Prophylactic Perioperative Antibiotic Use in Endoscopic Sinus Surgery: A Systematic Review and Meta-analysis
Amy M. Saleh, Katherine M. Torres, Mohammad H. Murad, Patricia J. Erwin and Colin L. W. Driscoll
Otolaryngology -- Head and Neck Surgery 2012 146: 533 originally published online 12 January 2012
DOI: 10.1177/0194599811434117

The online version of this article can be found at:
http://oto.sagepub.com/content/146/4/533

Published by:

SAGE
http://www.sagepublications.com

On behalf of:

AMERICAN ACADEMY OF
OTOLARYNGOLOGY–
HEAD AND NECK SURGERY

American Academy of Otolaryngology- Head and Neck Surgery

Additional services and information for Otolaryngology -- Head and Neck Surgery can be found at:

Email Alerts: http://oto.sagepub.com/cgi/alerts
Subscriptions: http://oto.sagepub.com/subscriptions
Reprints: http://www.sagepub.com/journalsReprints.nav
Permissions: http://www.sagepub.com/journalsPermissions.nav

>> Version of Record - Apr 2, 2012
OnlineFirst Version of Record - Jan 12, 2012

What is This?
Prophylactic Perioperative Antibiotic Use in Endoscopic Sinus Surgery: A Systematic Review and Meta-analysis

Amy M. Saleh, MD1, Katherine M. Torres, DO2, Mohammad H. Murad, MD3, Patricia J. Erwin, MLS3, and Colin L. W. Driscoll, MD1

No sponsorships or competing interests have been disclosed for this article.

Abstract

Context. Perioperative antibiotics are widely used to improve the outcomes of endoscopic sinus surgery.

Objective. The aim of this study was to summarize the evidence on the effect of perioperative antibiotic prophylaxis on outcomes of endoscopic sinus surgery.

Data Sources and Review Methods. We searched electronic databases from inception through May 2011 for any relevant clinical trials or observational studies. Two reviewers working independently extracted study characteristics, quality, and the outcomes of interest. Random-effects meta-analysis was used to pool the relative risks (RRs) and the standardized mean differences (SMDs) across trials.

Results. We found 4 eligible trials with varying quality, of which 3 were included in the quantitative analysis. Antibiotic prophylaxis was associated with a nonsignificant reduction in the incidence of infections (relative risk, 0.76; 95% confidence interval [CI], 0.64 to 1.09), symptoms scores (SMD, –0.04; 95% CI, –0.46 to 0.38), and endoscopic scores (SMD, –0.09; 95% CI, 0.30 to 0.13). The heterogeneity associated with the analysis was significant only for the outcome of change in symptoms score (I-squared values, 0%, 70%, and 0% for the 3 outcomes, respectively).

Conclusions. Trial data available to date are unable to demonstrate a statistically significant reduction in infection, symptom scores, or endoscopic scores to support the routine use of postoperative prophylactic antibiotics following endoscopic sinus surgery. Our analysis was limited by the number of published trials related to this topic.

Keywords

perioperative antibiotics, endoscopic sinus surgery, antibiotic prophylaxis

Received October 8, 2011; revised November 29, 2011; accepted December 6, 2011.

The use of perioperative (preoperative, intraoperative, and postoperative) antibiotics to prevent postsurgical infections was first established in the 1960s and is now used commonly as it has been found to be beneficial in preventing postoperative infection, particularly when a normally sterile area is contaminated by a nonsterile area. Its use has become widespread in otorhinolaryngology, where surgery is often categorized as clean-contaminated according to traditional definitions (Table 1). This practice has been adopted in endoscopic sinus surgery, with postoperative antibiotics being routinely used to improve postoperative healing and outcomes. Endoscopic sinus surgery has become widely performed as the standard surgical therapy for treating many conditions of the sinuses, with more than 250,000 surgeries performed every year. Commonly, patients are given a 7- to 14-day postoperative course of prophylactic oral antibiotics. Many surgeons cite not only reduction in postoperative infection but also improved surgical outcomes and reduction in morbidity if antibiotics are used routinely postoperatively.

Despite the routine use of postoperative antibiotic prophylaxis following endoscopic sinus surgery, there is a lack of published evidence to support this practice. Antibiotic use can be associated with increased bacterial resistance, added cost to the patient, and potential side effects such as allergic reaction or Clostridium difficile infection. Furthermore, other otolaryngological surgeries such as tonsillectomy and otologic surgery...
have been studied and reviewed in detail, with the findings that routine postoperative antibiotic use is not supported despite these surgeries also being in the clean-contaminated category.\(^7\)\(^8\) Finally, many other fields have studied the use of prophylactic antibiotics, and none support use beyond 48 to 72 hours, with the large majority supporting preoperative dosing only or a 24-hour maximum prophylaxis period.\(^9\) For these reasons, we felt a systematic review of the literature on the use of postoperative antibiotics in endoscopic sinus surgery was warranted.

**Methods**

**Study Identification**

An expert reference librarian (P.J.E.) designed and conducted the electronic search strategy with input from study investigators. There were no language, publication year, or publication status restrictions. Study designs included clinical trials and observational studies. The following databases were searched from their inception through May 2011: Ovid MEDLINE, Ovid EMBASE, Ovid EBM Reviews–Cochrane Central Register of Controlled Trials, ISI Web of Science, and Scopus. Search terms included *endoscopy*, *FESS*, *nose*, *paranasal sinus disease*, *nasal polyps*, *anti-bacterial agents*, *postoperative complications*, *intraoperative complications*, *preoperative care*, *premedication*, *antibiotic prophylaxis*, *bacterial infections*, *equipment contamination*, *endoscopic sinus surgery*, *chronic sinusitis*, *rhinosinusitis*, *sinusitis*, *anti-infective agent*, *postoperative infection*, and *infectious complication*. We scanned reference lists of identified studies for further trials. The detailed search strategy is available upon request and also in the appendix available at otol journal.org.

**Eligibility Criteria and Study Selection**

Studies included were any clinical trials or observational studies that enrolled patients undergoing endoscopic sinus surgery and investigated the use of systemic antibiotic prophylaxis aimed at reducing the infection rate or improving secondary outcomes (ie, healing, nasal symptoms) in the immediate postoperative period (30 days and less) and compared it with a placebo, no antibiotic, or a short course versus a longer course of antibiotics. Two authors (A.M.S. and K.M.T.) working independently and in duplicate used titles, keywords, and abstracts of the identified citations to exclude trials that clearly did not meet the inclusion criteria of the review. If one or both of the authors concluded that the trial might meet criteria, the full article was obtained for further study to determine eligibility. We compared the results of the 2 independent selections. We resolved disagreements by discussion.

**Data Extraction**

Two authors independently extracted data into a standardized data extraction form and assessed quality. We resolved disagreements by discussion. Data extracted included population (range of patients’ age, comorbid conditions, indication for surgery), intervention (onset of administration of prophylaxis, duration of administration, type of prophylaxis), exclusion criteria, surgical procedures, intraoperative condition, use of packing, other perioperative medications/interventions, duration of follow-up, study design and quality measures, and outcomes of interest (infection rates, symptoms scores, endoscopic scores, side effect profiles, antibiotic resistance profiles). The methodologic quality of randomized trials was assessed by evaluating randomization, allocation concealment, blinding, and loss to follow-up. We attempted to contact the original authors, when necessary, to clarify study methods or to obtain additional data.

**Statistical Analysis**

We estimated from each study the risk ratio (also called relative risk [RR]) for dichotomous outcomes and the standardized mean difference (SMD) for continuous outcomes. We chose SMD for the outcomes of symptoms score and endoscopic scores because studies used different scales. SMD makes the point estimates unitless and allows pooling across scales. Estimates were pooled across studies using a random effects meta-analysis. Heterogeneity across studies was estimated using the I-squared statistics, which represent the proportion of heterogeneity that is not attributable to chance. To facilitate pooling of data available, we assumed the choice for an antibiotic was a rational one and decided to make no distinction between different regimen/dosage patterns.

We conducted a sensitivity analysis by comparing the effect of inclusion and exclusion of studies of different quality and definitions of outcomes.

We had planned to conduct subgroup analyses for children and adults (adults >18); intraoperative condition (normal, inflamed, purulent); onset of administration; duration of administration; mode of administration (systemic vs topical); and patient risk factors (ie, diabetics). However, neither the original data nor additional data supplied by study authors allowed for sufficient quantitative analysis of the data.
Results

Description of Studies

A total of 524 articles were identified in our search, of which 4 were included in the review (Figure 1). Details of the participants, interventions, and outcomes in those studies are presented in Table 2 and 3. Three studies compared the use of systemic antibiotics with the use of a placebo or no antibiotic\(^{10-12}\) and provided data for meta-analysis.

A fourth study fulfilled the inclusion criteria of this review, but because of its different design, it is qualitatively described and not pooled in meta-analysis. This study evaluated the use of a single injection of antibiotic at the beginning of the procedure to a longer (24-hour) course.\(^ {13}\)

Studies that were excluded included one\(^ {14}\) that compared one antibiotic regimen to another for a prolonged course only, which did not meet our inclusion criteria, and another 2 studies\(^ {15,16}\) that used 3 months of macrolides postoperatively. We felt this put these studies outside the scope of prophylactic perioperative antibiotic use, so they were excluded.

Risk of Bias in Included Studies

The methodological quality of the included studies varied. All studies reported on randomized treatment allocation. One did not report allocation concealment (Maier and Strutz\(^ {13}\)). Two studies were blinded appropriately (Jorrisen et al\(^ {12}\) and Albu and Lucaciu\(^ {10}\)), and one was not blinded (Jiang et al\(^ {11}\)). The last did not mention blinding (Maier and Strutz\(^ {13}\)). Loss of follow-up was provided for all of the studies except one and ranged from 0% to 25%. One study was deemed to have high methodologic quality (Jorrisen et al\(^ {12}\)).

Individual Study Review

Jorrisen et al\(^ {12}\) designed a prospective double-blind placebo-controlled randomized control trial with 202 patients. The patients had a diagnosis of chronic rhinosinusitis or recurrent acute sinusitis and underwent endoscopic sinus surgery including at least one of the following: antrostomies, ethmoidectomies, sphenoidotomies, and frontal sinusotomies. Patients with concurrent other septal or rhino surgery, allergy, asthma, immune deficiency, pregnancy, or cystic fibrosis were excluded. A total of 101 patients postoperatively received placebo in one arm, and 101 patients received Zinnat (cefuroxime) 250 mg twice a day for 10 days in the other. No packing was used. All patients were placed on nasal saline rinses and given 5 days of betamethasone. They all also

Table 2. Characteristics of the Included Studies

<table>
<thead>
<tr>
<th>Study</th>
<th>Design</th>
<th>No. of Patients</th>
<th>Age, y</th>
<th>Sex</th>
<th>Antibiotic Used</th>
<th>Dose</th>
<th>Duration</th>
<th>Comparison Group</th>
<th>Definition of Infection</th>
<th>Length of Follow-up</th>
</tr>
</thead>
<tbody>
<tr>
<td>Jorrisen et al, 2000(^ {12})</td>
<td>Double-blind placebo-controlled RCT</td>
<td>202</td>
<td>Mean, 44 (range, 11-77)</td>
<td>M/F</td>
<td>Cefuroxime axetil</td>
<td>250 mg</td>
<td>BID</td>
<td>Placebo</td>
<td>Local and systemic signs (cellulitis or pus and fever)</td>
<td>4 weeks</td>
</tr>
<tr>
<td>Jiang et al, 2008(^ {11})</td>
<td>RCT</td>
<td>84</td>
<td>Mean, 30 (range, 9-83)</td>
<td>M/F</td>
<td>Amoxicillin/clavulanate</td>
<td>375 mg</td>
<td>TID</td>
<td>Nothing</td>
<td>Purulent secretions seen on endoscopic examination</td>
<td>3 weeks</td>
</tr>
<tr>
<td>Maier and Strutz, 1992(^ {13})</td>
<td>RCT</td>
<td>106</td>
<td>—</td>
<td>—</td>
<td>Cefuroxime 1.5 g</td>
<td>q8H</td>
<td>24 hours</td>
<td>Single preoperative dose</td>
<td>Did not explain, just yes or no</td>
<td>3 weeks</td>
</tr>
<tr>
<td>Albu and Lucaciu, 2010(^ {10})</td>
<td>Double-blind placebo-controlled RCT</td>
<td>100</td>
<td>Mean, 41 (range, 18-65)</td>
<td>M/F</td>
<td>Amoxicillin/clavulanate</td>
<td>625 mg</td>
<td>BID</td>
<td>Placebo</td>
<td>Signs and symptoms of an upper respiratory infection</td>
<td>4 weeks</td>
</tr>
</tbody>
</table>

Abbreviations: RCT, randomized control trial; M/F, male/female.
underwent the same debridement schedule at 3, 8, 15, and 22 days. They were evaluated at these intervals as well. The main outcome measure was infection (purulent secretions in the setting of fever or cellulitis) that developed within the first month after surgery. They also evaluated the patients with a symptom scale and endoscopically to evaluate healing as secondary outcomes. Twelve of 101 patients in the treatment group and 18 of 101 patient in the control group had recorded infections, with the difference being statistically insignificant (odds ratio [OR], 0.62; confidence interval [CI], 0.28-1.37). They also found no significant difference between total endoscopic scores and symptoms score at each of the evaluation points between the 2 groups. No major side effects from antibiotic use were reported. There was no loss to follow-up.

Jiang et al\textsuperscript{11} designed a nonblinded prospective randomized control trial with 84 patients. The patients had a diagnosis of chronic rhinosinusitis and underwent endoscopic sinus surgery including at least one of the following: antrostomies, ethmoidectomies, sphenoidotomies, and frontal sinusotomies. Patients with previous surgery, immunodeficiency, or preop antibiotics within 1 week were excluded. Forty patients received no antibiotics, and 31 received amoxicillin/clavulanate 375 mg 3 times a day for 3 weeks postoperatively. Gel foam packs were inserted bilaterally at the conclusion of surgery. No other perioperative medications were given, and the patients were debrided once at 3 weeks when they were evaluated. Outcome measures included symptom scale, endoscopic evaluation, culture rate, and antibiotic sensitivity. They did note the presence or absence of purulent secretions endoscopically but did not define infection beyond that. The authors found no statistically significant difference at the end of treatment for endoscopic scores, symptom scores, culture rate, or antibiotic sensitivity between the control and treatment groups. Their data revealed 15 of 31 patients with purulent secretions on endoscopic examination in the treatment group upon examination and 23 of 40 patients in the control group, the difference of which is not statistically significant (OR, 0.69; CI, 0.27-1.78).

Albu and Lucaciu\textsuperscript{10} designed a prospective double-blinded placebo-controlled randomized trial with 100 patients. The patients had a diagnosis of chronic rhinosinusitis and underwent endoscopic sinus surgery, including at least one of the following: antrostomy, ethmoidectomy, sphenoidotomy, or frontal sinusotomy without concurrent septal surgery. Patients with atrophic rhinitis, odontogenic sinusitis, cystic fibrosis, extramucosal mycotic sinusitis, NSAID intolerance, diabetes, history of previous nasal/sinus procedures, endocarditis prophylaxis, immunodeficiency, recent antibiotic use

Table 3. Characteristics of the Included Studies, Continued

<table>
<thead>
<tr>
<th>Study</th>
<th>Inclusion</th>
<th>Exclusion</th>
<th>Indication</th>
<th>Secretions Seen during Surgery</th>
<th>Other Postoperative Medications</th>
<th>Packing</th>
<th>Postoperative Debridement</th>
</tr>
</thead>
<tbody>
<tr>
<td>Jorrisen et al, 2000\textsuperscript{12}</td>
<td>Undergoing ESS</td>
<td>Concurrent other septal or rhinosurgery, allergy, asthma, immune deficiency, pregnancy, cystic fibrosis</td>
<td>Polyposis, CRS, RAS</td>
<td>Mucoid, none, purulent</td>
<td>Nasal saline rinse TID, betamethasone 2-1.5-1-0.5 mg/d for 5 days</td>
<td>No</td>
<td>Yes (3, 8, 15, 22 days)</td>
</tr>
<tr>
<td>Jiang et al, 2008\textsuperscript{11}</td>
<td>Undergoing ESS</td>
<td>Previous surgery, immunodeficiency, preop antibiotics within 1 week</td>
<td>CRS</td>
<td>None, thin, thick, or purulent</td>
<td>None</td>
<td>Yes (gel foam)</td>
<td>Yes (3 weeks)</td>
</tr>
<tr>
<td>Maier and Strutz, 1992\textsuperscript{13}</td>
<td>Undergoing ESS</td>
<td>Immunodeficiency or preop radiation, preop signs of purulence</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>Yes</td>
<td>—</td>
</tr>
<tr>
<td>Albu and Lucaciu, 2010\textsuperscript{10}</td>
<td>Undergoing ESS</td>
<td>Atrophic rhinitis, odontogenic sinusitis, cystic fibrosis, extramucosal mycotic sinusitis, NSAID intolerance, diabetes, history of previous nasal/sinus procedures, endocarditis prophylaxis, immunodeficiency, recent antibiotic use</td>
<td>CRS</td>
<td>None, thin, thick, or purulent</td>
<td>Saline irrigations QID</td>
<td>Yes (gel foam)</td>
<td>None</td>
</tr>
</tbody>
</table>

Abbreviations: ARS, allergic rhinosinusitis; CRS, chronic rhinosinusitis; ESS, endoscopic sinus surgery; NSAID, nonsteroidal anti-inflammatory drug.
patients were placed on nasal saline rinses 4 times a day postoperatively. No other medications were given. Gel foam packs were used for 1 day postoperatively then removed. No postoperative debridement was done, but the patients were evaluated at 5, 12, 21, and 30 days. The main outcome measures were a symptom scale and endoscopic scale score, but they also tracked infection rates (defined as in Jorrisen et al12) that developed within the first month after surgery. On day 5 there was a statistical difference in nasal obstruction symptoms, with the treatment group having a mean of 1 point less on a scale of 1 to 10 (4.02 vs 5.01, P = .01). There was also a significant difference for total endoscopic scores, with the treatment group having a better score of 14.2 vs 15.02 on a scale of 0 to 20 (P = .008) on day 5. On day 12, there remained a significant difference in endoscopic scores only (treatment group 9.05, control group 10.12, P = .009). On days 21 and 30, there were no longer any statistically significant differences in symptoms or endoscopic evaluation. During the course of the study, 5 of 40 patients in the treatment group and 7 of 35 patients in the control group experienced an uncomplicated upper respiratory tract infection; the difference between groups was not statistically significant (OR, 0.57; CI, 0.16–1.99). Four patients reported gastrointestinal disturbances with antibiotic use in the treatment group, and no patients reported this in the control group. No other side effects were experienced. There was 25% loss to follow-up in this study.

Maier and Strutz13 designed a study with 106 patients, but this study included patients undergoing not only endoscopic sinus surgery but also parotidectomy and neck dissection. There were 36 patients in the sinus subgroup, but the authors did not delineate how many were in each treatment arm. The patients were randomized to be given either a single dose preoperatively of cefuroxime 1.5 g intravenously only versus receiving 3 additional doses every 8 hours postoperatively. Other information as provided for the studies above was unavailable. They reported no infections or side effects for any patients in the sinus subgroup for either treatment arm.

Quantitative Analysis

Antibiotic prophylaxis was associated with a nonsignificant reduction in the incidence of infections (RR, 0.76; 95% CI, 0.64 to 1.09), symptoms scores (SMD, −0.04; 95% CI, −0.46 to 0.38), and endoscopic scores (SMD, −0.09; 95% CI, 0.30 to 0.13; Figure 2). The heterogeneity associated with the analysis was significant only for the outcome of change in symptoms score (I-squared values, 0%, 70%, and 0% for the 3 outcomes, respectively).

In sensitivity analysis, we excluded the study by Jiang et al11 in which the definition of infection was different (presence of purulent secretions only vs this plus systemic signs). The conclusions do not change (ie, nonsignificant reduction in the risk of infection; RR, 0.65; 95% CI, 0.37 to 1.16). Similarly, if only studies with high methodologic quality are included (0% loss to follow-up and clear allocation concealment; Jorrisen et al12), the conclusions do not change (ie, nonsignificant reduction in the risk of infection; RR, 0.67; 95% CI, 0.34 to 1.31).

Discussion

We conducted a systematic review and meta-analysis of randomized trials to evaluate the effect of systemic prophylactic antibiotics following endoscopic sinus surgery. We found 4 eligible trials. A meta-analysis of 3 trials demonstrates that routine postoperative antibiotic prophylaxis did not show a statistically significant reduction in the incidence of infection, endoscopic scores, and symptoms.

The strength of this systematic review includes using a comprehensive literature search that spans multiple databases, having 2 independent reviewers conduct the review to reduce bias, and employing an analysis using the random effects model, which incorporates between-study heterogeneity.

The main limitation of this report is the small number of patients and studies, which leads to imprecision and wide confidence intervals. Imprecision lowers the confidence of guideline developers and clinicians. It is plausible that patients with more complex clinical syndromes or anatomic abnormalities might derive an increased benefit from postoperative prophylaxis; however, published evidence to date does not allow for this type of multivariate analysis. At the present time, more evidence is needed to support the use of routine prophylaxis for patients undergoing endoscopic sinus surgery.

These studies do not address whether better disease control can be obtained by using long-term anti-inflammatory antibiotics.
such as macrolides (often for months), as was proposed in other studies. These studies are often cited in reviews on postoperative care after sinus surgery advocating the use of routine perioperative antibiotics but in fact are addressing an entirely different question. The use of long-term low-dose macrolides for control of other inflammatory conditions has been studied and may be beneficial but is beyond the scope of this review.

Future randomized trials are needed to evaluate the utility of prophylactic antibiotics in this setting. The results of future trials should ideally be stratified by different populations of patients, for example, elderly patients, patients with diabetes, or cystic fibrosis patients. This has not traditionally been done when investigating perioperative antibiotic use in the literature, but we believe it would be useful for further stratification of recommendations for prophylaxis. Trials evaluating topical or local antibiotics perioperatively are also needed. The existing evidence relating to topical therapy is limited by coadministration of varying systemic antibiotic protocols.

Conclusions

The current evidence does not support the routine use of prophylactic postoperative antibiotics following endoscopic sinus surgery. There was not sufficient evidence to evaluate whether a preoperative dose or intraoperative dosing affects the outcomes of endoscopic sinus surgery.

Acknowledgments

We would like to thank Drs Jorrisen, Jiang, and Albu for being so kind as to reply to requests for more details.

Author Contributions

Amy M. Saleh, concept, design, analysis, search, statistics, drafting and review of manuscript; Katherine M. Torres, design, analysis of data, revising and reviewing manuscript; Mohammad H. Murad, design, methods, statistics, review of manuscript; Patricia J. Erwin, design, search methods and executions, review of manuscript; Colin L. W. Driscoll, concept, design, revising, reviewing of the manuscript.

Disclosures

Competing interests: None.
Funding source: None.

Supplemental Material

Additional supporting information may be found at http://oto.sagepub.com/content/by/supplemental-data

References