Postoperative antibiotic use in patients with unilateral purulent chronic rhinosinusitis

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Abstract
Objectives: To describe our experience with the use of postoperative antibiotics in the management of unilateral chronic rhinosinusitis (CRS) patients with active infection at the time of surgery, and to evaluate the need for routine postoperative antibiotic administration in this population.

Methods: This retrospective chart review analyzed the medical records of all patients who underwent endoscopic sinus surgery for unilateral purulent CRS between November 2013 and September 2019 at a tertiary care center and who were not prescribed routine postoperative antibiotics. Duration of time until normalization of sinus cavities and whether antibiotics were ultimately prescribed for persistent infectious signs and symptoms were recorded. Patient characteristics and findings were analyzed to determine if any of the evaluated parameters were associated with the need for postoperative antibiotics.

Results: Sixty-nine patients were included in the study. Thirty-three (47.8%) did not require antibiotics during the postoperative period. The average time to sinus normalization was 8.1 weeks (range 1-24 weeks) for patients who received antibiotics and 5.7 weeks (range 1-16 weeks) for those who did not receive antibiotics ($P = .066$). No evaluated variables were associated with antibiotic use on univariate or multivariate analysis.

Conclusion: Postoperative antibiotics were not necessary to normalize infected sinus cavities for nearly half of patients with unilateral purulent CRS in this series. Further studies are needed to better delineate which patients would derive benefit from postoperative antibiotics.

Level of Evidence: Level IV.

Keywords
adult rhinology, allergy/rhinology, outcomes/cost effectiveness, quality of life
INTRODUCTION

Endoscopic sinus surgery (ESS) is an option for treatment of chronic rhinosinusitis (CRS) refractory to appropriate medical management, and proper postoperative care is associated with improved patient outcomes. However, an optimal postoperative regimen remains unknown and is currently a topic of controversy. Antibiotics are commonly prescribed in the postoperative period to minimize infection and improve healing, but recently their efficacy has been challenged in several studies. In 2020, Lehmann et al published a randomized, double-blind, placebo-controlled noninferiority clinical trial evaluating postoperative prophylactic antibiotics in patients undergoing ESS for CRS. The results of this study suggest that a placebo is noninferior to antibiotics regarding sinonasal-specific quality of life and the rate of postoperative infection, while significantly higher rates of diarrhea were observed in the antibiotic group.

Less is known about the role for postoperative antibiotics in patients diagnosed with unilateral purulent CRS. Observing purulence intraoperatively prompts many providers to universally prescribe postoperative antibiotics. In fact, evidence of discolored, purulent secretions is a common exclusion criterion in previous studies evaluating postoperative antibiotic use. A portion of unilateral purulent CRS patients may also have an odontogenic etiology of CRS, which has similarly been used as an exclusion criteria in previous studies of postoperative antibiotic use. As such, relatively little is known about the necessity of antibiotics in the unilateral purulent CRS population. These patients have often been treated with multiple and prolonged courses of antibiotics prior to surgery and are often reluctant to use additional antibiotics postoperatively due to either previous adverse antibiotic effects, or concern for developing them. Additionally, previous studies have demonstrated that infections leading to failure of ESS can be caused by both non-colonizing bacteria that were not present at the time of surgery, as well as persistent infections that are refractory to antibiotic treatment. This has led the senior authors of this manuscript (RAL, SML) to offer patients a watch-and-wait approach to postoperative antibiotic administration (with close observation), despite the presence of active infection at the time of surgery. Given the potential for side effects and increased microbial resistance, minimizing antibiotic use in the postoperative period is likely beneficial for reducing treatment-associated morbidity.

In this study, we describe our experience with minimizing the use of postoperative antibiotics in the management of unilateral CRS with active infection at the time of surgery, and we reevaluate the need for routine postoperative antibiotic administration in these patients.

MATERIALS AND METHODS

The Institutional Review Board of the New York University Grossman School of Medicine approved this retrospective chart review. Patients aged 18 to 80 who underwent ESS between November 2013 and September 2019 for unilateral CRS unresponsive to medical management were included. Preoperative medical management was not uniform and was generally prescribed by a referring otolaryngologist or

| TABLE 1 | Univariate comparisons between treatment groups |
|---------|---------------------------------------------|
|         | No antibiotics (n = 33) | Antibiotics (n = 36) | P-value |
| Age     | 53.8 (3.0) | 58.7 (2.4) | .26 |
| Sex (male) | 19 (58.6%) | 21 (58.3%) | .95 |
| Polyposis | 16 (48.5%) | 16 (44.4%) | .74 |
| Asthma   | 6 (18.2%) | 10 (27.8%) | .35 |
| Allergies | 6 (18.2%) | 6 (16.2%) | .87 |
| Diabetes | 2 (6.1%) | 4 (11.1%) | .68 |
| Hypertension | 12 (36.4%) | 15 (41.7%) | .65 |
| Smoker       | | | |
| Current | 5 (15.2%) | 1 (2.8%) | .12 |
| Never | 17 (51.5%) | 17 (47.2%) | |
| Former | 11 (33.3%) | 18 (50.0%) | |
| Pre-op steroids | 15 (45.5%) | 18 (50.0%) | .71 |
| Immunocompromised | 2 (6.1%) | 4 (11.1%) | .68 |
| Odontogenic source | 22 (66.7%) | 18 (50.0%) | .16 |
| Lund-Mackay score | 7.0 (0.62) | 7.3 (0.57) | .60 |
| Previous surgery | 5 (15.2%) | 6 (16.7%) | .86 |
| Post-op steroid rinses | 5 (15.2%) | 12 (33.3%) | .08 |
| Time to normalization (weeks) | 5.7 (0.84) | 8.1 (1.2) | .066 |
| Sinus normalization at 2 month follow-up | 32 (97.0%) | 32 (88.9%) | .36 |

Note: Continuous variables reported as mean values with standard errors. Statistical significance (p-value < 0.05) indicated by *.
primary care physician. Diagnosis of unilateral CRS was based upon a clinical history of rhinosinusitis for at least 12 weeks and nasal endoscopy/computed tomography (CT) findings. Patients with odontogenic sinusitis were also included; however, patients found to have a fungal ball or mycetoma were excluded.

Medical history of asthma, seasonal allergies, diabetes, hypertension, immunocompromised status and smoking history were recorded. The presence of a confirmed odontogenic source of CRS was also recorded. Preoperative disease extent was quantified by the Lund-Mackay staging system based on the pre-operative CT scan (score range 1-12, unilateral). Preoperative treatment with antibiotics and intranasal steroids, as well as intraoperative administration of antibiotics were also recorded.

All patients underwent ESS by one of two senior rhinologists (SML and RAL). Extent of surgery was at the discretion of the surgeon. Only patients found to have active infection at the time of surgery (identified intraoperatively by the presence of discolored, purulent secretions) were included in the study. Intraoperative antibiotics were not used in any subject. Non-absorbable packing was not used in any subject; however, silastic stents were placed in some patients who underwent concomitant septoplasty. Patients were offered a watch-and-wait approach after surgery during which antibiotics were not prescribed in the immediate postoperative period and the patients were closely monitored. Postoperative follow-up appointments typically occurred at 1 week, 1 month and 2 months after surgery, and then tailored to findings. Nasal endoscopy was performed at each visit. The desired endpoint following surgery was normalization of the paranasal sinus cavities defined as having no mucopurulent secretions, mucosal inflammation, or edema on endoscopy. Antibiotics were started if the patient failed to show continual improvement symptomatically and/or on nasal endoscopy. Patients with less than one month of follow-up were excluded from this study. Normalization of sinuses at the time of the most recent follow-up visit was recorded.

### 2.1 Statistical analyses

Patients were grouped by postoperative antibiotic use. Categorical variables were assessed using chi-square or Fisher's exact tests as appropriate. Continuous variables were assessed using two-sample T tests and Mann-Whitney U tests as appropriate. Multivariable logistic regression analysis was then used to determine whether patient characteristics were independently associated with the need for antibiotics. All analyses were performed using SPSS 27.0 (IBM, Armonk, New York). Significance testing was 2-sided with a 0.05 alpha level.

### 3 RESULTS

Sixty-nine patients were included in this study. Mean age was 56 years, and 40 patients (57.8%) were male. Forty patients (57.8%) had a likely or confirmed odontogenic source based on pre-operative radiographic findings and/or dental evaluation. The average number of pre-operative antibiotic courses prescribed prior to ESS was 2.6 (range 1-10).

Mean pre-operative Lund-Mackay CT score was 7.1 (SE = 0.96). Nasal polyposis was present in 32 (46.4%) patients. History of asthma, allergies, diabetes, or hypertension was noted in 16 (23.2%), 12 (17.4%), 6 (8.7%), 27 (39.1%) patients, respectively. Six (8.2%) patients were immunocompromised (HIV, diffuse large B-cell lymphoma, or follicular lymphoma). Six patients (8.7%) were current smokers and 29 (42.0%) were former smokers (Table 1). Seventeen patients (24.6%) were prescribed medicated rinses (budesonide or ciprofloxacin/dexamethasone) postoperatively. The average duration to sinus normalization was 8.2 weeks in patients given medicated rinses and 6.5 weeks in patients who only used saline rinses (P = .29).

Thirty-three (47.8%) patients did not require antibiotics in the postoperative period (Table 1). Of these patients, the average duration to sinus normalization was 8.1 weeks (range 1-24 weeks). None of the assessed characteristics was associated with the need for antibiotics on univariate or multivariate analysis (Table 2). If used, the choice of antibiotic was at the discretion of the surgeon and guided by intraoperative and postoperative cultures. Staphylococcus epidermidis was the most commonly isolated bacteria in both patient groups (Table 3).

### 4 DISCUSSION

In our patient population, 47.8% of patients did not require antibiotics in the postoperative period. None of the evaluated characteristics was associated with the use of postoperative antibiotics.
Intraoperative culture results

| Isolated organism                | No antibiotics (n = 36) (no. of isolates) | Antibiotics (n = 37) (no. of isolates) |
|---------------------------------|------------------------------------------|----------------------------------------|
| No culture sent                 | 13                                       | 11                                     |
| Staphylococcus epidermidis      | 8                                        | 14                                     |
| Staphylococcus aureus           | 4                                        | 4                                      |
| Beta-hemolytic Streptococcus    | 3                                        | 1                                      |
| Corynebacterium species         | 2                                        | 4                                      |
| Coagulase negative Staphylococcus | 2                                      | 0                                      |
| Streptococcus viridans          | 2                                        | 0                                      |
| Mixed pharyngeal flora          | 1                                        | 4                                      |
| Staphylococcus lugdunensis      | 1                                        | 4                                      |
| Escherichia coli                | 1                                        | 2                                      |
| Klebsiella oxytoca              | 1                                        | 2                                      |
| Streptococcus constellatus      | 1                                        | 2                                      |
| Aspergillus species             | 1                                        | 1                                      |
| Klebsiella aerogenes            | 1                                        | 1                                      |
| Prevotella melaninomica         | 1                                        | 1                                      |
| Streptococcus intermedius       | 1                                        | 1                                      |
| Aggregatibacter aphrophilus     | 1                                        | 0                                      |
| Bacillus species                | 1                                        | 0                                      |
| Cutibacterium acnes             | 1                                        | 0                                      |
| Eikenella corrodens             | 1                                        | 0                                      |
| Enterobacter cloacae            | 1                                        | 0                                      |
| Fusobacterium necrophorum       | 1                                        | 0                                      |
| Haemophilus influenza           | 1                                        | 0                                      |
| Proteus mirabilis               | 1                                        | 0                                      |
| Staphylococcus lentus           | 1                                        | 0                                      |
| Streptococcus arginosis         | 1                                        | 0                                      |
| Streptococcus mitis             | 0                                        | 2                                      |
| Acinetobacter calcoaceticus-    | 0                                        | 1                                      |
| baumannii complex               |                                           |                                         |
| Gemella morbillorum             | 0                                        | 1                                      |

Note: Some cultures grew out multiple isolates.

Contrary to conventional practice, nearly half of the patients with purulent infections at the time of surgery in our study group responded to surgery alone without the need for antibiotics. Interestingly, odontogenic etiology was not associated with need for postoperative antibiotics. It is important to note that the watch-and-wait approach for postoperative antibiotics was a joint decision between surgeon and patient, and the patients were made aware of the risks and lack of existing research into this methodology. Most patients opted for this approach and were frequently relieved to hear that they may not require additional antibiotics. All patients were aware that they could opt for a course of antibiotics at any time based on their symptoms.

To our knowledge, this is the first study to investigate the minimization of postoperative antibiotics specifically in patients with unilateral CRS with active infection at the time of surgery. Other studies have investigated the role of postoperative antibiotics on ESS clinical outcomes in general, with mixed results. Albu et al showed improved symptoms and endoscopic appearance with a 2-week course of antibiotics post-ESS.14 However, Jiang et al showed no difference in outcomes after a prolonged course of antibiotics with a 3-week follow-up period.4 Importantly, these studies did not distinguish between patients with unilateral or bilateral CRS, and they did not specifically analyze patients with purulence noted intra-operatively.

There are several limitations to this study. First, this was a purely observational study in which the success of treatment was based on clinical exam findings rather than an objective outcome measure, which may have introduced bias. Given the retrospective nature of the study, the rhinologists who performed the postoperative examinations were aware whether each patient received antibiotics and thus not blinded when making their assessments. Moreover, the number of preoperative antibiotic courses, as well as CT scan data were missing in approximately 20% of patients, preventing the inclusion of these characteristics in the multivariate analysis. For patients who were referred to the senior rhinologists by outside providers, information regarding treatment prior to their referral is largely unavailable. Data pertaining to the dental treatment of patients with odontogenic sinusitis was also unavailable. Less than 10% of patients were active smokers, diabetic, or immunocompromised, potentially limiting the conclusions that can be drawn about these characteristics. Additionally, the postoperative regimen of patients was not uniform; all patients were prescribed nasal saline irrigations in the postoperative period, but 15 patients were also prescribed budesonide or ciprofloxacin/dexamethasone rinses. No significant association was found between the use of these medications and the need for postoperative antibiotics (P = .06). Moreover, these were not associated with time to sinus normalization (P = .29). Another limitation is that only patients who agreed to the avoidance of immediate postoperative antibiotic use were included in the study. Prior to surgery, the surgeons discussed the risks, benefits and alternatives of antibiotic avoidance. While most patients agreed with this approach, some were given antibiotics at their request, and such patients were not included in the study. This is likely to have introduced some selection bias in our patient population, and thus it significantly limits the conclusions we can draw from the data. Although the decision to start antibiotics in the postoperative period was based upon continued...
symptoms/endoscopic findings, this was at the discretion of the surgeon in discussion with the patient, not standardized, and likely quite variable. Finally, we grouped all patients under the heading of unilateral purulent sinusitis, even though this represents a heterogeneous group of patients (eg, odontogenic sinusitis, and CRS with and without polyposis). Nevertheless, an effort was made to reduce this heterogeneity through the exclusion of certain pathologies such as mycetoma and fungal balls. These inconsistencies limit the ability to draw conclusions based on the outcomes.

We believe our experience provides valuable data regarding this specific CRS patient population and can be used to inform our patients. Although more than half of our patients ultimately required antibiotics, the remainder of our patients with active unilateral infection at the time of surgery improved with restoration of functional drainage alone. When weighing the risks and benefits of antibiotic treatment, we feel this is an important data point to make an informed decision. Furthermore, we did not see any significant adverse events from not immediately initiating antibiotic treatment, and all infections eventually resolved.

5 | CONCLUSION

In our study population, nearly half of the patients with unilateral CRS with active infection at the time of surgery did not require postoperative antibiotics to achieve normalization of their sinus cavities. Further studies with prospective design and larger sample size are needed to better elucidate which patients in this specific CRS population would benefit from antibiotic use in the postoperative period.

CONFICT OF INTEREST

The authors have no conflicts of interest or financial disclosures.

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