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Are multiple sinus cultures necessary during sinus surgery for chronic rhinosinusitis?

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Abstract

Background—Multiple cultures are commonly obtained from different sinuses where purulence is encountered during endoscopic sinus surgery (ESS). This brings into question the utility and necessity of obtaining multiple cultures. The purpose of this study was to evaluate if multiple cultures obtained during a single case is informative in finding additional pathogens or if it is a redundant, cost-increasing practice. We hypothesized that multiple sinus cultures are necessary to identify the pathogens responsible for an individual's sinus disease. We seek to add information on the utility of performing multiple sinus cultures from a patient care and a health economics standpoint.

Methods—This study was a retrospective review of a single rhinologist's surgical database from 2008 to 2016. Patients that underwent ESS for chronic rhinosinusitis (CRS) and had multiple cultures obtained during surgery were included. Culture difference was recorded as a discrepancy of an infectious pathogen between cultures.

Results—We identified 231 patients with multiple sinus cultures. Of those, 39.4% had a difference of pathogens noted on culture between different sinuses. Only 5% of the cohort received clinically relevant benefit from the second culture obtained in regard to a change in antibiotics.

Conclusion—In this retrospective review we showed that, for the practitioner who obtains sinus cultures intraoperatively, limiting this practice to a single culture rather than multiple is cost-effective and sufficient for identifying the pathogen to be treated. This study, and the resultant change in practice, has the potential to reduce healthcare costs associated with the surgical care of the patient with CRS.

Keywords

chronic rhinosinusitis; CRS; disease severity; endoscopic sinus surgery; ESS; sinus cultures; therapeutics

Chronic rhinosinusitis (CRS) is a prevalent condition, affecting between ~1–4% of the U.S. population.^{1,2} The pathophysiology of CRS is debated, but the inflammatory and infectious interaction is the basis of treatment, specifically anti-inflammatory medications, surgery, and antibiotics.³ The nasal microbiome is important for innate immunity and studies have

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suggested that dysregulation of natural nasal flora by bacteria such as *Staphylococcus aureus* and *Pseudomonas* may play a role in persistence of rhinosinusitis.⁴ Although the use of antibiotics in CRS is at the discretion of the practitioner, the role of endoscopic-guided cultures and culture-directed antibiotics and the benefit on quality of life outcomes have been demonstrated.⁵ Additionally, Zhang et al. showed that postoperative antibiotics that do not cover intraoperative cultures led to decreased quality of life outcomes compared with culture-appropriate antibiotics.⁶ Furthermore, consensus guidelines and expert opinion routinely recommend short courses of culture-directed antibiotics for acute exacerbations of CRS.^{7–10} Occasionally during sinus surgery, when phenotypically distinct mucopurulence is seen, multiple cultures are obtained from the sinuses in order to identify the range of organisms contributing to the infectious aspect of sinusitis.

Sinus cultures provide information on the pathogens present and help guide antibiotic choice. A single sinus culture with gram stain and sensitivity and susceptibility analysis leads to a significant cost to the patient and healthcare system. When necessary, the culture can provide beneficial information to guide treatment. However, when multiple cultures are obtained, these charges can quickly build and increase healthcare costs.

We sought to determine if taking multiple sinus cultures from the same patient during sinus surgery yields different, unique pathogens or if it is a redundant, and therefore cost-increasing, practice. We hypothesized that sinus surgical patients with multiple sinus cultures taken at surgery would demonstrate unique pathogens between cultures in the majority of cases. We also sought to perform a cost-benefit analysis to evaluate the cost-effectiveness of obtaining multiple sinus cultures based on the need to change antibiotic regimen due to multiple unique pathogens present or antibiotic resistance profiles.

This evaluation will help guide the paradigm of obtaining sinus cultures and help improve cost-effective use of medical resources.

Methods

After approval from the University of Washington Institutional Review Board and waiver of consent, a retrospective review was performed on patients that underwent endoscopic sinus surgery (ESS) by the senior author during the period from September 1, 2010 to November 1, 2017. Patients that had multiple sinus cultures obtained during sinus surgery were identified.

The decision to take multiple sinus cultures during surgery was not standardized, but normally related to the appearance of phenotypically unique mucopurulence (Fig. 1). The decision to obtain multiple cultures was entirely based on surgeon preference. However, the practice of the senior rhinologists is to obtain a culture when pockets of mucopurulence with distinct appearance, texture, or color are encountered. This distinction is a comparison made against previously noted pockets from earlier in the case. Cultures were obtained using BD ESwab Collection & Transport system (BD Diagnostics, Sparks, MD). This is a single-swab liquid-based system for collection and transport, with uniquely designed nylon-flocked swabs. Sinus culture is performed in aerobic, anaerobic, and fastidious conditions. In our

institution, a single sinus culture with gram stain and sensitivity and susceptibility analysis is charged \$215.00.

Pathogens for each culture were compared to the other cultures and uniqueness was determined based on bacteria identification and antibiotic sensitivity profile from the specimen description in the microbiology laboratory result of the medical record. Pathogens were considered different if the infectious pathogen was different between the 2 cultures. That is to say, if 1 culture showed *S. aureus* and the other showed *Pseudomonas aeruginosa*, this was recorded as distinct pathogens. Similarly, if a pathogen such as *P. aeruginosa* was present on both cultures, yet the sensitivity profiles were different and distinct, then those were recorded as distinct pathogens. However, if the same pathogen with similar antibiotic sensitivity profiles was cultured from different sinus sites, then this was recorded as the same, not distinct, pathogens.

Patients were prescribed antibiotics immediately post-operatively based either on knowledge of previous culture data or empiric treatment. Due to surgeon preference and experience, the default antibiotic choice for the majority of patients without contraindication or previous culture that demonstrated resistance was trimethoprim-sulfamethoxazole. Initial antibiotic prescribed was compared with sensitivity profile for identified pathogen. The need for change in antibiotic based on culture results was recorded as a binary variable (yes/no).

Additional variables collected included demographics, comorbidities (asthma, cystic fibrosis, nasal polyposis, and ciliary dyskinesia), sinus where each culture obtained, initial antibiotic choice, and presence of purulence during the case.

Once patients with different pathogens between cultures were identified, these cohorts were separated by change in antibiotic due to culture identification (Fig. 2). Examining the group with difference in pathogens and change in antibiotics based on culture data, we performed a simulation to determine if performing a single culture on these individuals would have yielded the same information necessary to lead to a change in culture. To do this, the order of cultures obtained was identified in the nursing record; the first culture obtained was compared with the pathogen identified that led to a change in antibiotic regimen. Analysis was performed to determine if the first culture obtained was sufficient to lead to a change in antibiotic regimen. In order to control for potential randomness of cultures obtained, we then reversed the order of cultures obtained to determine if the second culture obtained was sufficient to lead to change in the antibiotic regimen.

Analysis

Descriptive statistics of the study population were performed with frequencies and proportions being calculated for all variables. Change in antibiotic regimen was recorded and calculated as proportion of overall patients. In order to estimate the cost associated with multiple sinus cultures, we calculated the Number Needed to Treat (NNT) with 95% confidence intervals (CIs). NNT was calculated by isolating the number of patients that required information from the second culture in order to lead to change in antibiotic regimen and comparing it to the total cohort of patients that had multiple intraoperative sinus

cultures. Cost analysis was performed using the NNT. This calculation was based on institutional data on charged amount associated with sinus cultures.

Results

Initial review of all patients that underwent sinus surgery for CRS yielded a total of 762 unique cases. Of this, 287 cases (37.6%) had no cultures obtained intraoperatively, 244 (32.1%) had a single culture obtained, and 231 (30.3%) had multiple intraoperative sinus cultures obtained. Thus, a total of 231 patients were included based on undergoing ESS and having multiple sinus cultures obtained intraoperatively. Of 231 cases, 114 (49.3%) had cultures obtained from contralateral sides, while the remaining had cultures obtained from the same side, but from different sinuses.

The average age of patients was 50 years and 55% of patients were male. Demographics are listed in Table 1. Difference in pathogens between cultures was identified in 39.4% of patients ($n = 91$). Overall change in antibiotic treatment was 25.5% in the entire cohort ($n = 59$) (Fig. 2).

Patients with difference in pathogen between cultures were identified as a distinct cohort. We then identified the first culture obtained based on nursing records from the operating room. The microbiology of the first culture was analyzed for antibiotic susceptibilities and then cross-referenced with the second culture result to identify if the antibiotic appropriate for the first culture would be adequate for coverage of the pathogen identified by the second culture. This analysis demonstrated that the first culture obtained was sufficient to lead to the change in antibiotic regimen in 57% ($n = 16$) (Fig. 3). In other words, in 12 patients with a difference in pathogen and a postoperative change in antibiotics, the second culture obtained provided clinically relevant pathogen information that led to the change in antibiotics prescribed. Therefore, in the entire case series, only 12 patients (5.2%) gained significant results from their multiple cultures in order to lead to a clinically useful change in antibiotic treatment.

When reversing the order of cultures obtained, meaning if we had taken the second culture before the first culture, we found only 13 patients (5.6%) gained significant results from their multiple cultures in order to lead to a clinically useful change in antibiotic treatment.

The most common results found on culture demonstrated commensal sinonasal bacteria. The next most common pathogens identified were methicillin sensitive *S. aureus* followed by *Pseudomonas/Stenotrophomonas* species.

In 12 of 231 cases, multiple cultures led to a change in antibiotic treatment that would not have been achieved with only a single culture. Therefore, the number needed to treat is 20 (95% CI, 11.1 to 33.3). With the charge in our institution of approximately \$215.00 per sinus culture, this leads to \$4300.00 to obtain a culture result that leads to an antibiotic change in a single patient. In other words, 20 patients would undergo sinus surgery with multiple intraoperative cultures in order to identify 1 patient that had a clinically relevant result from the second culture obtained that would lead to a change in postoperative antibiotic selection. We observed no difference when applying the same analysis to the

second culture independently of the first; ie, assuming the second culture was the only culture obtained.

Discussion

To our knowledge, this is the first study assessing the utility and cost-effectiveness of multiple sinus cultures in CRS. We identified 231 patients that had multiple sinus cultures obtained during ESS; 39.4% of patients demonstrated difference in pathogens between sinus cultures; of these, change in postoperative antibiotics due to culture results occurred in 30.7%. When limited to first culture obtained to assess if only 1 culture would have been enough to identify a pathogen and select an appropriate antibiotic, this first culture was sufficient to lead to change in treatment, or demonstrated susceptibility to empiric treatment, in 94.8% of patients. In just 12 of the 231 patients (5%) investigated, the second culture provided unique information used to guide antibiotic treatment (NNT = 20). This leads to \$4300.00 to obtain a culture result that leads to an antibiotic change in a single patient.

We acknowledge that antibiotic selection and management of CRS with antibiotics is not well understood. Whether or not appropriate antibiotic selection alters the clinical course of CRS is debated and likely is dependent more on CRS phenotype and endotype than the specific pathogen. This study does not aim to perform a cost analysis based on antibiotic use and therefore questions regarding this require further study and investigation. Our cost analysis is based on the precedent and widespread practice of therapies directed at the infectious component of CRS.

The most common initially prescribed antibiotic was trimethoprim/sulfamethoxazole (TMP/SMX) followed by fluoroquinolones (Fig. 3). Subsequent antibiotic selection after culture results continued to show TMP/SMX being the most common antibiotic to cover pathogen antibiotic sensitivity. At our institution, empiric postoperative antibiotic choice is typically TMP/SMX due to its coverage of methicillin-sensitive *S. aureus* (MSSA), as well as methicillin-resistant *S. aureus* (MRSA), in addition to other gram-positive organisms. We demonstrated a rate of change in empiric antibiotic based on endoscopically guided culture of 57%. This is similar to previously published rates of change based on endoscopic-guided cultures.¹⁰

Whether or not multiple sinus cultures are necessary or appropriate is currently based on surgeon preference. The International Consensus Statement on Allergy and Rhinology (ICAR) consensus statement noted a small benefit for antibiotic treatment in patients with CRS and leaves it as an option based on patient and provider preference.¹¹ As mentioned in the introduction culture-directed antibiotics have demonstrated improvement in quality of life measures in patients with CRS. Additionally, previous studies have demonstrated the importance of postoperative antibiotic adjustment based on culture results to facilitate recovery following ESS.⁶ This study did not seek to evaluate the effect of antibiotic treatment on long-term effect of culture-directed antibiotic treatments on patients' clinical course. Our analysis did show that a single culture is sufficient for obtaining necessary culture information if desired to guide antibiotic therapy in the vast majority of patients (95%).

We acknowledge a number of limitations in this study. First, the majority of patients in this study were prescribed TMP/SMX for empiric antibiotic choice. This medication covers the majority of common sinus pathogens. We acknowledge that other practitioners may elect a different antibiotic as first-line treatment. This may result in a different rate of change of postoperative antibiotic. A second limitation is the lack of standardized protocol for obtaining multiple cultures. At our tertiary institution, it is up to the surgeon to decide where and when to take an intraoperative culture. Although most instances of multiple cultures were obtained in cases of phenotypically distinct mucopurulence, there is no formal protocol for when these were obtained. This may have influenced our results. Additionally, previous studies have demonstrated poor sensitivity of standard clinical culture methods compared with more sensitive bacterial detection techniques such as 16SrRNA gene sequencing.¹² Our study demonstrated a low rate of completely negative culture results; however, there is a possibility for obtaining more useful pathogen information using these more costly microbial detection techniques. At the current time, these tools are prohibitive based on cost and turnaround time and thus not an option for routine use.

Future directions for this work will center on identifying the most appropriate and cost-effective empiric postoperative antibiotic. We plan to conduct a prospective modeling study using culture data obtained on patients with exacerbations of their sinusitis. Utilizing the information obtained on routine sinus cultures, we plan to perform a modeling study to identify the most effective antibiotic for postoperative treatment. This study will be improved by sampling data from around the country to ensure appropriateness of antibiotic selection irrespective of geographic location. Additional future directions will incorporate longitudinal review of culture data to evaluate change in pathogen following culture-directed antibiotic treatment.

Conclusion

In this retrospective review we showed that for the sinus surgeon who obtains sinus cultures intraoperatively, this study supports limiting this practice to a single culture rather than taking multiple cultures. This study and the resultant change in practice have the potential to reduce healthcare costs associated with the surgical care of the patient with CRS.

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FIGURE 1.
Example of phenotypically distinct mucopurulence from a single patient.

FIGURE 2.

Results of review of patients with multiple sinus cultures obtained during ESS for CRS. When limiting to first culture obtained in individuals with difference between cultures and change in treatment to identify if first culture would be sufficient to lead to change in treatment (red box). CRS = chronic rhinosinusitis; ESS = endoscopic sinus surgery.

FIGURE 3.

Comparison of antibiotic choice prescribed postoperatively based on surgeon preference compared to antibiotic patient was taking on POD 7. This reflects the change in antibiotic-based on culture results. Amox/Clav = amoxicillin/clavulanate potassium; POD 7 = postoperative day 7; SMX = sulfamethoxazole; TMP = trimethoprim.

TABLE 1

Age	51 years (15-89)
Gender	
Male	122 patients (52.8%)
Difference in Pathogen present between cultures	91 patients (39.4%)
Comorbidity present	18 patients (6.1%)
(CF, ciliary dyskinesia, AERD)	