity of bleeding when steroids are administered. Although no study specified indications to undergo a reintervention in the event of bleeding, this procedure usually suggests that the bleeding was significant enough to require an emergency procedure. Bleeding events requiring reintervention are more likely to be noticed and reported in a publication as opposed to minor events. Therefore, reinterventions to manage bleeding events may be a more objective and reliable outcome to assess clinically significant bleeding events after tonsillectomy.

Conclusions and policy implications

We did not observe an increased incidence of postoperative bleeding events following administration of systemic steroids during tonsillectomy. We did, however, observe a significant increase in the incidence of operative reintervention associated with the use of steroids, which may be related to an increased severity of a given bleeding episode. Considering the potential for harm and the availability of other drugs to prevent postoperative nausea and vomiting, we recommend that steroids should be used with caution; risks and benefits must be weighted; and steroids should not be used routinely for such purposes, especially in children. Further studies should be designed to answer concerns about the safety of the perioperative use of steroids in tonsillectomy procedures.

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Contributors: JP, AFT, RZ, FL, LM, and DAF contributed to the conception and design of the study. JP and LV determined eligibility of search results and extracted data from included studies. JP, AB, and AFT performed and reviewed the analyses, and drafted the manuscript.

What is already known on this topic

Tonsillectomy is one of the most commonly performed ear, nose, and throat surgeries worldwide, but has a high underlying risk of postoperative nausea and vomiting

Systemic use of steroids to reduce postoperative nausea and vomiting is increasing, and recommended in addition to the use of 5-HT_3 antagonists in recent guidelines

A recent study has linked such use of steroids with an increased incidence of postoperative bleeding after tonsillectomy

What this study adds

Overall, the risk of postoperative bleeding did not increase after perioperative administration of systemic steroids in patients undergoing tonsillectomy

However, the incidence of reinterventions for bleeding episodes did increase overall with steroids, and especially among children, which could represent a greater severity of bleeding associated with use of steroids

Systemic steroids should be used with caution; risks and benefits must be weighted, and steroids should not be used routinely to prevent postoperative nausea and vomiting after tonsillectomy, especially in children

All authors participated in the interpretation of the data and the critical review of the manuscript, and approved the version to be published. AFT is the guarantor.

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Ethical approval: This study did not require ethical approval.

Data sharing: No additional data available.

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Tables

Table 1| Characteristics of included studies in meta-analysis

Study (reference)	No of participants		Age inclusion criteria (years)	Procedure	Dissection technique	Drug regimen		NSAID use	Duration of follow-up	Bleeding outcome definition
	Steroids	Control				Steroids	Control			
Catlin et al. (1991)[32]	10	15	4 to 12	T, or T and A	Combined	Dexamethasone IV, 8 mg/m², before induction	Placebo	No	3 weeks	NR
Volk et al. (1993)[55]	25	25	4 to 12	T, or T and A	Combined	Dexamethasone IV, 10 mg, at induction	Placebo	No	7 to 10 days	NR
Ohlms et al. (1995)[47]	34	35	3 to 18	T, or T and A	Cold, combined	Dexamethasone IV, 0.5 mg/kg (max 12 mg), immediately before surgery	Placebo	No	3 to 4 weeks	NR
April et al. (1996)[30]	41	39	3 to 15	T and A	Hot	Dexamethasone IV, 1 mg/kg (max 16 mg), after induction	Placebo	NR	24 h	NR
Tom et al. (1996)[53]	26	32	1 to 18	T and A	Hot	Dexamethasone IV, 1 mg/kg (max 10 mg), after induction	Placebo	No	10 days	NR
Kim et al. (1998)[39]	40	20	3 to 15	T, or T and A	Combined	Dexamethasone IV, 1 mg/kg (max 15 mg), after induction or in the postanaesthetic care unit	No treatment or placebo	Yes	3 days	NR
Carr et al. (1999)[31]	15	14	Adults	T	Hot	Dexamethasone IV, 20 mg, during surgery	Placebo	No	10 days	NR
Holt et al. (2000)[36]	68	60	2 to 14	T, or T and A	Cold	Tropisetron and dexamethasone IV, 0.5 mg/kg (max 8 mg), after induction	Tropisetron alone, 0.1 mg/kg (max 2 mg)	NR	6 days	NR
Nawasreh et al. (2000)[46]	62	58	4 to 14	T, or T and A	Hot	Dexamethasone IV, 1 mg/kg (max 16 mg), 1 h before surgery	Placebo	NR	24 h	NR
Palme et al. (2000)[48]	25	25	≥5	T, or T and A	Hot, combined	Prednisolone given orally, 10 mg daily (age 5-11 years) or 0.5 mg/kg daily (age ≥12 years), postoperative day 1 to 7	Placebo	No	2 weeks	NR
Giannoni et al. (2002)[33]	25	25	3 to 15	T	Hot	Dexamethasone IV, 1 mg/kg (max 16 mg), after induction	Placebo	Yes	10 days	NR
Güne et al. (2002)[34]	15	45	3 to 12	T	NR	Dexamethasone IV, 0.15 mg/kg, after induction	3 groups: placebo, ondansetron, 0.15 mg/kg, or droperidol, 0.075 mg/kg	NR	6 h	NR
Stewart et al. (2002)[52]	132	68	≥16	T	Hot	Dexamethasone alone or dexamethasone and piroxicam (same dose as controls); dexamethasone IV, 8 mg at induction, 2 mg on the night of surgery, 2 mg twice daily for 4 days, 2 mg daily for 4 days	Piroxicam alone, given orally: 10 mg given 2 h before surgery, 10 mg given on the night of surgery; 10 mg given twice daily for 4 days; 10 mg given daily for 4 days	Yes	2 weeks	NR
Hanasono et al. (2004)[35]	106	113	≤12	T, or T and A	Hot, combined	Dexamethasone IV, 1 mg/kg (max 50 mg), at the start of surgery	Placebo	NR	3 days	NR
Samarkandi et al. (2004)[51]	29	31	2 to 12	T	Hot	Dexamethasone IV, 0.5 mg/kg, after induction	Placebo	NR	24 h	NR
Malde et al. (2005)[41]	45	45	>3	T	Cold	Dexamethasone IV, 0.15 mg/kg, after induction	Placebo	NR	7 days	NR

Table 1 (continued)

Study (reference)	No of participants		Age inclusion criteria (years)	Procedure	Dissection technique	Drug regimen		NSAID use	Duration of follow-up	Bleeding outcome definition
	Steroids	Control				Steroids	Control			
Trujillo et al. (2005)[54]	35	34	3 to 15	T, or T and A	NR	Dexamethasone IV; 1 mg/kg (max 8 mg); immediately before surgery, 8 h after operation, 16 h after operation	Placebo	NR	6 days	NR
Kaan et al. (2006)[37]	32	30	4 to 12	T, or T and A	Cold	Dexamethasone IV, 0.5 mg/kg (max 16 mg), after induction	Placebo	NR	8 h	NR
Kaufmann et al. (2006)[38]	101	103	2 to 16	T and A	NR	Dexamethasone IV, 0.5 mg/kg (max 10 mg), during surgery	No treatment or placebo	NR	10 days	NR
McKean et al. (2006)[43]	37	35	16 to 70	T	Combined	Dexamethasone IV, 10 mg, at induction	Placebo	Yes	7 days	NR
Mohammad et al. (2006)[45]	25	25	3 to 18	T, or T and A	Cold, combined	Dexamethasone IV, 1 mg/kg (max 12 mg), during surgery	Unclear (placebo or no drug)	Yes (steroid group 20%, controls 52%)	24 h	NR
Alajmi et al. (2008)[28]	42	38	5 to 18	T, or T and A	Cold, combined	Dexamethasone IV, 1 mg/kg (max 16 mg), after induction	Placebo	Yes (steroid group 14.3%, controls 47.4%)	16 days	NR
Czarnetzki et al. (2008)[12]	161	54	2 to 17	T, or T and A	Cold, hot, combined	3 groups: dexamethasone IV, 0.05 mg/kg, 0.15 mg/kg, 0.5 mg/kg (max 20 mg); after induction	Placebo	Yes (steroid subgroups 38%, 43%, and 38%; controls 65%)	10 days	History of bleeding leading to readmission, with or without evidence of bleeding at examination or need for emergency reoperation
Lachance et al. (2008)[40]	41	61	18 to 45	T	Combined, 2 cold dissections in control group	Dexamethasone IV (8 mg during surgery), dexamethasone given orally (8 mg at home on day of surgery; 6, 4, and 2 mg twice daily on postoperative days 1, 2, and 3, respectively)	Placebo	No	7 days	NR
Rujirojindakul et al. (2008)[50]	25	25	15 to 60	T	Hot	Dexamethasone IV, 20 mg, after induction	Placebo	No	7 days	NR
Ammar et al. (2009)[29]	30	30	Adults and children	T, or T and A	Cold	Dexamethasone IV, 5 mg to children, 10 mg to adults, for 4 days after surgery	Placebo	Yes	5 days	NR
Mohamed et al. (2009)[44]	100	50	2 to 12	T, or T and A	Hot	2 groups: dexamethasone alone or dexamethasone and glossopharyngeal nerve block (same dose as controls); dexamethasone IV, 0.15mg/kg (max 8 mg), before surgery	Bilateral glossopharyngeal nerve block alone with 3 mL of 0.5% bupivacaine	No	Until discharge time (up to 24 h)	NR
Rabbani et al. (2010)[49]	30	30	Adults and children	T, or T and A	NR	Dexamethasone IV, 0.1 mg/kg for age <12 years or 8 mg for >12 years, at induction	Ondansetron, 0.1 mg/kg for age <12 years, 4 mg for age >12 years	NR	24 h	NR

Table 1 (continued)

Study (reference)	No of participants		Age inclusion criteria (years)	Procedure	Dissection technique	Drug regimen		NSAID use	Duration of follow-up	Bleeding outcome definition
	Steroids	Control				Steroids	Control			
Mathiesen et al. (2011)[42]	48	99	18 to 50	T	Combined	Dexamethasone IV, 8 mg, with paracetamol and pregabalin (same dose as controls) before induction	2 groups: paracetamol alone, 1000 mg, or paracetamol and pregabalin, 300 mg	No	2 weeks	Bleeding episodes requiring reoperation

A=adenoidectomy; cold=dissection with cold steel instruments, haemostasis with gauze compression, or ligatures; combined=cold dissection with use of electrocautery for haemostasis; hot=dissection and haemostasis with electric device; IV=intravenous; max=maximum; NR=not reported; NSAID=non-steroidal anti-inflammatory drug; T=tonsillectomy.

Table 2| **Risk of bias and methodological quality assessment of included studies**

Study (reference)	Sequence generation	Allocation concealment	Blinding	Incomplete outcome data	Selective reporting	Other bias	Follow-up period (>24 h)	Summary
Catlin et al. (1991)[32]	Unclear	Unclear	Low	High	Unclear	Unclear	Low	Unclear
Volk et al. (1993)[55]	Unclear	Low	Low	High	Low	High	Low	Unclear
Ohlms et al. (1995)[47]	Unclear	Low	Low	High	Low	Low	Low	Unclear
April et al. (1996)[30]	Low	Low	Low	Low	Low	Low	High	High
Tom et al. (1996)[53]	Unclear	Low	Low	High	Low	Unclear	Low	Unclear
Kim et al. (1998)[39]	Unclear	High	High	Unclear	Low	High	Low	High
Carr et al. (1999)[31]	Low	Unclear	Low	High	Low	Low	Low	Unclear
Holt et al. (2000)[36]	Low	Low	Low	Low	Low	Low	Low	Low
Nawasreh et al. (2000)[46]	Unclear	High	High	Low	High	Unclear	High	High
Palme et al. (2000)[48]	Unclear	Low	Low	Unclear	Low	Unclear	Low	Unclear
Giannoni et al. (2002)[33]	Low	Low	Low	Low	Low	Low	Low	Low
Güne et al. (2002)[34]	Unclear	High	Unclear	Low	Low	Unclear	High	High
Stewart et al. (2002)[52]	Low	Low	Low	High	Low	Low	Low	Unclear
Hanasono et al. (2004)[35]	Low	Low	Low	Low	Low	Low	Low	Low
Samarkandi et al. (2004)[51]	Low	Unclear	Low	Low	Unclear	Low	High	High
Malde et al. (2005)[41]	Low	Low	Low	Low	Low	Low	Low	Low
Trujillo et al. (2005)[54]	Low	Unclear	Low	Low	Unclear	Low	Low	Unclear
Kaan et al. (2006)[37]	Low	Unclear	Low	Low	Low	Low	High	High
Kaufmann et al. (2006)[38]	Unclear	High	High	High	Low	High	Low	High
McKean et al. (2006)[43]	Low	Low	Low	High	Low	Low	Low	Unclear
Mohammad et al. (2006)[45]	Unclear	Unclear	High	Unclear	Unclear	High	Unclear	High
Alajmi et al. (2008)[28]	High	High	High	Low	Low	High	Low	High
Czarnetzki et al. (2008)[12]	Low	Low	Low	Low	Low	High	Low	Unclear
Lachance et al. (2008)[40]	Low	Low	Low	Low	Low	Low	Low	Low
Rujirojindakul et al. (2008)[50]	Low	Low	Low	Low	Low	Low	Low	Low
Ammar et al. (2009)[29]	Unclear	Unclear	Low	Unclear	Low	Low	Low	Unclear
Mohamed et al. (2009)[44]	Unclear	High	Low	Low	Low	Low	High	High
Rabbani et al. (2010)[49]	High	High	High	Low	Unclear	High	High	High
Mathiesen et al. (2011)[42]	Low	Low	Low	Low	Low	Low	Low	Low

Table 3| Sensitivity analysis of post-tonsillectomy bleeding outcome

Subgroups	No of studies	No of participants	Odds ratio (95% CI)	I^2 (%)
Methodological quality				
Low risk of bias	7	786	0.82 (0.38 to 1.74)	0
High risk of bias	11	986	0.71 (0.31 to 1.61)	0
Blinding				
Double blinded	22	2040	1.04 (0.68 to 1. 56)	0
No blinding or unclear	7	634	0.67 (0.27 to 1.70)	0
Sample size				
<100 patients	20	1189	1.15 (0.60 to 2.42)	0
≥100 patients	9	1485	0.88 (0.55 to 1.40)	0
Duration of follow-up				
≤24 h	8	642	0.92 (0.30 to 2.82)	0
>24 h	21	2032	0.96 (0.64 to 1.44)	0
Age group				
Children only	19	1809	1.24 (0.74 to 2.08)	0
Adults only	6	605	0.73 (0.41 to 1.30)	0
Surgical technique				
Cold or combine dissection	13	861	0.82 (0.43 to 1.56)	0
Hot dissection	9	592	0.76 (0.42 to 1.40)	0
Dose regimen of steroid				
≤0.5 mg/kg	19	1784	1.05 (0.68 to 1.61)	0
>0.5 mg/kg	9	840	0.77 (0.34 to 1.74)	0
Coadministration of NSAID				
NSAID	8	787	0.92 (0.52 to 1.62)	26
No NSAID	20	1683	1.00 (0.60 to 1.65)	0
Type of comparator				
Placebo	20	1615	1.32 (0.80 to 2.20)	0
Other drugs	6	745	0.62 (0.33 to 1.16)	0
Moment of bleeding episode				
Primary bleedings	9	952	0.93 (0.33 to 2.59)	0
Secondary bleedings	14	1437	0.97 (0.61 to 1.56)	18

Cold=dissection with cold steel instruments, haemostasis with gauze compression, or ligatures; combined=cold dissection with use of electrocautery for haemostasis; hot=dissection and haemostasis with electric device; NSAID=non-steroidal anti-inflammatory drug.

Table 4| **Sensitivity analysis of operative reintervention to treat post-tonsillectomy bleeding**

Subgroups	No of studies	No of participants	Odds ratio (95% CI)	I^2 (%)
Methodological quality				
Low risk of bias	3	299	0.91 (0.22 to 3.68)	0
High risk of bias	4	320	3.31 (0.51 to 21.61)	0
Blinding				
Double blinded	9	938	2.22 (0.95 to 5.18)	0
No blinding or unclear	3	240	2.64 (0.31 to 22.41)	0
Sample size				
<100 patients	7	394	3.85 (1.13 to 13.17)	0
≥100 patients	5	784	1.57 (0.56 to 4.38)	0
Follow-up				
≤24 h	3	260	3.06 (0.37 to 25.07)	0
>24 h	9	918	2.16 (0.92 to 5.06)	0
Age group				
Children only	8	679	3.43 (1.29 to 9.13)	0
Adults only	4	499	1.07 (0.29 to 4.03)	0
Surgical technique				
Cold or combined dissection	6	453	1.45 (0.50 to 4.20)	0
Hot dissection	4	450	3.84 (0.53 to 28.00)	0
Dosage regimen of steroid				
≤0.5 mg/kg	8	816	2.45 (1.04 to 5.76)	0
>0.5 mg/kg	4	362	1.52 (0.21 to 11.20)	0
Coadministration of NSAID				
NSAID	3	475	4.10 (0.99 to 16.97)	0
No NSAID	9	703	1.75 (0.68 to 4.50)	0

Cold=dissection with cold steel instruments, haemostasis with gauze compression, or ligatures; combined=cold dissection with use of electrocautery for haemostasis; hot=dissection and haemostasis with electric device; NSAID=non-steroidal anti-inflammatory drug.

Table 5| **Summary of evidence for key outcomes**

Outcome	No of participants/studies	Quality of evidence (GRADE)	Summary	
			Relative effect, odds ratio (95% CI)	Study events rates (steroid/control groups (%))
Post-tonsillectomy bleeding episodes	2674/29	Very low	0.96 (0.66 to 1.40)	4.6/4.2
Admission	1722/17	Very low	1.16 (0.68 to 2.00)	4.1/3.1
Reintervention	1178/12	High	2.27 (1.03 to 4.99)	3.0/1.5

Figures

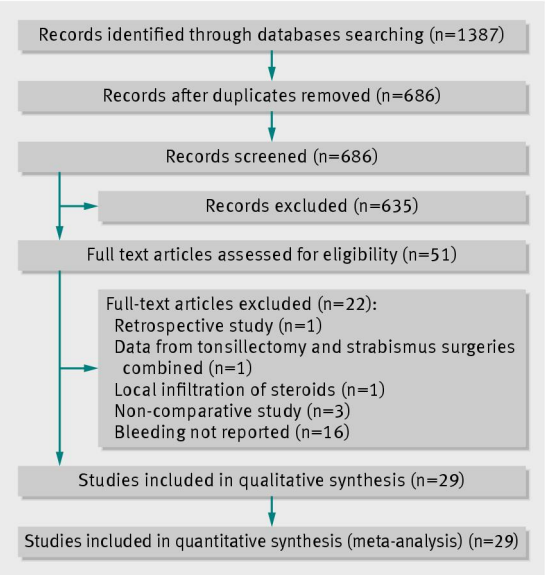

Fig 1 Flow diagram of studies

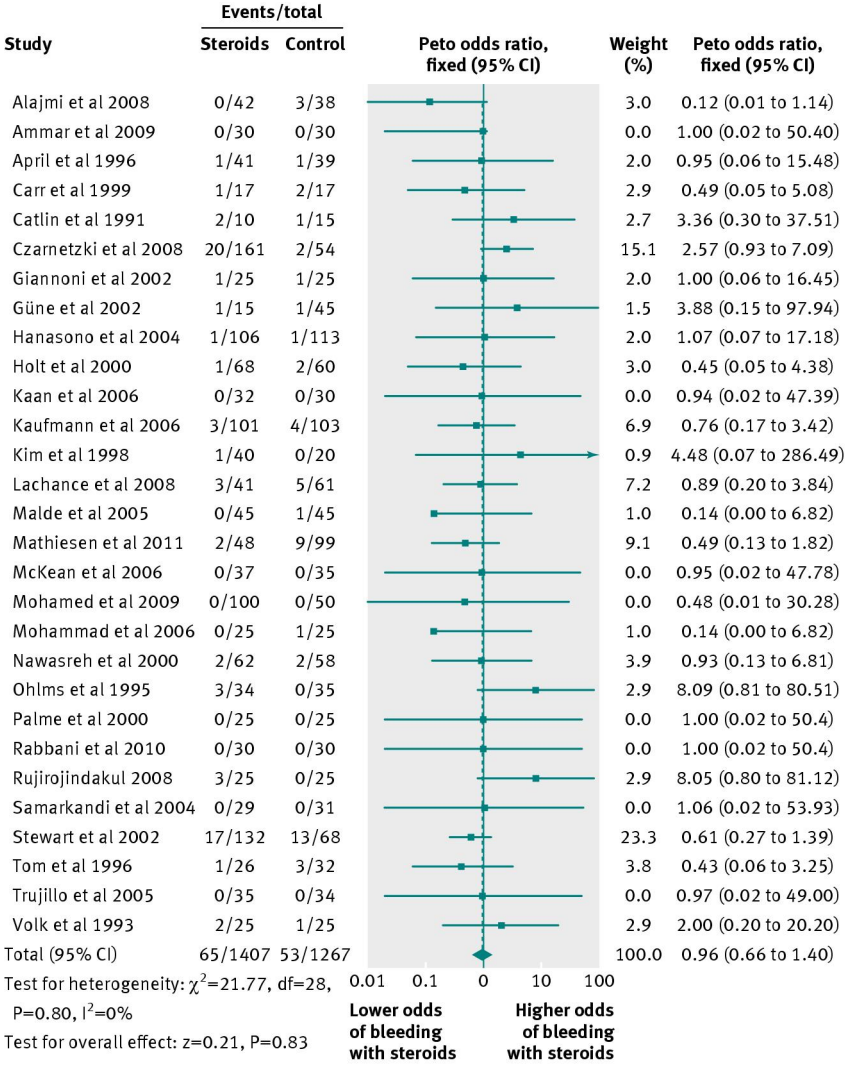

Fig 2 Post-tonsillectomy bleeding. For Peto odds ratio, continuity correction k=0.5 was used when there was no event in both groups

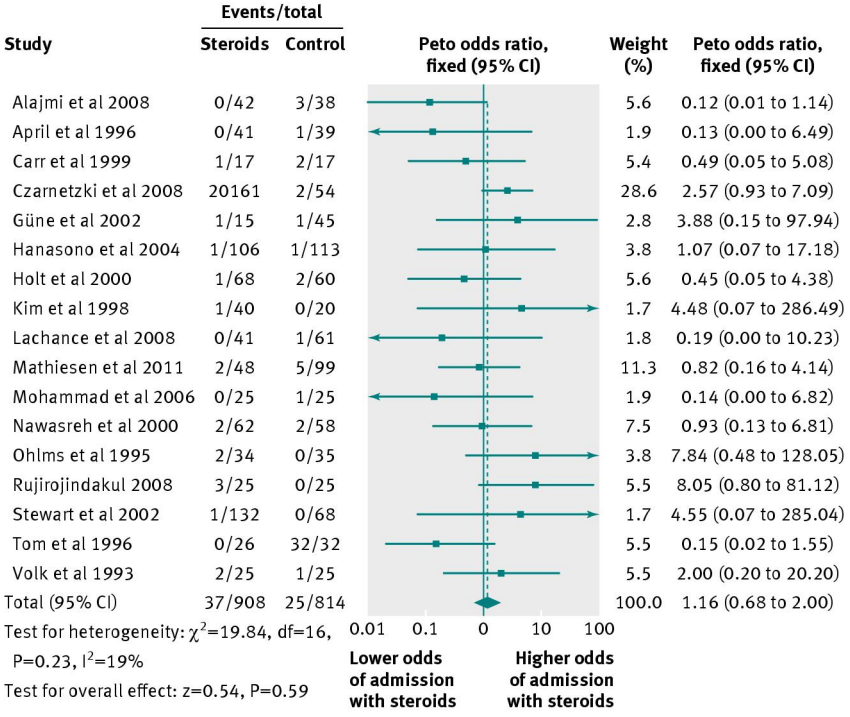

Fig 3 Admission for post-tonsillectomy bleeding

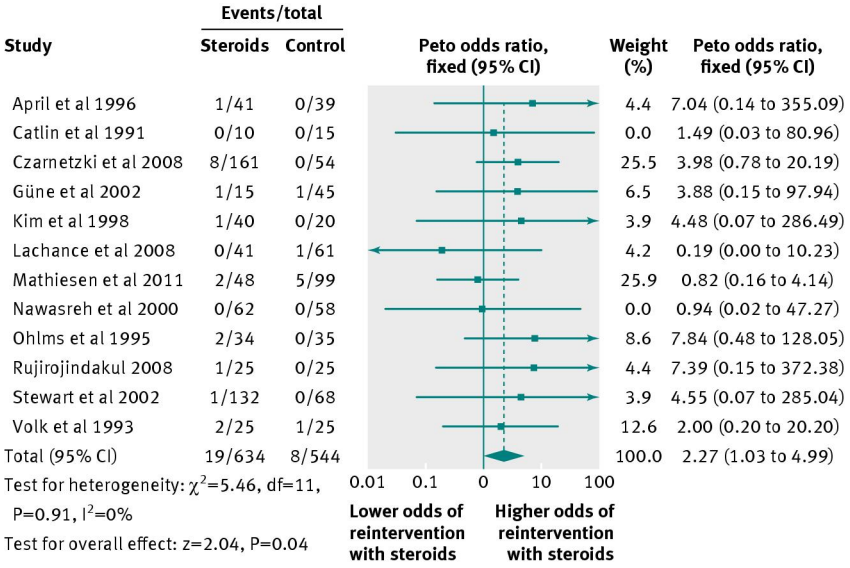

Fig 4 Reintervention for post-tonsillectomy bleeding. For Peto odds ratio, continuity correction k=0.5 was used when there was no event in both groups