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Steroids for improving recovery following tonsillectomy in children (Review)

Steward DL, Grisel J, Meinzen-Derr J

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Cochrane Database of Systematic Reviews 2011, Issue 8. Art. No.: CD003997.
DOI: 10.1002/14651858.CD003997.pub2.

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[Intervention Review]

Steroids for improving recovery following tonsillectomy in children

David L Steward[1], Jedidiah Grisel[2], Jareen Meinzen-Derr[3,4]

[1]Otolaryngology - Head and Neck Surgery, University of Cincinnati College of Medicine, Cincinnati, OH, USA. [2]Department of Otolaryngology, University of Cincinnati Academic Health Center, Cincinnati, OH, USA. [3]Department of Otolaryngology, Division of Pediatric Otolaryngology, Cincinnati Children's Hospital Medical Center, Cincinnati, OH, USA. [4]Division of Biostatistics and Epidemiology, Cincinnati Children's Hospital, Cincinnati, USA

Contact address: David L Steward, Otolaryngology - Head and Neck Surgery, University of Cincinnati College of Medicine, 231 Sabin Way, ML 0528 - Dept of OTO-HNS, Cincinnati, OH, 45267-0528, USA. stewardd@ucmail.uc.edu.

Editorial group: Cochrane ENT Group.
Publication status and date: New search for studies and content updated (conclusions changed), published in Issue 8, 2011.

Citation: Steward DL, Grisel J, Meinzen-Derr J. Steroids for improving recovery following tonsillectomy in children. *Cochrane Database of Systematic Reviews* 2011, Issue 8. Art. No.: CD003997. DOI: 10.1002/14651858.CD003997.pub2.

ABSTRACT

Background

This is an update of a Cochrane Review first published in *The Cochrane Library* in Issue 1, 2003.

Tonsillectomy continues to be one of the most common surgical procedures performed worldwide. Despite advances in anesthetic and surgical techniques, post-tonsillectomy morbidity remains a significant clinical problem.

Objectives

To assess the clinical efficacy of a single intraoperative dose of dexamethasone in reducing post-tonsillectomy morbidity.

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Web of Science; BIOSIS Previews; Cambridge Scientific Abstracts; ISRCTN; and additional sources for published and unpublished trials. The date of the most recent search was 29 October 2010, following a previous search in September 2002.

Selection criteria

Randomized, double-blind, placebo-controlled trials of a single dose of intravenous, intraoperative corticosteroid for pediatric patients (age < 18 years) who underwent tonsillectomy or adenotonsillectomy.

Data collection and analysis

The first author extracted data regarding the primary outcome measures and measurement tools from the published studies. The first author also recorded data regarding study design, patient ages, procedures performed, dose of corticosteroid and method of delivery, as well as methodological quality. When data were missing from the original publications, we contacted the authors for more information. We performed data analysis with a random-effects model, using the RevMan 5.1 software developed by the Cochrane Collaboration.

Main results

We included 19 studies (1756 participants). We selected only randomized, placebo-controlled, double-blinded studies to minimize inclusion of poor quality studies. However, the risk of bias in the included studies was not formally assessed. Children receiving a single intraoperative dose of dexamethasone (dose range = 0.15 to 1.0 mg/kg) were half as likely to vomit in the first 24 hours compared to children receiving placebo (risk ratio (RR) 0.49; 95% confidence interval (CI) 0.41 to 0.58; P < 0.00001). Routine use in five children would be expected to result in one less patient experiencing post-tonsillectomy emesis (risk difference (RD) -0.24; 95% CI -0.32 to -0.15; P < 0.00001). Children receiving dexamethasone were also more likely to advance to a soft/solid diet on post-tonsillectomy day one (RR 1.45; 95% CI 1.15 to 1.83; P = 0.001) than those receiving placebo. Finally, postoperative pain was improved in children receiving dexamethasone as measured by a visual analog scale (VAS, 0 to 10) (MD -1.07; 95% CI -1.73 to -0.41; P = 0.001), which correlates clinically to a reduction in pain (on a VAS of 0 to 10) from 4.72 to 3.65. No adverse events were noted in the included studies.

Authors' conclusions

The evidence suggests that a single intravenous dose of dexamethasone is an effective, safe and inexpensive treatment for reducing morbidity from pediatric tonsillectomy.

PLAIN LANGUAGE SUMMARY

Steroids for improving recovery following tonsillectomy in children

After children have a tonsillectomy or adenotonsillectomy (surgery to remove the adenoids and/or tonsils), pain, nausea, vomiting and delays to return to eating are common. The corticosteroid drug dexamethasone is sometimes given in a single intravenous dose (through the veins) during surgery to try to prevent vomiting after the operation. We included 19 randomized controlled trials in the review, with a total of 1756 patients. The review of trials found that a dose of corticosteroid during tonsillectomy or adenotonsillectomy can prevent vomiting for one out of every five children who gets the drug. Children also return to a normal diet more quickly and they have less pain after surgery.

BACKGROUND

This is an update of a Cochrane Review first published in *The Cochrane Library* in Issue 1, 2003.

Tonsillectomy continues to be one of the most common surgical procedures performed worldwide. Despite advances in anesthetic and surgical techniques, post-tonsillectomy morbidity (emesis, poor oral intake, pain and bleeding) remains a significant clinical problem for the patient, family and physician (Randall 1998).

During the past 40 years, investigators have studied the effects of systemic corticosteroids in reducing post-tonsillectomy morbidity (Papangelou 1972). Results of randomized, placebo-controlled studies of single intravenous steroid dosing have been conflicting; some demonstrating benefit and others showing no benefit (Aouad 2001; April 1996; Catlin 1991; Ohlms 1995; Pappas 1998; Splinter 1996; Tom 1996; Volk 1993; Vosdoganis 1999). For this reason, a Cochrane systematic review was completed in 2003 (Steward 2003), which showed that a single dose of intraoperative, intravenous steroids reduced postoperative emesis by half and children were more likely to return to a soft/solid diet by day one. Although pain was a predefined outcome measure in the 2003 review, due to inconsistencies in pain measurement we could not analyze this outcome, although a systematic review focusing specifically on pain was performed in 2006 (Afman 2006). Additionally, multiple randomized, double-blind, placebo-controlled trials have been performed during the intervening years since the initial review in 2003, which has created the need for an update of the current literature.

In an attempt to consolidate current research findings for emesis, return to diet and pain outcomes, and to update the Cochrane Review performed in 2003, we performed a systematic overview of published clinical trials using established meta-analysis techniques with a predetermined protocol (Boissel 1989; Saks 1987). Our hypothesis that a single intraoperative dose of dexamethasone re-

duces morbidity following pediatric tonsillectomy or adenotonsillectomy is based upon clinical experience and published randomized studies demonstrating reduction in post-tonsillectomy morbidity. Our goals were to determine if a meta-analysis of randomized studies would still statistically support this hypothesis and to determine if a statistically significant result would have clinical relevance.

OBJECTIVES

To assess the clinical efficacy of a single intraoperative dose of dexamethasone in reducing post-tonsillectomy morbidity.

METHODS

Criteria for considering studies for this review

Types of studies

Randomized, double-blind, placebo-controlled trials.

Types of participants

Pediatric patients (age < or = 18 years) who underwent tonsillectomy or adenotonsillectomy.

Types of interventions

Single dose of intravenous, intraoperative corticosteroid.

Types of outcome measures

1. The number of children experiencing emesis during the first 24 hours after surgery.
2. The number of children returning to a soft or solid diet by postoperative day one.
3. Pain at 24 hours as measured by a visual analog scale (VAS) normalized to a 0 to 10 range (0 = least pain, 10 = most pain).

Note: in the Cochrane Review of 2003, return to diet by post-tonsillectomy day three was also analyzed. In that review, only two studies (Catlin 1991; Volk 1993) met the inclusion criteria for day three analysis, and the results did not show any statistical significance between the steroid group and placebo (Steward 2003). Since 2003, return to diet by day three has not been measured with any consistency. For this reason, day three diet was eliminated from the current review. Additionally, several studies have measured time to first oral intake (hours). This outcome measure was not included in the 2003 review, and an improvement in this measure was felt to add little additional information separate from the 'return to diet by day one' measure. Therefore, this measure was not included in the current review.

Search methods for identification of studies

We conducted systematic searches for randomized controlled trials. There were no language, publication year or publication status restrictions. The date of the last search was 29 October 2010, following a previous search in September 2002.

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* 2010, Issue 4); PubMed; EMBASE; CINAHL; LILACS; KoreaMed; IndMed; PakMediNet; CAB Abstracts; Web of Science; BIOSIS Previews; CNKI; ISRCTN; ClinicalTrials.gov; ICTRP; and Google.

We modeled 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 randomized 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 major databases including CENTRAL are provided in Appendix 1.

Searching other resources

We scanned the reference lists of identified publications for additional trials and contacted trial authors where necessary. In addition, we searched PubMed, TRIPdatabase, NHS Evidence - ENT and Audiology, and Google to retrieve existing systematic reviews relevant to this systematic review, so that we could scan their reference lists for additional trials. In previous searches in 2002, we contacted leading experts in the fields of pediatric otolaryngology and pediatric anesthesiology for information on any relevant unpublished data.

Data collection and analysis

Selection of studies

We reviewed the titles and abstracts of all studies obtained by the search and two authors independently selected trials meeting the eligibility criteria. We obtained the full texts of the articles if there was insufficient information to make a decision and arranged

translations where necessary. We resolved any disagreements by discussion until a consensus was reached. We documented our justification for the exclusion of studies in the Characteristics of excluded studies table.

Data extraction and management

The first author extracted data regarding the primary outcome measures and measurement tools from the published studies. The first author also recorded data regarding study design, patient ages, procedures performed, dose of corticosteroid and method of delivery, as well as methodological quality. When data were missing from the original publications, we contacted the authors for more information.

Assessment of risk of bias in included studies

We specifically designed our protocol to select only randomized, placebo-controlled, double-blinded studies to minimize inclusion of poor quality studies. While we did not rank studies based upon quality, the authors did assess the methodological quality of included studies. Two of the authors (DLS, JG) worked independently to assess trials for methodological quality using the following criteria: allocation concealment (blinding of randomization), blinding of intervention, completeness of follow up and blinding of outcome measurement/assessment. We added information about allocation concealment to the table Characteristics of included studies under the 'Risk of bias' tables.

Data synthesis

We performed all meta-analyses of the included trials using the RevMan 5.1 software developed by the Cochrane Collaboration (RevMan 2011). We performed all data analyses with random-effects models and reported Mantel-Haenszel risk ratios for dichotomous outcomes. For continuous outcomes, we derived a pooled risk difference from a random-effects model. When a study collected but did not report data regarding one of the three primary outcome measures, we excluded that study from the meta-analysis of that particular outcome measure. When a measurement tool for an outcome from one study differed from other studies in such a way as to prevent pooling of data, we excluded that study and provided the reasons in the results section. Lastly, we excluded studies that did not collect data regarding a particular outcome measure from analysis of that outcome measure. We made decisions regarding the exclusion of studies from analysis based on the above criteria with the investigators blinded to the results of the studies. RevMan calculates measures of heterogeneity with the Chi^2 test and I^2 statistic, which measures the inconsistency of effects across interventions. We performed sensitivity analyses to assess statistically the impact of study exclusion due to missing data or different measurement tools (Boissel 1989). We also performed sensitivity analysis to assess the potential impact of publication bias or missed studies (Rosenthal 1979).

RESULTS

Description of studies

Results of the search

From the update searches in 2010, we retrieved a total of 514 references: 302 of these were removed in first-level screening (i.e. removal of duplicates and clearly irrelevant references), leaving 101 references for further consideration. The searches conducted in 2002 had yielded over 180 titles and abstracts for review.
We reviewed all titles and abstracts for possible inclusion. We evaluated foreign language publications based upon available English translations or translated them for evaluation. We then reviewed any potential studies in full. Of these, 10 met the above inclusion criteria, which we combined with the studies included in the 2003 review (see Characteristics of included studies). Other searches, using the 'clinical query' filter of the PubMed (MEDLINE) database, *The Cochrane Library* database and other search terms (CORTICOSTEROIDS, DEXAMETHASONE and MORBIDITY), yielded no additional studies meeting the selection criteria. Likewise, no other studies meeting the selection criteria were identified through cross-referencing, nor through contacting experts in the field.

Included studies

We included 19 studies in the current review (1756 participants). Ten of these studies were new for the current update and nine were included from the previous version of the review (Steward 2003). A summary of the included studies is as follows:

Design

All included studies were randomized, placebo-controlled and double-blinded.

Setting

Studies were all performed in academic health centers from international locations.

Participants

Only children were included and ages ranged from nine months to 18 years.

Interventions

The studied intervention was a single, intraoperative dose of corticosteroid (dexamethasone), ranging from 0.15 mg/kg to 1.0 mg/kg.

Outcomes

Measured outcomes included:

1. the number of children experiencing emesis during the first 24 hours after surgery;
2. return to a soft or solid diet by postoperative day one; and
3. pain at 24 hours as measured by a visual analog scale (VAS) normalized to a 0 to 10 range (0 = least pain, 10 = most pain).

Excluded studies

Forty-three studies addressing steroid treatment to reduce post-tonsillectomy morbidity failed to meet the selection criteria and were excluded (see Characteristics of excluded studies). Thirteen studies did not meet the allocation requirement (not randomized, placebo-controlled or double-blinded). Twenty-three studies did not involve intravenous administration of steroids. Eleven studies were not limited to children. Fifteen studies did not limit the experimental group to steroids only. Two studies included procedures other than tonsillectomy/adenoidectomy (uvulopalatopharyngoplasty in both cases). One study did not report any of the outcomes included in this review, and one study was terminated early.

Risk of bias in included studies

To address problems of quality in meta-analysis, some authors have suggested methods to assign relative value to studies based upon assessment of quality (Chalmers 1981). However, this technique has not gained universal acceptance (Boissel 1989). We specifically designed our protocol to select only randomized, placebo-controlled, double-blinded studies to minimize inclusion of poor quality studies.

While we did not rank studies based upon quality, the authors did assess the methodological quality of included studies. Two of the authors (DLS, JG) worked independently to assess trials for methodological quality using the following criteria: allocation concealment (blinding of randomization), blinding of intervention, completeness of follow up, and blinding of outcome measurement/assessment. We added information on allocation concealment to the table Characteristics of included studies in the 'Risk of bias' tables.

Only six studies reported adequate allocation concealment (April 1996; Catlin 1991; Elhakim 2003; Giannoni 2002; Hanasono 2004; Volk 1993), while the remaining studies were unclear on this point. Performance bias included surgical and anesthetic techniques, which were controlled in nine of the studies (Aouad 2001; Bhattacharya 2009; Catlin 1991; Elhakim 2003; Giannoni 2002; Hanasono 2004; Kaufmann 2006; Ohlms 1995; Pappas 1998). Surgical technique was not controlled in four studies (Kaan 2006; Khani 2009; Samarkandi 2004; Splinter 1996), while anesthetic technique was not controlled in six studies (Al Shehri 2007; April 1996; Splinter 1996; Tom 1996; Volk 1993; Vosdoganis 1999), one of which used blocked randomization to address this issue (Splinter 1996). Attrition bias did not appear to be significant within any of the studies and all studies reported the number of subjects excluded from analysis. Outcome measurements differed amongst studies and are discussed specifically in the results section for each outcome measure. Reporting bias (not reporting data with no statistical significance) was present in one study for the emesis outcome (Catlin 1991), two studies for dietary outcomes (Catlin 1991; Volk 1993) and four studies for pain outcomes (April 1996; Catlin 1991; Tom 1996; Volk 1993). Based on this analysis, the authors feel that the risk of bias is low, however we did not perform a formal assessment.

Effects of interventions

Emesis

We evaluated emesis by analyzing the number of patients who experienced an emetic event during the first 24 hours following tonsillectomy. For this outcome measure, we pooled the data from 15 studies (1273 participants). The result of the meta-analysis suggests a statistically significant risk ratio, favoring steroids (RR 0.49; 95% confidence interval (CI) 0.41 to 0.58; P < 0.00001) (Analysis 1.1). In addition, patients who received steroids had lower rate of emesis (21%) compared to patients who received placebo (48%). The pooled risk difference for this analysis was statistically significant (RD -0.24; 95% CI -0.32 to -0.15; P < 0.00001) (Analysis 1.2). No significant heterogeneity regarding the risk ratio was noted in this meta-analysis (I^2 = 14%; P = 0.3), although significant heterogeneity was present regarding the risk difference (I^2 = 71%; P < 0.0001).

Sensitivity analysis (emesis)

We checked the sensitivity of this analysis to potential reporting bias (not reporting data with a null result) first by deleting and then by assuming a null result for the Giannoni et al study (Giannoni 2002). The results were not significantly different for either the deleted (RR 0.48; 95% CI 0.40 to 0.58; P < 0.00001) or null assumption analyses (RR 0.50; 95% CI 0.41 to 0.60; P < 0.00001). We also conducted sensitivity analysis by assuming a null result for the Catlin et al study (Catlin 1991). Again, the results were not different including Catlin et al with a null assumption (RR 0.49; 95% CI 0.41 to 0.59; P < 0.00001). To check the sensitivity of the emesis analysis to possible publication bias (not publishing studies with a null result) and/or studies missed by the search strategy,

we calculated the fail-safe N as described by Rosenthal (Rosenthal 1979). The result of this analysis suggests that 129 studies with a null risk ratio (i.e. RR = 1) would be required to raise the overall risk ratio to statistical non-significance.

Diet (day one)

We evaluated diet by analyzing the number of patients that advanced to a soft or solid diet during post-tonsillectomy day one. We pooled the data from five studies (452 participants) in the day one diet analysis. The result of this meta-analysis suggests statistical significance using both risk ratio (RR 1.45; 95% CI 1.15 to 1.83; P = 0.001) (Analysis 1.3) and risk difference (RD 0.21; 95% CI 0.10 to 0.31; P < 0.0001) (Analysis 1.4). Although moderate heterogeneity was noted regarding both the risk ratio (I^2 = 46%; P = 0.12) and the risk difference (I^2 = 44%; P = 0.13), neither was statistically significant.

Sensitivity analyses (day one diet)

To determine the impact of potential reporting bias, we performed sensitivity analysis assuming a null result for the two studies with missing data (Catlin 1991; Volk 1993). The missing proportions in each group for each study were set equal to the observed average over all studies (0.58). The risk ratio is reduced, but still suggests statistical significance (RR 1.35; 95% CI 1.13 to 1.61; P = 0.001). To assess the impact of possible selection bias resulting from exclusion of the studies by Pappas et al, Aouad et al and Kaan et al, we performed sensitivity analysis by also including these studies (Aouad 2001; Kaan 2006; Pappas 1998). The result suggests statistical significance (RR 1.52; 95% CI 1.18 to 1.97; P = 0.001) even when including the null assumption for the missing data as described above (RR 1.23; 95% CI 1.04 to 1.46; P = 0.01).

Pain

Eight studies (652 participants) were included in this analysis (Elhakim 2003; Giannoni 2002; Hanasono 2004; Kaan 2006; Khani 2009; Ohlms 1995; Volk 1993; Vosdoganis 1999). The result of this meta-analysis suggests statistical difference in the mean difference regarding mean pain scores (mean difference (MD) -1.07; 95% CI -1.73 to -0.41; P = 0.001) (Analysis 1.5). We excluded three studies because they did not report pain as an outcome (Aouad 2001; Kyrou 2001; Splinter 1996). Six studies (Al Shehri 2007; April 1996; Bhattacharya 2009; Catlin 1991; Kaufmann 2006; Samarkandi 2004) that evaluated pain as an outcome measure did not publish enough data for analysis, and thus were excluded. Pappas et al reported analgesic use as a pain outcome measure and Tom et al reported the frequency of pain between study groups; both studies were also excluded (Pappas 1998; Tom 1996). Significant heterogeneity was noted in this meta-analysis (I^2 = 86%; P < 0.00001).

Sensitivity analysis (pain)

To determine the impact of potential reporting bias, we performed sensitivity analysis assuming a null result for the six studies that did record pain scores, but did not adequately report results for inclusion (Al Shehri 2007; April 1996; Bhattacharya 2009; Catlin 1991; Kaufmann 2006; Samarkandi 2004). This was done by assuming a null result for the additional studies and recalculating the pooled difference in means. Including the additional studies reduced the pooled mean difference, but the results remained significant (MD -0.59; 95% CI -1.18 to 0.0; P = 0.05).
We detected significant heterogeneity in the meta-analysis of pain scores, therefore we also performed a sensitivity analysis to determine whether the heterogeneity was due to the presence of one or two outlying studies. Each study was subsequently removed from the analysis and the pooled results were recalculated to determine which study(ies) contributed the most to the heterogeneity. Results indicated that both of the studies by Elhakim et al (Elhakim 2003) and Khani et al (Khani 2009) contributed the most to the I^2. After excluding these two studies, the I^2 was 0% (P = 0.67) (MD -0.48; 95% CI -0.85, -0.10; P = 0.01).

DISCUSSION

Meta-analysis

With certain limitations, meta-analysis is a valuable tool that can provide a more objective evaluation of a group of studies than a traditional narrative review (Alsarraf 2000). Limitations of meta-analysis are well described and can be grouped into problems of combinability, selection bias and the quality of the original studies (Sharpe 1997). Combinability problems result from 'mixing apples and oranges'. In our study this relates to pooling data from studies with different surgical techniques, surgical procedures, anesthetic techniques, dexamethasone dosages, patient populations and outcome measurement tools. To address this problem, we accepted the inherent heterogeneity amongst the trials and utilized a random-effects model for analysis, rather than a fixed-effect model. This has the advantage of allowing for variability within the patient populations and also for variability in treatment effect (Boissel 1989).
To address problems of selection bias in our meta-analysis, we performed sensitivity analyses to determine the impact on our results due to exclusion of studies: potentially missed or unpublished; with missing data; or with a significantly different measurement tool (Boissel 1989; Rosenthal 1979). The results for the emesis and day one diet outcome measures remained significant even after the sensitivity analysis. For the pain outcome, the pooled mean difference (MD) changed from -1.07 (95% confidence interval (CI) -1.73 to -0.41; P = 0.001) to -0.59 (95% CI -1.18 to 0.0; P = 0.05).

To address problems of quality in meta-analysis, some authors have suggested methods to assign relative value to studies based upon assessment of quality (Chalmers 1981). However, this technique has not gained universal acceptance (Boissel 1989). We specifically designed our protocol to select only randomized, placebo-controlled, double-blinded studies to minimize inclusion of poor quality studies. As such, we think it unlikely that quality issues significantly impact the result of our analyses.

Emesis

Our results suggest a statistically significant reduction in chance of experiencing episodes of post-tonsillectomy emesis during the first 24 hours with dexamethasone versus placebo for pediatric patients.

The mechanism by which dexamethasone may exert an anti-emetic effect remains unknown (Brunton 1996). However, dexamethasone has been shown to be an effective anti-emetic in randomized trials with emetogenic chemotherapy (Hesketh 1994; Research 1995). Additionally, randomized studies of a serotonin antagonist plus either dexamethasone or placebo have shown a statistically significant reduction in emesis after pediatric tonsillectomy in the dexamethasone-treated group (Fujii 1996; Holt 2000). Thus, despite the fact that the mechanism is not yet understood, an anti-emetic effect of corticosteroids is supported by other studies (Goldman 2000; Henzi 2000) and widely accepted (Schimmer 1996).

The number needed to treat (NNT = 1/risk difference) is a statistical inference of the size of therapeutic effect one might expect in clinical practice. The NNT of 4.17 predicts that routine use of a single intravenous dose of dexamethasone in approximately five patients would result in one less patient experiencing post-tonsillectomy emesis. This suggests therapeutic benefit with a clinically relevant effect size. This therapeutic benefit is consistent with the previous review in 2003. In clinical practice, whether or not an individual patient responds will likely be dependent upon patient factors, anesthetic technique, narcotic use and possibly the amount of blood swallowed during tonsillectomy.

Diet

An earlier return to a regular diet following tonsillectomy as a result of dexamethasone therapy could be the result of mood elevation, appetite stimulation, anti-emetic effect or a combination of these (Schimmer 1996). Our results of the day one diet outcome measure demonstrate a statistically significant increase in the number of patients returning to a soft/solid diet during the first 24 hours. In 2003, the systematic review also demonstrated a statistically significant difference (RR 1.69, P = 0.04). The current review reduces the chance of a type I error from 4% to 0.1%.

The NNT of 4.76 suggests that routine use of dexamethasone in five children would result in one more child advancing to a soft/solid diet on post-tonsillectomy day one. This suggests a clinically significant effect size. These results are consistent with and support the findings of the 2003 systematic review (Steward 2003).

Pain

In the 2003 Cochrane Review, pain was listed as a predefined outcome, but there were insufficient data to analyze the results. Since that time, eight studies have rigorously measured postoperative pain using a visual analog scale (VAS). (Elhakim 2003; Giannoni 2002; Hanasono 2004; Kaan 2006; Khani 2009; Ohlms 1995; Volk 1993; Vosdoganis 1999). The results of meta-analysis of these studies demonstrate a statistically significant improvement in postoperative pain for patients in the steroid group (MD -1.07; 95% CI -1.73 to -0.41; P = 0.001). These data are consistent with the results of a systematic review devoted specifically to this issue (Afman 2006).

The clinical significance of this observed pain reduction must be considered. Each study measured pain on a visual analog scale (VAS) with 0 corresponding to 'least pain' and 10 corresponding to 'most pain' (studies with different pain scales were normalized to a 0 to 10 scale). The mean score in the placebo group was 4.72 and the steroid group was reduced to 3.65. The sensitivity analysis decreased this pain reduction benefit (MD -0.59; 95% CI -1.18 to 0.0; P = 0.05). Therefore, while dexamethasone was associated with reduction in pain, the clinical significance of this finding should be interpreted with caution. The effect size of the estimated benefit on postoperative pain appeared to be, in part, driven by specific studies.

Safety

One of the excluded studies was terminated prematurely because the steroid group demonstrated significant postoperative hemorrhage compared to placebo (Czarnetzki 2008). Several methodological questions have been raised regarding this study, including non-standardization of diagnosis, administration of ibuprofen, non-standard surgical technique and attributing primary hemorrhage to dexamethasone use (Gunter 2009). Indeed, four of eight patients requiring surgical re-intervention had bleeding on the day of surgery. The use of ibuprofen perioperatively is also controversial. Ibuprofen is known to have antiplatelet effects and some practice guidelines discourage its perioperative use (Douketis 2008), although a recent prospective study comparing tonsillectomy patients recovered with ibuprofen did not observe increased bleeding rates compared to placebo (Yaman 2011).

The findings published by Czarnetski et al resulted in several retrospective chart reviews representing 3318 patients receiving intraoperative, intravenous dexamethasone (Brigger 2010; Shakeel 2010). These studies did not show any increase in bleeding rates associated with steroid use. None of the other included or excluded studies for this review demonstrated any increased bleeding risk.

It should also be considered that the findings of Czarnetski et al were a type I error. Duplication under more appropriate study conditions should be performed before serious consideration can be made of their claim.

Other risks to patients of single-dose dexamethasone appear minimal. A single dose of corticosteroid, even a large one, has been considered to be virtually without harmful effects (Schimmer 1996). The most concerning potential risks of corticosteroid therapy include immune system suppression resulting in severe systemic infection and avascular joint necrosis. Disseminated varicella infection (chicken pox) is described in patients undergoing immune suppressive steroid therapy. A systematic review of avascular joint necrosis found that while risk is associated with increased daily steroid dosage, no increased risk was observed with single bolus dosing (Felsen 1987). While neither complication has been reported as a consequence of a single perioperative dose during tonsillectomy, this does not imply that these complications are not possible. Appropriate discussion of the risks and benefits of therapy should occur between patient, family and physician.

The cost of dexamethasone is relatively low, which makes routine use seem reasonable. This modest increase in cost may be offset by a reduction in cost resulting from rescue anti-emetic therapy, prolonged hospitalization or both. However, its cost-effectiveness remains to be studied.

A previously published version of this meta-analysis suggested improved anti-emetic effect with increasing dexamethasone dose (Steward 2001). Though meta-analysis lends itself to subset analysis (Boissel 1989; Saks 1987), caution should be used in evaluating this result as these studies were not designed to assess dose effect and patients were not randomized to different dosages. Additionally, because both mg/kg dose and the maximum dose given varied amongst these studies, statistical results of regression analysis of only the former are questionable. Therefore, the question of appropriate dosing remains unanswered and final recommendations must await randomized dose-control trials

Generalizability

As this analysis excluded studies with adult patients, these results cannot be generalized to the adult population. However, dexamethasone has been shown to be an effective anti-emetic in adult patients undergoing emetogenic chemotherapy, suggesting a role for further study in adult tonsillectomy patients. Previous randomized, placebo-controlled studies of adult patients have focused primarily on pain as an outcome measure (Carr 1999; Tewary 1993).

AUTHORS' CONCLUSIONS

Implications for practice

Tonsillectomy is one of the most commonly performed surgical procedures worldwide. Despite changes in anesthetic and surgical techniques, however, postoperative morbidity remains a significant clinical problem. The results of our meta-analysis suggest a statistically significant reduction in postoperative morbidity with single-dose dexamethasone therapy given during pediatric tonsillectomy or adenotonsillectomy. Specifically, our results suggest a statistically significant reduction in post-tonsillectomy emesis events during the first 24 hours and an increase in the number of patients advancing to a soft/solid diet on postoperative day one. Postoperative pain is also reduced with dexamethasone use. Moreover, single-dose dexamethasone therapy is inexpensive and, if harmful effects occur, they are exceptionally rare. Given the frequency with which tonsillectomy is performed; the low cost and safety of single-dose intravenous dexamethasone; and the benefit from emesis reduction, return to a soft/solid diet and pain reduction, the evidence suggests that routine use would significantly reduce morbidity from pediatric tonsillectomy.

Implications for research

Further study is still warranted to determine optimum dexamethasone dosing. Additionally, further study is suggested to determine possible benefit in the adult tonsillectomy patient. Lastly, any suggestion that single-dose dexamethasone increases bleeding risk needs to be substantiated with further studies.

ACKNOWLEDGEMENTS

Statistical support was provided by the Center for Epidemiology and Biostatistics at Cincinnati Children's Medical Center, Cincinnati, OH.

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* *Indicates the major publication for the study*

CHARACTERISTICS OF STUDIES

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

Al Shehri 2007

Methods	Randomized, double-blind, placebo-controlled	
Participants	150 patients enrolled age 2 to 6 years undergoing tonsillectomy with or without adenoidectomy (electrodissection)	
Interventions	Dexamethasone 0.5 mg/kg (max dose 8 mg) IV or dexamethasone 1.0 mg/kg (max dose 16 mg) IV or 2 mL normal saline	
Outcomes	Incidence of early (PACU) and late (ward) vomiting; total incidence Time to first oral intake (hours) Postoperative pain score (recorded but not reported)	
Notes	Anesthetic not controlled; surgery controlled	
Risk of bias		
Bias	**Authors' judgement**	**Support for judgement**
Allocation concealment (selection bias)	Unclear risk	Unclear

Aouad 2001

Methods	Randomized, double-blind, placebo-controlled	
Participants	110 patients enrolled age 2 to 12 years undergoing tonsillectomy or adenotonsillectomy (electrosurgery) 106 patients completed (53 placebo and 53 steroid)	
Interventions	Dexamethasone 0.5 mg/kg (max dose 8 mg) IV or normal saline	
Outcomes	Emesis 24 hours Day 1 diet (rated based upon child requesting food, accepts when offered, accepts when coaxed, refuses) Time to first oral intake Outcomes not included: day 3 diet; pain	
Notes	Anesthesia and surgery controlled	
Risk of bias		
Bias	**Authors' judgement**	**Support for judgement**

Aouad 2001 (*Continued*)

Allocation concealment (selection bias)	Unclear risk	Unclear

April 1996

Methods	Randomized, double-blind, placebo-controlled
Participants	80 patients age 3 to 15 years undergoing tonsillectomy or adenotonsillectomy (electro-surgery) (41 steroid and 39 placebo)
Interventions	Dexamethasone 0.5 mg/kg (max dose 8 mg) IV or normal saline
Outcomes	Emesis 6 hours Day 1 diet Pain (scale and analgesic use) recorded but not reported Outcomes not included: day 3 diet
Notes	Anesthesia not controlled; surgery controlled

Risk of bias

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

Bhattacharya 2009

Methods	Randomized, double-blind, placebo-controlled
Participants	100 patients enrolled age 6 to 15 years undergoing tonsillectomy (no electrocautery)
Interventions	Dexamethasone 8 mg IV or normal saline Diclofenac patch applied to all participants
Outcomes	Emesis 24 hours Day 1 diet (obtained by communication) Pain score (VAS) (obtained by communication)
Notes	Anesthesia and surgery controlled

Risk of bias

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

Catlin 1991

Methods	Randomized, double-blind, placebo-controlled	
Participants	25 patients age 3 to 12 years undergoing tonsillectomy or adenotonsillectomy (cold) (10 steroid and 15 placebo)	
Interventions	Dexamethasone 1.0 mg/kg (max dose 16 mg) IV or normal saline	
Outcomes	Emesis 24 hours recorded but not reported Day 1 diet recorded but not reported Day 3 diet Pain (score and analgesic use) recorded but not reported	
Notes	Anesthesia and surgery controlled	
Risk of bias		
Bias	**Authors' judgement**	**Support for judgement**
Allocation concealment (selection bias)	Low risk	Adequate

Elhakim 2003

Methods	Randomized, double-blind, placebo-controlled	
Participants	120 patients age 4 to 11 years undergoing tonsillectomy or adenotonsillectomy (electro-cautery)	
Interventions	Dexamethasone 0.5 mg/kg (max dose 8 mg) IV or normal saline	
Outcomes	Emesis 24 hours (steroid 20% versus placebo 56%) Time to first oral intake Pain score 24 hours (VAS)	
Notes	Anesthesia and surgery controlled	
Risk of bias		
Bias	**Authors' judgement**	**Support for judgement**
Allocation concealment (selection bias)	Low risk	Adequate

Giannoni 2002

Methods	Randomized, double-blind, placebo-controlled
Participants	50 patients age 3 to 15 years undergoing tonsillectomy or adenotonsillectomy (electrocautery)
Interventions	Dexamethasone 1.0 mg/kg (max dose 16 mg) IV or normal saline
Outcomes	Emesis 24 hours (recorded but not reported) Pain score 24 hours (VAS) Quality of life survey
Notes	Surgery and anesthesia controlled

Risk of bias

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

Hanasono 2004

Methods	Randomized, double-blind, placebo-controlled
Participants	219 patients age 9 months to 12 years undergoing tonsillectomy (62 electrocautery and steroids, 44 cold and steroids, 56 electrocautery and placebo, 57 cold and placebo)
Interventions	Dexamethasone 1 mg/kg IV or placebo
Outcomes	Episodes of emesis Percentage of oral intake Patient related pain score (VAS)
Notes	Surgery and anesthesia controlled

Risk of bias

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

Kaan 2006

Methods	Randomized, double-blind, placebo-controlled
Participants	66 patients age 4 to 12 years undergoing tonsillectomy or adenotonsillectomy
Interventions	Dexamethasone 0.5 mg/kg (max dose 8 mg) or saline

Kaan 2006 (*Continued*)

Outcomes	Emesis at at least 8 hours Time to first oral intake Number of patients requesting oral intake or accepting when offered Pain (VAS), rated 1 to 5 and multiplied by 2 to get a 10-point scale; steroid 2.0 (SD 0.4) versus placebo 4.0 (SD 1.0)
Notes	Anesthesia controlled

Risk of bias

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

Kaufmann 2006

Methods	Randomized, placebo-controlled (does not report blinding)
Participants	230 children ages 2 to 16 years undergoing tonsillectomy or adenotonsillectomy (combination hot/cold technique); 204 completed study (steroid 101 versus placebo 103)
Interventions	Dexamethasone 0.5 mg/kg (max dose 10 mg) IV versus no treatment
Outcomes	Emesis 24 hours: only recorded number of patients with more than 1 episode Day 1 diet Pain score (VAS): recorded but not reported
Notes	Surgery and anesthesia controlled

Risk of bias

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

Khani 2009

Methods	Randomized, double-blind, placebo-controlled
Participants	66 patients age 4 to 12 years undergoing tonsillectomy or adenotonsillectomy (method unclear)
Interventions	Dexamethasone 0.5 mg/kg (max dose 8 mg) IV or saline
Outcomes	Emesis 24 hours: only measured at 8 hours Day 1 diet: only measured as time to first oral intake

Khani 2009 (*Continued*)

	Pain score (VAS): recorded but not reported	
Notes	Anesthesia controlled	
Risk of bias		
Bias	**Authors' judgement**	**Support for judgement**
Allocation concealment (selection bias)	Unclear risk	Unclear

Kyrou 2001

Methods	Randomized, double-blind, placebo-controlled	
Participants	60 patients age 4 to 14 years undergoing tonsillectomy or adenotonsillectomy	
Interventions	Dexamethasone 0.2 mg/kg IV AND metoclopramide 0.15 mg/kg IV or metoclopramide 0.15 mg/kg IV	
Outcomes	Emesis 24 hours (steroid 10% versus placebo 37%)	
Notes	Anesthesia and surgery control not reported	
Risk of bias		
Bias	**Authors' judgement**	**Support for judgement**
Allocation concealment (selection bias)	Unclear risk	Unclear

Ohlms 1995

Methods	Randomized, double-blind, placebo-controlled
Participants	69 patients age 3 to 18 years undergoing tonsillectomy or adenotonsillectomy (cold) (34 steroid and 35 placebo)
Interventions	Dexamethasone 0.5 mg/kg (max dose 12 mg) IV or normal saline
Outcomes	Emesis 24 hours Day 1 diet Day 3 diet Pain score Analgesic doses
Notes	Anesthesia and surgery controlled

Ohlms 1995 (*Continued*)

Risk of bias		
Bias	**Authors' judgement**	**Support for judgement**
Allocation concealment (selection bias)	Unclear risk	Unclear

Pappas 1998

Methods	Randomized, double-blind, placebo-controlled
Participants	130 patients age 2 to 12 years undergoing tonsillectomy or adenotonsillectomy (electrosurgery) (63 steroid and 65 placebo)
Interventions	Dexamethasone 1.0 mg/kg (max dose 25 mg) IV or normal saline
Outcomes	Emesis 24 hours ("retch" or emesis) Day 1 diet (rated based upon child requesting food, accepts when offered, accepts when coaxed, refuses) Pain: analgesic use in PACU Outcomes not included: day 3 diet
Notes	Anesthesia and surgery controlled

Risk of bias		
Bias	**Authors' judgement**	**Support for judgement**
Allocation concealment (selection bias)	Unclear risk	Unclear

Samarkandi 2004

Methods	Randomized, double-blind, placebo-controlled
Participants	60 patients age 2 to 12 years undergoing tonsillectomy (electrocautery)
Interventions	Dexamethasone 0.5 mg/kg IV or saline (steroid 29 versus placebo 31)
Outcomes	Emesis 24 hours (steroid 38% versus steroid 74%); data collected only until time of discharge Pain (VAS) recorded but not reported Oral intake recorded only as number of patient taking oral intake within first 3 postoperative hours
Notes	Anesthetic controlled

Risk of bias

Samarkandi 2004 (*Continued*)

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

Splinter 1996

Methods	Randomized, double-blind, placebo-controlled
Participants	133 patients age 2 to 12 years undergoing tonsillectomy or adenotonsillectomy (mixed technique) (63 steroid and 70 placebo)
Interventions	Dexamethasone 0.5 mg/kg (max dose 8 mg) IV or normal saline
Outcomes	Emesis 24 hours Outcomes not included: diet; pain
Notes	Anesthesia controlled; surgery not controlled

Risk of bias

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

Tom 1996

Methods	Randomized, double-blind, placebo-controlled
Participants	58 patients age 1 to 18 years undergoing adenotonsillectomy (electrosurgery) (26 steroid and 32 placebo)
Interventions	Dexamethasone 0.15 mg/kg (max dose 8 mg) IV or normal saline
Outcomes	Emesis 24 hours Day 1 diet Day 3 diet Pain Analgesic doses recorded but not reported
Notes	Anesthesia not controlled; surgery controlled

Risk of bias

Bias	Authors' judgement	Support for judgement

Tom 1996 (*Continued*)

Allocation concealment (selection bias)	Unclear risk	Unclear

Volk 1993

Methods	Randomized, double-blind, placebo-controlled
Participants	49 patients age 4 to 12 years undergoing tonsillectomy or adenotonsillectomy (cold) (24 steroid and 25 placebo)
Interventions	Dexamethasone 10 mg IV or normal saline
Outcomes	Day 1 diet mean scores Day 3 diet mean scores Pain score Analgesic Outcomes not included: emesis
Notes	Anesthesia not controlled; surgery controlled

Risk of bias

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

Vosdoganis 1999

Methods	Randomized, double-blind, placebo-controlled
Participants	41 patients age 2 to 12 years undergoing tonsillectomy or adenotonsillectomy (cold with electrosurgical hemostasis) (22 steroid and 19 placebo)
Interventions	Dexamethasone 0.4 mg/kg (max dose 8 mg) IV or normal saline
Outcomes	Emesis 24 hours Day 1 diet (by personal communication) Time (hours) to first solid diet Pain score Analgesic Outcomes not included: day 3 diet
Notes	Anesthesia not controlled; surgery controlled

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**

Vosdoganis 1999 (*Continued*)

Allocation concealment (selection bias)	Unclear risk	Not used

IV: intravenous
PACU: post-anesthesia care unit
VAS: visual analog scale

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

Study	Reason for exclusion
Alajmi 2008	Allocation: not double-blinded
Alavoine 1969	Allocation: not randomized, double-blinded and placebo-controlled
Ammar 2009	Interventions: not intraoperative IV administration
Anderson 1975	Participants: not limited to children Interventions: not intravenous route (tonsil fossa injection)
Atherino 1966	Interventions: not corticosteroid only (corticosteroid + antibiotic) Not intravenous route (tonsil fossa injection)
Bonaccorsi 1965	Interventions: not corticosteroid only (steroid + antihistamine)
Carr 1999	Participants: not limited to children
Celiker 2004	Allocation: not placebo-controlled
Cho 1998	Interventions: not corticosteroid only (steroid + propofol or enflurane)
Cupero 2003	Participants: not limited to children Not intravenous route (tonsil fossa injection)
Czarnetzki 2008	Study was terminated for bleeding in steroid group; patients were recovered with ibuprofen
Del 1970	Interventions: not corticosteroid only (estriol) Not intravenous route (topical)
Egeli 1997	Participants: not limited to children Interventions: not intravenous route (tonsil fossa injection)
El Sabiee 2004	Interventions: not corticosteroid only (steroid + ketamine versus droperidol + ketamine)

(*Continued*)

Ewah 2006	Allocation: not randomized, double-blind or placebo-controlled
Fazel 2007	Outcomes: none of the outcomes of interest were reported
Fujii 1996	Interventions: not corticosteroid only (granisetron versus granisetron + steroid)
Gunter 2006	Allocation: not placebo-controlled
Hirunwiwatkul 2001	Allocation: not randomized, double-blinded and placebo-controlled Participants: not limited to children Not tonsillectomy or adenotonsillectomy only (UP3) Interventions: not intravenous route (tonsil fossa injection)
Holt 2000	Interventions: not corticosteroid only (tropisetron versus tropisetron + steroid)
Inci 2009	Interventions: not corticosteroid only; not intravenous route (topical and systemic)
Karaman 2009	Allocation: not double-blinded
Kaygusuz 2003	Interventions: not intravenous route (tonsil fossa injection)
Kerekhanjanarong 01	Allocation: not randomized, double-blinded and placebo-controlled Interventions: not intravenous route (tonsil fossa injection)
Kim 2007	Allocation: not placebo-controlled
King 1967	Interventions: not corticosteroid only Not intravenous route (tonsil fossa injection)
Liu 1996	Allocation: not randomized, double-blinded and placebo-controlled Participants: not limited to children Interventions: not intravenous route (topical)
Malde 2005	Participants: not limited to children
McKenna 1972	Interventions: not corticosteroid only (antibiotic + anesthetic + steroid) Not intravenous route (tonsil fossa injection)
Mohamed 2009	Interventions: not intravenous route (IV and tonsil fossa injection)
Montazeri 2009	Interventions: not intravenous route (tonsil fossa injection)
Palme 2000	Interventions: not single intravenous route of corticosteroid (oral) Participants: not limited to children

(*Continued*)

Papangelou 1972	Allocation: not randomized, double-blinded and placebo-controlled Participants: not limited to children Interventions: not single intravenous route of corticosteroid (oral)
Pedersen 1967	Interventions: not corticosteroid only (estriol) Not intravenous route (topical)
Rundle 1967	Interventions: not corticosteroid only (antibiotic + anesthetic + steroid) Not intravenous route (tonsil fossa injection)
Schlorhaufer 1965	Interventions: not intravenous route (terra cortyl spray)
Skvirskaia 1980	Interventions: not corticosteroid only (oxycyclosol) Not intravenous route (topical)
Smith 1964	Interventions: not corticosteroid only Not intravenous route (tonsil fossa injection)
Splinter 1997	Allocation: not placebo-controlled (perphenazine versus dexamethasone)
Stol'tser 1971	Allocation: not randomized, double-blinded and placebo-controlled
Tewary 1993	Participants: not limited to children
Vilar 1967	Interventions: not corticosteroid only (estriol) Not intravenous route (topical)
Williams 1999	Participants: not limited to children Not tonsillectomy or adenotonsillectomy only (UP3)

IV: intravenous
UP3: uvulopalatopharyngoplasty

DATA AND ANALYSES

Comparison 1. Steroid versus placebo

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Emesis - risk ratio	15	1273	Risk Ratio (M-H, Random, 95% CI)	0.49 [0.41, 0.58]
2 Emesis - risk difference	15	1273	Risk Difference (M-H, Random, 95% CI)	-0.24 [-0.32, -0.15]
3 Day 1 diet - risk ratio	5	452	Risk Ratio (M-H, Random, 95% CI)	1.45 [1.15, 1.83]
4 Day 1 diet - risk difference	5	452	Risk Difference (M-H, Random, 95% CI)	0.21 [0.10, 0.31]
5 Pain score	8	652	Mean Difference (IV, Random, 95% CI)	-1.07 [-1.73, -0.41]

Analysis 1.1. Comparison 1 Steroid versus placebo, Outcome 1 Emesis - risk ratio.

Review: Steroids for improving recovery following tonsillectomy in children

Comparison: 1 Steroid versus placebo

Outcome: 1 Emesis - risk ratio

Study or subgroup	Steroid n/N	Placebo n/N	Risk Ratio M-H,Random,95% CI	Weight	Risk Ratio M-H,Random,95% CI
Al Shehri 2007	15/100	17/50		7.5 %	0.44 [0.24, 0.81]
Aouad 2001	12/53	27/53		8.4 %	0.44 [0.25, 0.78]
April 1996	2/41	10/39		1.5 %	0.19 [0.04, 0.81]
Bhattacharya 2009	4/50	15/50		2.8 %	0.27 [0.10, 0.75]
Elhakim 2003	11/55	31/55		8.1 %	0.35 [0.20, 0.63]
Giannoni 2002	2/25	1/25		0.6 %	2.00 [0.19, 20.67]
Kaan 2006	6/32	10/30		3.8 %	0.56 [0.23, 1.36]
Khani 2009	6/33	17/33		4.6 %	0.35 [0.16, 0.78]
Kyrou 2001	3/30	11/30		2.2 %	0.27 [0.08, 0.88]
Ohlms 1995	2/34	3/35		1.1 %	0.69 [0.12, 3.85]
Pappas 1998	30/63	57/65		23.4 %	0.54 [0.41, 0.71]
Samarkandi 2004	11/29	23/31		10.0 %	0.51 [0.31, 0.85]
Splinter 1996	25/63	50/70		18.2 %	0.56 [0.40, 0.78]

(*Continued* . . .)

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Study or subgroup	Steroid n/N	Placebo n/N	Risk Ratio M-H,Random,95% CI	Weight	Risk Ratio M-H,Random,95% CI
Tom 1996	1/26	15/32		0.8 %	0.08 [0.01, 0.58]
Vosdoganis 1999	10/22	10/19		7.1 %	0.86 [0.46, 1.61]
Total (95% CI)	**656**	**617**		**100.0 %**	**0.49 [0.41, 0.58]**

Total events: 140 (Steroid), 297 (Placebo)

Heterogeneity: $Tau^2 = 0.02$; $Chi^2 = 16.21$, df = 14 (P = 0.30); $I^2 = 14\%$

Test for overall effect: Z = 7.91 (P < 0.00001)

Test for subgroup differences: Not applicable

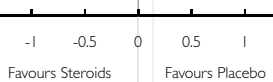
Analysis 1.2. Comparison 1 Steroid versus placebo, Outcome 2 Emesis - risk difference.

Review: Steroids for improving recovery following tonsillectomy in children

Comparison: 1 Steroid versus placebo

Outcome: 2 Emesis - risk difference

Study or subgroup	Steroid n/N	Placebo n/N	Risk Difference M-H,Random,95% CI	Weight	Risk Difference M-H,Random,95% CI
Al Shehri 2007	15/100	17/50		7.4 %	-0.19 [-0.34, -0.04]
Aouad 2001	12/53	27/53		6.8 %	-0.28 [-0.46, -0.11]
April 1996	2/41	10/39		7.3 %	-0.21 [-0.36, -0.06]
Bhattacharya 2009	4/50	15/50		7.4 %	-0.22 [-0.37, -0.07]
Elhakim 2003	11/55	31/55		6.9 %	-0.36 [-0.53, -0.20]
Giannoni 2002	2/25	1/25		7.8 %	0.04 [-0.09, 0.17]
Kaan 2006	6/32	10/30		5.8 %	-0.15 [-0.36, 0.07]
Khani 2009	6/33	17/33		5.8 %	-0.33 [-0.55, -0.12]
Kyrou 2001	3/30	11/30		6.1 %	-0.27 [-0.47, -0.06]



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Study or subgroup	Steroid n/N	Placebo n/N	Risk Difference M-H,Random,95% CI	Weight	Risk Difference M-H,Random,95% CI
Ohlms 1995	2/34	3/35		8.0 %	-0.03 [-0.15, 0.09]
Pappas 1998	30/63	57/65		7.4 %	-0.40 [-0.55, -0.25]
Samarkandi 2004	11/29	23/31		5.4 %	-0.36 [-0.60, -0.13]
Splinter 1996	25/63	50/70		7.1 %	-0.32 [-0.48, -0.16]
Tom 1996	1/26	15/32		6.5 %	-0.43 [-0.62, -0.24]
Vosdoganis 1999	10/22	10/19		4.1 %	-0.07 [-0.38, 0.23]
Total (95% CI)	**656**	**617**		**100.0 %**	**-0.24 [-0.32, -0.15]**

Total events: 140 (Steroid), 297 (Placebo)

Heterogeneity: $Tau^2 = 0.02$; $Chi^2 = 47.75$, df = 14 (P = 0.00001); $I^2 = 71\%$

Test for overall effect: Z = 5.66 (P < 0.00001)

Test for subgroup differences: Not applicable

Analysis 1.3. Comparison 1 Steroid versus placebo, Outcome 3 Day 1 diet - risk ratio.

Review: Steroids for improving recovery following tonsillectomy in children

Comparison: 1 Steroid versus placebo

Outcome: 3 Day 1 diet - risk ratio

Study or subgroup	Steroids n/N	Placebo n/N	Risk Ratio M-H,Random,95% CI	Weight	Risk Ratio M-H,Random,95% CI
April 1996	17/41	7/39		7.7 %	2.31 [1.08, 4.96]
Kaufmann 2006	90/101	70/103		42.8 %	1.31 [1.13, 1.52]
Ohlms 1995	6/34	5/35		4.1 %	1.24 [0.42, 3.67]
Tom 1996	19/26	10/32		12.6 %	2.34 [1.33, 4.11]
Vosdoganis 1999	22/22	15/19		32.9 %	1.26 [0.99, 1.61]
Total (95% CI)	**224**	**228**		**100.0 %**	**1.45 [1.15, 1.83]**

Total events: 154 (Steroids), 107 (Placebo)

Heterogeneity: $Tau^2 = 0.03$; $Chi^2 = 7.34$, df = 4 (P = 0.12); $I^2 = 46\%$

Test for overall effect: Z = 3.18 (P = 0.0015)

Test for subgroup differences: Not applicable

Analysis 1.4. Comparison 1 Steroid versus placebo, Outcome 4 Day 1 diet - risk difference.

Review: Steroids for improving recovery following tonsillectomy in children

Comparison: 1 Steroid versus placebo

Outcome: 4 Day 1 diet - risk difference

Study or subgroup	Steroids n/N	Placebo n/N	Risk Difference M-H,Random,95% CI	Weight	Risk Difference M-H,Random,95% CI
April 1996	17/41	7/39		17.7 %	0.24 [0.04, 0.43]
Kaufmann 2006	90/101	70/103		30.6 %	0.21 [0.10, 0.32]
Ohlms 1995	6/34	5/35		20.2 %	0.03 [-0.14, 0.21]
Tom 1996	19/26	10/32		13.7 %	0.42 [0.18, 0.65]
Vosdoganis 1999	22/22	15/19		17.8 %	0.21 [0.02, 0.40]
Total (95% CI)	**224**	**228**		**100.0 %**	**0.21 [0.10, 0.31]**

Total events: 154 (Steroids), 107 (Placebo)

Heterogeneity: $Tau^2 = 0.01$; $Chi^2 = 7.17$, df = 4 (P = 0.13); $I^2 = 44\%$

Test for overall effect: Z = 3.94 (P = 0.000081)

Test for subgroup differences: Not applicable

Analysis 1.5. Comparison 1 Steroid versus placebo, Outcome 5 Pain score.

Review: Steroids for improving recovery following tonsillectomy in children

Comparison: 1 Steroid versus placebo

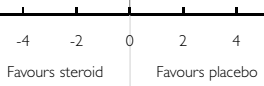
Outcome: 5 Pain score

Study or subgroup	Steroid N	Mean(SD)	Placebo N	Mean(SD)	Mean Difference IV,Random,95% CI	Weight	Mean Difference IV,Random,95% CI
Elhakim 2003	55	0.8 (0.4)	55	2.9 (0.9)		16.8 %	-2.10 [-2.36, -1.84]
Giannoni 2002	25	4.7 (2.4)	25	5 (2.4)		10.1 %	-0.30 [-1.63, 1.03]
Hanasono 2004	106	4.3 (4.9)	113	5.6 (4.9)		10.3 %	-1.30 [-2.60, 0.00]
Kaan 2006	32	5 (1)	30	5.4 (1)		15.7 %	-0.40 [-0.90, 0.10]
Khani 2009	33	2 (0.4)	33	4 (1)		16.4 %	-2.00 [-2.37, -1.63]
Ohlms 1995	34	5 (3)	35	5.8 (2.5)		10.3 %	-0.80 [-2.10, 0.50]
Volk 1993	19	6.9 (2.5)	16	7.9 (2.5)		8.2 %	-1.00 [-2.66, 0.66]
Vosdoganis 1999	22	3.3 (1.65)	19	3.3 (1.65)		12.2 %	0.0 [-1.01, 1.01]
Total (95% CI)	**326**		**326**			**100.0 %**	**-1.07 [-1.73, -0.41]**

Heterogeneity: $Tau^2 = 0.66$; $Chi^2 = 55.70$, df = 7 (P<0.00001); $I^2 = 87\%$

Test for overall effect: Z = 3.19 (P = 0.0014)

Test for subgroup differences: Not applicable



APPENDICES

Appendix 1. Search strategies

CENTRAL	PubMed	EMBASE (Ovid)	CINAHL (EBSCO)
#1 MeSH descriptor Tonsillectomy explode all trees #2 MeSH descriptor Palatine Tonsil explode all trees with qualifier: SU #3 MeSH descriptor Palatine Tonsil explode all trees	#1 "Tonsillectomy" [Mesh] OR "Palatine Tonsil/surgery" [Mesh] OR tonsillectom* [tiab] OR tonsilectom* [tiab] OR adenotonsillectom* [tiab] OR adenotonsilectom*	1 exp tonsillectomy/ 2 (tonsillectom* OR tonsilectom* OR adenotonsillectom* OR adenotonsilectom* OR tonsillotom* OR tonsilotom*).tw.	S1 (MH "Tonsillectomy") OR TX tonsillectom* OR tonsilectom* OR adenotonsillectom* OR adenotonsilectom* OR tonsillotom* OR tonsilotom*

(*Continued*)

#4 MeSH descriptor Tonsillitis explode all trees #5 (tonsil* OR adenotonsil*) #6 (#3 OR #4 OR #5) #7 MeSH descriptor Surgical Procedures, Operative explode all trees #8 (surg* or excis* or extract* or remov):ti #9 (#7 OR #8) #10 (#6 AND #9) #11 (tonsillectom* OR tonsilectom* OR adenotonsillectom* OR adenotonsilectom* OR tonsillotom* OR tonsilotom*) #12 (#1 OR #2 OR #10 OR # 11) #13 MeSH descriptor Steroids explode all trees #14 MeSH descriptor Adrenal Cortex Hormones explode all trees #15 MeSH descriptor Anti-Inflammatory Agents explode all trees #16 MeSH descriptor Anti-Inflammatory Agents, Non-Steroidal explode all trees #17 (#15 AND NOT #16) #18 (steroid* or corticosteroid* or glucocorticoid* or beclomethasone or betamethasone or budesonide or cortisone or dexamethasone or flunisolide or fluticasone or fludrocortisone or hydrocortisone or cortisol or methylprednisolone or mometasone or prednisolone or prednisone or triamcinolone) #19 (#13 OR #14 OR #17 OR #18) #20 (#12 AND #19)	[tiab] OR tonsillotom* [tiab] OR tonsilotom* [tiab] #2 ("Tonsillitis" [Mesh] OR "Palatine Tonsil" [Mesh] OR tonsil [tiab] OR adenotonsil* [tiab]) AND ("Surgery" [Mesh] OR surg* [ti] OR excis* [ti] OR extract* [ti] OR remov* [ti]) #3 #1 OR #2 #4 "STEROIDS" [Mesh] OR "Adrenal Cortex Hormones" [Mesh] OR "Adrenal Cortex Hormones" [Pharmacological Action] OR ("ANTI-INFLAMMATORY AGENTS" [Mesh] NOT "Anti-Inflammatory Agents, Non-Steroidal"[Mesh]) #5 steroid* [tiab] OR corticosteroid* [tiab] OR glucocorticoid* [tiab] OR beclomethasone [tiab] OR betamethasone [tiab] OR budesonide [tiab] OR cortisone [tiab] OR dexamethasone [tiab] OR flunisolide [tiab] OR fluticasone [tiab] OR fludrocortisone [tiab] OR hydrocortisone [tiab] OR cortisol [tiab] OR methylprednisolone [tiab] OR mometasone [tiab] OR prednisolone [tiab] OR prednisone [tiab] OR triamcinolone [tiab] #6 #4 OR #5 #7 #3 AND #6	3 (tonsil* or adenotonsil*).tw. 4 exp tonsil/ or tonsillitis/ 5 exp surgery/ 6 (surg* or excis* or extract* or remov*).ti. 7 3 OR 4 8 5 OR 6 9 7 AND 8 10 1 OR 2 OR 9 11 exp Steroid/ 12 exp Antiinflammatory Agent/ not exp Nonsteroid Antiinflammatory Agent/ 13 (steroid* or corticosteroid* or glucocorticoid* or beclomethasone or betamethasone or budesonide or cortisone or dexamethasone or flunisolide or fluticasone or fludrocortisone or hydrocortisone or cortisol or methylprednisolone or mometasone or prednisolone or prednisone or triamcinolone).tw. 14 11 OR 12 OR 13 15 10 AND 14	S2 (MH "Tonsil") OR (MH "Tonsillitis") S3 TX tonsil* OR adenotonsil* S4 S2 or S3 S5 surg* or excis* or extract* or remov* S6 S4 and S5 S7 S1 or S6 S8 (MH "Steroids+") S9 (MH "Adrenal Cortex Hormones+") S10 (MH "Antiinflammatory Agents, Steroidal+") S11 (MH "Antiinflammatory Agents, Non-Steroidal+") S12 S10 NOT S11 S13 TX steroid* or corticosteroid* or glucocorticoid* or beclomethasone or betamethasone or budesonide or cortisone or dexamethasone or flunisolide or fluticasone or fludrocortisone or hydrocortisone or cortisol or methylprednisolone or mometasone or prednisolone or prednisone or triamcinolone
Web of Science/BIOSIS Previews	**Cochrane Ear, Nose and Throat Disorders Group Trials Register**	**CAB Abstracts (Ovid)**	**ISRCTN (mRCT)**

(*Continued*)

#1 TS=(tonsillectom* OR adenotonsillectom*) #2 TI=((tonsil* OR adenotonsil*) AND (surg* or excis* or extract* or remov*)) #3 #2 OR #1 #4 TS=(steroid* or corticosteroid* or glucocorticoid* or beclomethasone or betamethasone or budesonide or cortisone or dexamethasone or flunisolide or fluticasone or fludrocortisone or hydrocortisone or cortisol or methylprednisolone or mometasone or prednisolone or prednisone or triamcinolone) #5 #3 AND #4	(tonsil* OR adenotonsil* OR posttonsil*) AND (steroid* or corticosteroid* or glucocorticoid* or beclomethasone or betamethasone or budesonide or cortisone or dexamethasone or flunisolide or fluticasone or fludrocortisone or hydrocortisone or cortisol or methylprednisolone or mometasone or prednisolone or prednisone or triamcinolone)	1 (tonsillectom* OR tonsilectom* OR adenotonsillectom* OR adenotonsilectom* OR tonsillotom* OR tonsilotom*).tw. 2 (tonsil* or adenotonsil*).tw. 3 exp tonsil/ or tonsillitis/ 4 exp surgery/ 5 (surg* or excis* or extract* or remov*).ti. 6 2 OR 3 7 4 OR 5 8 6 AND 7 9 1 OR 8 10 (steroid* or corticosteroid* or glucocorticoid* or beclomethasone or betamethasone or budesonide or cortisone or dexamethasone or flunisolide or fluticasone or fludrocortisone or hydrocortisone or cortisol or methylprednisolone or mometasone or prednisolone or prednisone or triamcinolone).tw. 11 9 AND 10	(tonsil% OR adenotonsil%) AND (steroid% or corticosteroid% or glucocorticoid% or beclomethasone or betamethasone or budesonide or cortisone or dexamethasone or flunisolide or fluticasone or fludrocortisone or hydrocortisone or cortisol or methylprednisolone or mometasone or prednisolone or prednisone or triamcinolone)

WHAT'S NEW

Date	Event	Description
1 February 2011	New search has been performed	New searches run October 2010.
1 February 2011	New citation required and conclusions have changed	The current review differs from the 2003 review in several ways Two authors (JA Welge and CM Myer) were no longer involved and two new authors (JJ Grisel and J Meinzen-Derr) joined We included 10 new studies and excluded 17 additional studies. This review does not include diet at day three as an outcome measure (included in 2003), but it does now include pain as measured by a visual analog scale. Children in the steroid group were two times less likely to vomit than children in the placebo group. They were also

(*Continued*)

		more likely to advance to a diet by day one and less likely to experience pain. These results strengthen the results found in the 2003 review

HISTORY

Date	Event	Description
27 October 2008	Amended	Converted to new review format.

CONTRIBUTIONS OF AUTHORS

Drs Steward and Grisel designed the study and developed the protocol according to the methods outlined in the 2003 Cochrane Review. Dr Grisel extracted the data from the original studies. Drs Steward, Grisel and Meinzen-Derr made decisions regarding study inclusion or exclusion for each outcome measure. Dr Meinzen-Derr performed the statistical analysis and wrote the results section. Drs Steward and Grisel wrote the discussion and conclusion based upon the results of the review.

DECLARATIONS OF INTEREST

None known.

SOURCES OF SUPPORT

Internal sources

- Center for Epidemiology and Biostatistics at Cincinnati Children's Medical Center, Cincinnati, OH, USA.

External sources

- No sources of support supplied

DIFFERENCES BETWEEN PROTOCOL AND REVIEW

There was no preceding protocol for this review. Changes from the previous version of the review: we have added details of study selection; day three diet has been eliminated as an outcome measure; and we have been able to analyze pain as an outcome.

INDEX TERMS

Medical Subject Headings (MeSH)

Adenoidectomy [*adverse effects]; Antiemetics [*therapeutic use]; Convalescence; Dexamethasone [*therapeutic use]; Glucocorticoids [*therapeutic use]; Pain, Postoperative [prevention & control]; Postoperative Nausea and Vomiting [*prevention & control]; Time Factors; Tonsillectomy [*adverse effects]; Treatment Outcome

MeSH check words

Adolescent; Child; Humans