

Effects of endoscopic endonasal sinus surgery on nasal flora in patients with chronic rhinosinusitis with nasal polyps

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Abstract

Aim: This study aimed to evaluate the alterations in the nasal flora in patients who underwent endoscopic endonasal surgery for chronic rhinosinusitis with nasal polyps (CRSwNP).

Material and Methods: This prospective study included 30 patients diagnosed with CRSwNP who were resistant to medical treatment and recommended for surgery. The nasal cavity was sampled two times, first preoperatively on the day of operation and postoperatively in the 4th week. Patients were divided into two groups according to their culture results, including normal flora bacteria and potential pathogen production.

Results: In the preoperative swab samples, 3 (11.1%) patients had no bacterial growth, 16 (59.3%) patients had a normal flora, and potential pathogens were detected in 8 (29.6%) patients. However, postoperatively, 3 (11.1%) patients had no bacterial growth, 13 (48.1%) patients had a normal flora, and potential pathogens were detected in 11 (40.7%) patients during the postoperative period. No significant difference was found between preoperative and postoperative culture results in terms of the number of patients with normal flora, potential pathogens, and no bacterial growth ($p=0.67$). The most common microorganism in the normal flora group preoperative and postoperative period was coagulase-negative Staphylococcus (77.8%, 51.9%, respectively), and the most common microorganism in the potential pathogen group was Staphylococcus aureus (18.5% and 25.9%, respectively). Comparing preoperative and postoperative culture results according to isolated potential pathogen microorganism types, no statistically significant difference was observed for any microorganism in the potential pathogen group ($p>0.05$).

Conclusion: As a result, no correlation between nasal polyps' surgery and potential pathogens was detected.

Keywords: Chronic rhinosinusitis; culture; nasal polyps; flora; potential pathogens; bacteria; *Staphylococcus aureus*; coagulase; transnasal endoscopic surgery; pseudomonas.

INTRODUCTION

Human microbiota research has significantly changed the perspective on the diversity and functions of human-related microorganisms. Moreover, these studies have also shown that microbiota change according to the health condition of the host. In healthy individuals, the mucosal surface of the upper respiratory tract is colonized by a wide variety of bacterial microbiota, whereas the lower airways have low bacterial diversity and load. On the

contrary, chronic inflammatory disease has an opposite trend in bacterial diversity and load in patients with airway diseases. Also, the mucosal microbiota is different in composition. In these patients, the mucosal microbiota is associated with the characteristics of the disease and is rich in known or suspected pathogenic species (1). Chronic rhinosinusitis (CRS) is defined as the presence of two of four major criteria, defined as nasal obstruction, hyposmia or anosmia, facial pressure, and purulent

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discharge, and when the inflammation is radiologically or endoscopically demonstrated to last longer than 12 weeks. Chronic rhinosinusitis has two subgroups: with nasal polyps (CRSwNP) and without nasal polyps (CRSsNP) (2). Despite the high prevalence of CRSwNP in the nasal cavity and paranasal sinus, the etiology is unclear (3). It is suggested that allergies, asthma, infection, cystic fibrosis, and hypersensitivity for aspirin are crucial in the etiology of CRSwNP (4). However, CRS involves the impairment of nasal microbiology and increase in the number of fungal species or some organisms such as *Staphylococcus aureus* (5). Microbial interaction with the host is critical in the onset and persistence of CRS (6).

This study aimed to evaluate the alterations in the nasal flora in patients who underwent endoscopic endonasal surgery for chronic rhinosinusitis with nasal polyps.

MATERIAL and METHODS

This prospective study included 30 patients diagnosed with bilateral diffuse CRSwNP who were resistant to medical treatment and recommended for surgery. Computed tomography of the paranasal sinus was carried out after the ear, nose, and throat examinations of the patients. Two nasal swabs were taken from the patients, first on the day of the operation and then postoperatively in the fourth week after recovery of the nasal cavity. The samples were taken from only one nasal cavity (right or left). Postoperative samples were also taken from the same side. The samples were taken from the polyp surface in patients with complete obliteration of the nasal cavity from the middle meatus level during the preoperative period. Patients who used antibiotics 1 week before the surgery or had immunodeficiency, autoimmune diseases, diabetes, ciliary dyskinesia, cardiac pathology requiring infective endocarditis prophylaxis, and liver/renal dysfunction were not included in the study. All patients underwent endoscopic sinus surgery (ESS) under general anesthesia and intraoperative antibiotic treatment was not used. Nasal lavage with physiological saline solution was recommended during the postoperative period for four times a daily. Additionally oral antibiotics were used for the first postoperative week. Systemic or topical nasal steroid therapy was not given to the patients during the postoperative four week. As analgesics, oral paracetamol was given to the patients during the postoperative period. During the postoperative period, the patients were called weekly for control appointments for nasal cavity care. Three patients who did not come for their appointments during the postoperative period were excluded from the study.

Microbiological analysis

Samples were delivered to the microbiology laboratory as soon as possible in the carrier medium (Sterile Stuart transport medium, BTR, Turkey). Each swab was placed in a tube containing 1 mL of sterile saline solution and vortexed for 1 min at 500 rpm. The same sample solution was used for each medium, and the samples were planted separately in 5% sheep blood agar (OR-BAK, Turkey), eosin

methylene blue agar (TM Media, India), and chocolate agar (TM Media, India) with a standard rounded tip (0.01 mL) and incubated at 37°C in 5% carbon dioxide environment for 24–48 h. Bacteria, whose reproduction was detected in the culture, were identified using conventional methods and semi-automated identification systems (API system, BioMerieux, France) according to colony morphology and gram staining characteristics. α-Hemolytic *Streptococcus*, nonhemolytic *Streptococcus*, coagulase-negative *Staphylococcus* (CNS), nonpathogenic *Neisseria* spp., *Corynebacterium* spp. (*diphtheria bacilli*), and nonpathogenic *Bacillus* spp. was defined as normal flora. *Staphylococcus aureus*, β-hemolytic streptococci, *Streptococcus pneumoniae*, *Moraxella catarrhalis*, *Haemophilus influenzae*, *Escherichia coli*, *Pseudomonas* spp., *Proteus* spp., *Enterococcus* spp., *Klebsiella* spp., and *Citrobacter* spp. were defined as pathogens.

Patients were divided into two groups according to their culture results, including normal flora bacteria growths and potential pathogen growths.

Ethical committee approval

The study was conducted with the permission of Clinical Research Ethics Committee (Ethics Committee Decision No: 174).

Statistical analyses

Data were analyzed using SPSS for Windows 11.5 software program. Chi-square and Fisher exact tests were used to investigate the differences between microorganism production status and microorganism types before and after the operation. The statistical significance limit was accepted as 0.05.

RESULTS

Twenty-seven patients who underwent ESS for CRSwNP and delivered culture samples were included in the study. The mean age of the patients was 35.59 ± 8.12 (23–54) years; 20 (74.1%) were males and 7 (25.9%) were females. In the preoperative swab samples, 3 (11.1%) patients had no bacterial growth, 16 (59.3%) patients had a normal flora, and potential pathogens were detected in 8 (29.6%) patients. However, postoperatively, 3 (11.1%) patients had no bacterial growth, 13 (48.1%) patients had a normal flora, and potential pathogens were detected in 11 (40.7%) patients during the postoperative period. Additionally, although not statistically significant, the number of patients in which normal flora was produced, decreased and the number of the patients, in which the potential pathogens were isolated, increased (Table 1). When the microorganism groups were compared in terms of culture results before and after the operation, no significant difference was detected ($p = 0.676$) (Table 1). The most common microorganism in the normal flora group preoperative and postoperative period was CNS (77.8%, 51.9%, respectively), and the most common microorganism in the potential pathogen group was *S. aureus* (18.5% and 25.9%, respectively) (Table 2 and Figure 1). Further, 85.7% of the preoperatively isolated

CNS included methicillin-sensitive CNS (MSCNS), and all the *S. aureus* isolates were sensitive to methicillin (MSSA). All CNS isolates isolated during the postoperative period and 85.7% of the *S. aureus* isolates were found to be methicillin-sensitive. *Pseudomonas* spp. was the second most common microorganism to grow among potential pathogens (14.8% and 11.1%, respectively). Comparing preoperative and postoperative culture results according to isolated microorganism types, no statistically significant difference was observed for any microorganism in the potential pathogen group ($p > 0.05$). In the normal flora group, however, coagulase-negative staphylococci, *Corynebacterium* spp., and *Bacillus* spp. were found to be statistically lower in number postoperatively.

Table 1. Comparison of microorganism groups before and after the surgery

| Microorganism Groups | Preoperative, n (%) | Postoperative, n (%) | p |
|----------------------|---------------------|----------------------|---------|
| Normal Flora | 16 (59.3) | 13 (48.1) | 0.676 ξ |
| Potential Pathogen | 8 (29.6) | 11 (40.7) | |
| No Bacterial Growth | 3 (11.1) | 3 (11.1) | |

ξ: Chi-Square test

Table 2. Comparison of preoperative and postoperative culture results with respect to the production of microorganisms

| | Preoperative n (%) | Postoperative n (%) | p |
|---------------------------------|-----------------------|------------------------|---------|
| Normal Flora | | | |
| CNS | 21(77.8) | 14 (51.9) | |
| <i>Corynebacterium</i> spp | 5 (18.5) | 1 (3.7) | |
| <i>Bacillus</i> spp | 1 (3.7) | 0 (0.0) | |
| α-Hemolytic Streptococcus | 0 (0.0) | 0 (0.0) | 0.001 ξ |
| Nonhemolytic Streptococcus | 0 (0.0) | 0 (0.0) | |
| <i>Neisseria</i> spp. | 0 (0.0) | 0 (0.0) | |
| Potential Pathogens | | | |
| <i>Staphylococcus aureus</i> | 5 (18.5) | 7 (25.9) | 0.513 ξ |
| <i>Pseudomonas</i> spp. | 4 (14.8) | 3 (11.1) | 0.500 Ω |
| <i>Citrobacter</i> spp. | 2 (7.4) | 0 (0.0) | 0.150 Ω |
| <i>Enterococcus</i> spp. | 1(3.7) | 0 (0.0) | 0.500 Ω |
| <i>Klebsiella</i> spp. | 0 (0.0) | 1(3.7) | 0.500 Ω |
| β-hemolytic streptococci | 0 (0.0) | 0 (0.0) | ---- |
| <i>Streptococcus pneumoniae</i> | 0 (0.0) | 0 (0.0) | ---- |
| <i>Moraxella catarrhalis</i> | 0 (0.0) | 0 (0.0) | ---- |
| <i>Haemophilus influenzae</i> | 0 (0.0) | 0 (0.0) | ---- |
| <i>Proteus</i> spp. | 0 (0.0) | 0 (0.0) | ---- |
| <i>Escherichia coli</i> | 0 (0.0) | 0 (0.0) | ---- |

ξ: Chi-Square test,

Ω: Fisher-Exact test

CNS: Coagulase-Negative Staphylococcus

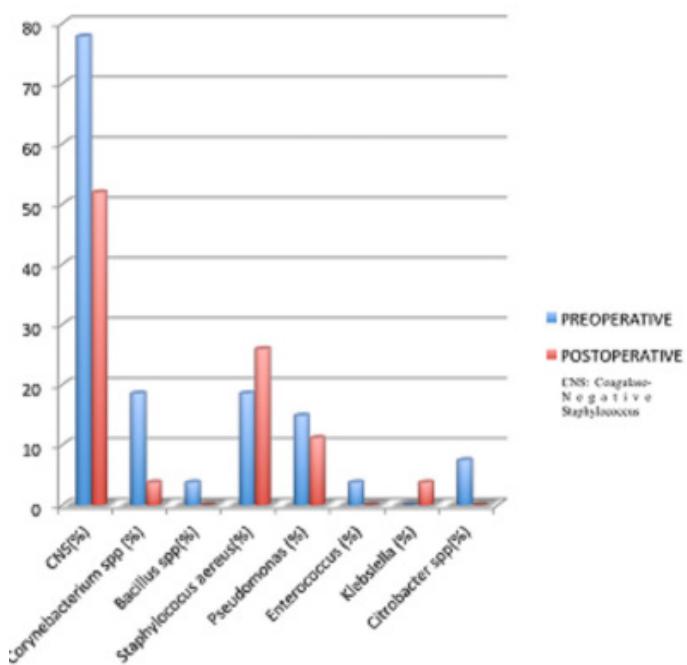


Figure 1. Comparison of pre and postoperative results of normal flora and potential pathogens

DISCUSSION

In patients with CRS, paranasal sinuses are colonized with bacteria. CNS, *S. aureus*, *S. viridans*, *Corynebacterium* spp., and anaerobes often produce in these patients (7). The role of bacteria in CRS is not well known (8). Some of these pathogens have been reported to contribute to the inflammatory component of CRS (7). For example, *S. aureus* and its superantigen have been reported to be involved in the pathogenesis of CRSwNP in a variety of studies (9-11). *S. aureus* and its superantigens are associated with the severity of the disease in patients with CRSwNP (11). In patients with massive polyposis, *S. aureus* is the most common bacteria found in the nasal mucus, and enterotoxins produced by these bacteria are reported to be the causative agent of damage to the lateral nasal wall. Superantigens (enterotoxins) cause the up-regulation of cytokine production by lymphocytes, and these cytokines are responsible for increase in the number of lymphocytes, eosinophils, and macrophages, the most common inflammatory cells in nasal polyps (10). In addition, recent studies have reported that loss of bacterial diversity in sinus microbiota is common in patients with CRS and preoperative sinus microbiota diversity is associated with good postoperative outcomes (12-14). However, another study reported that the cure rate in patients with nasal polyps without production in culture is higher than the rate in those with normal flora and production in culture. Also, the culture results of aspirate samples taken from the intraoperative maxillary sinus may serve as a prognostic factor predict ESS results (15).

Bacterial growth rates in cultures from patients with nasal polyps range from 77% to 97% (15-18). In the present study,

88.9% of the cultures were found to have bacterial growth, which is in accordance with the literature. In a study conducted, *S. aureus* (15.2%), α -hemolytic streptococci (13%), microaerophilic streptococci (10.9%), *H. influenzae* (8.7%), and *M. catarrhalis* (8.7%) were reported as the most isolated bacteria in aspirate samples of patients with CRSwNP (17). In the present study, CNS (77.8%-51.9%), *S. aureus* (18.5%-25.9%), *Corynebacterium* spp. (18.5% - 3.7%), and *Pseudomonas* spp. (14.8% -11.1%) were the most isolated bacteria during the preoperative and postoperative periods. In a study by Bendouah et al., respiratory pathogens such as *P. aeruginosa* or *S. aureus* have found to be common in patients with CRS (19). Nevertheless, these microorganisms generally are combined with various microorganisms and hence cannot be isolated on their own. This may explain clinical and immunological diversity in a patient with CRS (1). In a study on asymptomatic patients after ESS, the majority of the flora comprised CNS (69%) and diphtheroids (25%). *S. aureus* was found in 31% of the patients. This study showed that these bacteria persisted in healthy sinus cavities during the postoperative period (18). In patients with CRS, biofilm intensities were obviously reduced, but not completely eliminated, after ESS. CNS and *S. aureus* are most frequently produced in these patients before and after the treatment (20). In another study, 59% of cultures taken from patients who underwent ethmoidectomy after completed epithelialization showed production, 17% showed normal flora, and 23% showed no production. The most commonly produced gram-positive bacterium was *Staphylococcus* species (21). The presence of bacterial biofilm, especially the presence of polymicrobial biofilm or biofilm containing *S. aureus*, has negative prognostic value and is found to be correlated with high nasal endoscopy scores and symptoms after surgery and severe sinus diseases (6). In the present study, *S. aureus* and *P. aeruginosa*, which are biofilm-related pathogens, were the most isolated respiratory pathogens before and after the surgery and the isolation rates of these microorganisms did not significantly change due to surgery. Stern et al. reported a positive pathogenic culture rate of 78% in CRSwNP and 64% in CRSsNP. They also reported that the most commonly produced gram-positive bacterium was *S. aureus* and the most commonly produced gram-negative bacterium was *Citrobacter* spp. Gram-negative bacteria were more often found in patients with polyps (2). Our study, positive pathogenic culture rate of 29.6% was found during the preoperative period and 40.7% during the postoperative period. The most commonly produced gram-positive bacterium was *S. aureus* and the most commonly produced gram-negative bacterium was *Pseudomonas* spp. Although not statistically significant, the number of gram-positive bacteria increased, whereas the number of gram-negative bacteria decreased during the postoperative period. Niederfuhr et al. reported that CNS and *Corynebacterium* species were predominant in CRSwNP and CRSsNP and no significant difference was observed in bacteriological characteristics between the two groups (22). Similarly, Uhliarova et al. showed

no bacteriological difference between patients with CRSwNP and CRSsNP (16). In the present study, CNS and *Corynebacterium* spp were more isolated than other normal flora during the pre- and postoperative period, which was in accordance with the literature. The ratios of these commensal microorganisms decreased after the surgery, with no significant differences in the number of potential pathogens.

Some studies in the literature have supported the role of bacteria in the pathogenesis of polyps (23), whereas others have reported no such effect (16,22). Chronic colonization of bacteria and fungi has been detected in patients with CRSwNP, but it is not known whether this colonization results in nasal polyps or part of the underlying inflammatory process (9). The presence of microbial community, predominantly of *Corynebacteria* species, is associated with increased interleukin (IL)-5 gene expression and increased risk of nasal polyposis (1). Ba et al. reported that the absence of IL-5 expression in nasal polyps in patients with CRSwNP was associated with gram-negative bacterial colonization and the presence of IL-5 expression with gram-positive bacterial colonization (24).

CRS is a chronic inflammatory disease affecting more than 10% of the adult population, which leads to a reduced quality of life, loss of work, loss of time, and more than one million surgical interventions (5). Examinations of host and microbial interactions in patients with CRS may clarify disease mechanisms and help in designing effective treatment protocols (6). This study compared preoperative and postoperative culture results in terms of potential pathogens in patients with CRSwNP. Individual factors such as age, diet, hormonal status, and hygiene, which influenced the microbial structure, were minimized by comparing healthy individuals and patients with polyps in the same patient population. Thus, this study aimed to understand the relationship between nasal polyps and potential pathogens by investigating the alteration of potential pathogens after nasal polyps were removed during ESS. No changes were found in terms of potential pathogens before and after ESS. However, a limitation was that this study did not evaluate anaerobic bacteria. Hence, further prospective studies are needed to evaluate the entire microbiota in wider patient populations.

CONCLUSION

Endoscopic sinus surgery does not alter the nasal flora in patients with chronic rhinosinusitis with nasal polyps. The association of nasal microorganisms and chronic rhinosinusitis with nasal polyps can be understood better with long term follow up of these patients when some of them might have a recurrence of the disease.

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