

Bacterial Flora in the Sphenoid Sinus Changes with Perioperative Prophylactic Antibiotic Administration

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Abstract

The complications of endonasal transsphenoidal surgery (ETSS) include meningitis and sinusitis, and these complications are troublesome. Some reports have investigated the type of bacteria and the susceptibility of sphenoid sinus mucosal flora to drugs. However, most specimens can be collected after perioperative antibiotic administration. In this study, 95 and 103 sphenoid sinus mucosal samples collected during ETSS from September 2013 to February 2015 and from June 2017 to January 2019, respectively, were examined for bacterial culture. Sphenoid sinus mucosal samples were collected after antibiotic administration in the first period, whereas samples were collected before antibiotic administration in the second period. Hence, the specimens in the second period were not affected by antibiotics. Moreover, drug susceptibility tests for the detected bacteria were performed. Overall, 52 and 51 bacterial isolates were collected during both periods. Gram-positive cocci (GPCs), including *Staphylococcus aureus* and *Staphylococcus epidermidis*, were more common in the non-antibiotic group than in the antibiotic group ($p < 0.01$). However, the proportion of gram-negative rods (GNRs) did not significantly differ between the two groups ($p = 0.54$). The antibiotic group had a significantly higher proportion of bacteria resistant to ampicillin ($p < 0.01$) and first-generation cephalosporin ($p = 0.01$) than the non-antibiotic group. In conclusion, there was a difference in bacterial flora in the sphenoid sinus mucosal samples collected before and after intraoperative antibiotic administration.

Keywords: transsphenoidal surgery, bacterial flora, sphenoid sinus

Introduction

Endonasal transsphenoidal surgery (ETSS) is the most common procedure in managing pituitary lesions, and annually, this surgery has been increasingly performed.¹⁾ Meningitis and sinusitis are the most common infectious complications associated with ETSS. The incidence of meningitis after ETSS ranges from 0.7% to 10%.^{2–10)} There are no global guidelines on the use of prophylactic antibiotics prior to ETSS, and recent systematic reviews have not identified any effective antibiotics.¹¹⁾ Moreover, the American Society of Health-System Pharmacists guidelines

stated that there are no appropriate antibiotics for endoscopic sinus surgery.¹²⁾ Although there is no strong evidence supporting the use of perioperative antibiotics for ETSS, surgeons commonly use prophylactic drugs to safely perform the procedure.^{13,14)}

A previous report has shown that the bacterial flora detected in the nasal cavity before ETSS differs from that in the sphenoid sinus during surgery. Moreover, the bacterial flora in the sphenoid sinus had a high rate of drug resistance; therefore, the use of perioperative prophylactic antibiotics for ETSS should not be determined based on the type of nasal bacteria alone.¹⁵⁾ Nasal mucosal samples can be preoperatively collected, and sphenoid sinus mucosal samples can only be obtained intraoperatively. In previous reports, sphenoid sinus mucosal samples were collected after prophylactic antibiotic administration.^{15,16)} However, no study has assessed whether samples should be collected before or after the administration of prophylactic antibiotics. Hence,

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Table 1 Clinical characteristics of patients in two groups

Characteristics	Sample collection method	
	Antibiotic	Non-antibiotic
Total number of patients (n)	93	89
Sex (n)		
male	35	38
female	58	51
Age, years (mean \pm SD)	51.0 \pm 16.9	56.3 \pm 13.9
Disease (n)		
Non-functioning pituitary adenoma	39	34
Functioning pituitary adenoma	35	24
Rathke's cleft cyst	8	13
Meningioma	3	3
Craniopharyngioma	1	3
Germinoma	1	0
Chordoma	1	2
Others	5	10

samples were commonsensically assumed to be collected after the administration of prophylactic antibiotics, which might have resulted in the selective detection of resistant bacteria. That is, the examination of an appropriate perioperative antibiotic based on these results may not be accurate. We hypothesized that the culture results of specimens collected after antibiotic administration are affected by the drug and that there may be differences between specimens collected before and after antibiotic administration. Therefore, the current study aimed to identify the difference in sphenoid sinus flora before and after antibiotic administration.

Materials and Methods

Study participants

Overall, 121 and 109 consecutive ETSS were performed from September 2013 to February 2015 and from June 2017 to January 2019, respectively, at Nippon Medical School Hospital. Then, 93 and 89 patients were included in the study. Although there was a gap of several years between these two periods, the surgical procedure performed by the same surgeon who was proficient in pituitary surgery, including surgical instruments and disinfectant (0.02% benzalkonium chloride solution), did not change. In addition, we compared the bacterial flora of the entire hospital in the two groups based on bacteriological surveillance reports, and there was no apparent difference

between the bacterial strains isolated during the two periods.

A previous report has shown that the sphenoid sinus mucosal samples of patients with pituitary apoplexy differed.¹⁶⁾ Thus, patients with this condition, with the main purpose of cerebrospinal fluid (CSF) leakage repair, and those without an appropriate specimen were excluded. Patient characteristics are summarized in Table 1. Sphenoid sinus mucosal samples were collected during ETSS and were examined for bacterial culture. Samples were obtained after antibiotic administration in the first period and before antibiotic administration in the second period. The former was referred to as the antibiotic group and the latter the non-antibiotic group because the samples were not affected by antibiotic administration (Fig. 1). In the antibiotic group, sulbactam 0.5 g/ampicillin 1.0 g was immediately administered before surgery and every 3 hours thereafter. In cases in which CSF leakage was expected before surgery (e.g., patients requiring extended endoscopic ETSS), cefotaxime 1.0 g was administered. In the non-antibiotic group, antibiotics were selected using the same selection method and were immediately administered after sample collection, not before surgery and during the start of surgery. The time from the start of surgery to specimen collection was approximately 30 minutes to 1 hour in all cases. When collecting sphenoid sinus mucosal samples, caution was taken to prevent the collection device and sample from contacting the nasal corridor.

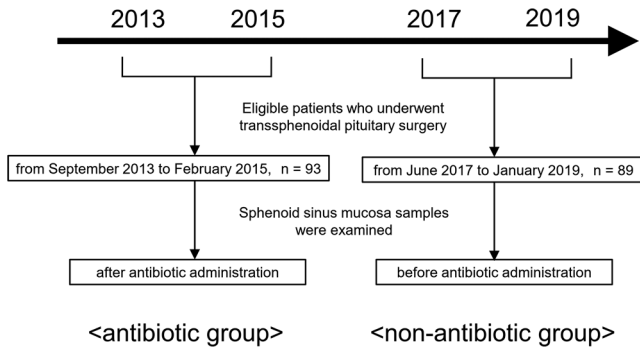


Fig. 1 Flowchart of patient selection during the two collection periods.

Bacterial culture

All specimens were subjected to culture tests with MicroScan WalkAway (Beckman Coulter, Inc., Brea, CA, USA). Then, drug susceptibility tests for the detected bacteria were performed. In this study, the drugs examined were ampicillin and first-generation (cefaclor and cefazolin), second-generation (cefmetazole, cefotiam, and flomoxef), and third-generation

(cefcape pivoxil, cefdinir, cefditoren pivoxil, cefixime, cefotaxime, ceftazidime, ceftriaxone, and sulbactam/cefoperazone) cephalosporins. The study design and protocol were approved by the Ethics Review Committee of Nippon Medical School (approval number: R1-08-1178), and a written informed consent was obtained from all patients.

Statistical analysis

Statistical differences were assessed using the chi-square test and Fisher’s exact test, and p values of <0.05 were considered statistically significant. All statistical analyses were performed using the Statistical Package for the Social Sciences version 25.0 (IBM Corp., Armonk, NY, USA).

Results

Table 2 shows the bacterial species detected on culture tests in the two groups. In some cases, multiple bacterial species were detected in one sample, and they were all counted. No bacteria were detected in 47 and 45 patients in the antibiotic

Table 2 Bacterial isolates from sphenoid sinus mucosal samples in the two groups

Isolated bacteria	Sample collection method	
	Antibiotic	Non-antibiotic
<i>Enterococcus faecalis</i>		1
<i>Microccosus sp.</i>	1	
MRSA	1	2
<i>Parvimonas micra</i>	1	
<i>Peptostreptococcus</i>	6	1
<i>Staphylococcus aureus</i>		10
<i>Staphylococcus capitis</i>	1	3
<i>Staphylococcus epidermidis</i>	15	23
<i>Staphylococcus lugdunensis</i>	2	1
<i>Viridans Streptococcus</i>		1
<i>Coryneform bacteria</i>	12	4
<i>Gram-positive rod</i>	1	
<i>Propionibacterium</i>	9	2
<i>Neisseria species</i>		1
<i>Citrobacter koseri</i>		1
<i>Enterobacter aerogenes</i>	1	
<i>Pseudomonas aeruginosa</i>		1
Normal bacterial flora	2	
Total number of patients (n)	93	89

Blank indicates no detection. MRSA: methicillin-resistant staphylococcus aureus.

Table 3 Gram-positive cocci and gram-negative rods isolated from sphenoid sinus mucosa samples in the two groups

Detected bacteria	Sample collection method		p value
	Antibiotic	Non-antibiotic	
Gram-positive coccus	27	42	<0.01
Gram-negative rod	1	2	0.62
Total number of bacterial isolates	52	51	
Total number of patients	93	89	

Table 4 Distribution of bacterial species in the cultures of sphenoid sinus mucosal samples in the two groups
antibiotic group

	Total number of isolates	Ampicillin resistant	Cephalosporin resistant		
			First generation	Second generation	Third generation
Gram-positive coccus	27	15	9	4	2
Gram-negative rod	1	1	1	1	0
Total	28	16 (57.1%)	10 (35.7%)	5 (17.8%)	2 (7.1%)

non-antibiotic group

	Total number of isolates	Ampicillin resistant	Cephalosporin resistant		
			First generation	Second generation	Third generation
Gram-positive coccus	42	10	5	0	0
Gram-negative rod	2	1	0	0	1
Total	44	11 (25.0%)	5 (11.3%)	0 (0%)	1 (2.2%)

and non-antibiotic groups, respectively. *Staphylococcus aureus* and *Staphylococcus epidermidis* were more common in the non-antibiotic group than in the antibiotic group.

In general, gram-positive coccus (GPC) and gram-negative rod (GNR) frequently cause surgical site infection.^{7,17,18)} Hence, in the current analysis, the bacteria were classified into two groups and were then compared (Table 3). The proportion of GPCs was significantly higher in the non-antibiotic group than in the antibiotic group ($p < 0.01$). However, there was no significant difference in proportion of GNRs between the two groups ($p = 0.62$).

Table 4 shows the detected bacteria and the number of bacteria resistant to antibacterial agents. The proportion of bacteria resistant to ampicillin ($p < 0.01$) and first-generation cephalosporin ($p = 0.01$) in the antibiotic group was significantly higher than that in the non-antibiotic group.

Discussion

In the current research, the bacteria detected in the cultures of sphenoid sinus mucosal samples collected before and after antibiotic administration differed, and the results were evident. However, similar findings were not observed in previous studies. Furthermore, the rate of resistance to ampicillin and first-generation cephalosporin among bacteria detected in the sphenoid sinus mucosal samples collected before antibiotic administration was significantly lower than that in the samples collected after antibiotic administration. These results support the hypothesis that bacterial flora in the sphenoid sinus mucosal samples collected after antibiotic administration is affected by the drug.

The bacterial species in the antibiotic group in our study and those in previous studies^{15,16)} were similar. That is, *S. epidermidis* and *Propionibacterium*, but

not *S. aureus*, species were commonly detected. This result implied that no previous research has examined (or at least specified) the flora via sampling before antibiotic administration.

In this study, the proportion of GPCs was higher in the non-antibiotic group than in the antibiotic group. Therefore, some bacteria sensitive to the administered antibiotic were killed, and drug-resistant bacteria were selectively detected. Sulbactam/ampicillin, which was effective against most *Staphylococcus* species, was used in most cases. The rate of resistance to ampicillin and first-generation cephalosporin was significantly higher in the antibiotic group than in the non-antibiotic group. The detection of bacteria resistant to the antibiotics administered might have attributed to this result.

Previous reports have recommended the use of third-generation cephalosporin because of high resistance to first-generation cephalosporins.^{15,19} In the current study, the drug resistance rate (11.3% and 0% for the first- and second-generation cephalosporin, respectively) among unaffected bacteria in sphenoid sinus mucosal samples was not extremely high. The resistance rate was similar to that of the third-generation cephalosporin in the antibiotic group (7.1%). Hence, first-generation cephalosporins, including cefazolin, or second-generation cephalosporins, such as cefotiam, can be an effective prophylactic antibiotic. The Japanese practice guidelines on the proper use of antibacterial agents for postoperative infection recommend the use of cefazolin as a prophylactic antibacterial agent for endoscopic sinus surgery.^{13,19–21} This finding supports our results. However, postoperative CSF leakage is a risk factor for the development of postoperative meningitis after ETSS,^{2,3,22,23} and patients with diabetes or immunosuppressive drugs are at high risk, even without CSF leakage.^{24–29} Thus, we do not negate the use of third-generation cephalosporins in cases in which CSF leakage is expected preoperatively. After cephalosporins, penicillin-based antibiotics, including ampicillin, are the most commonly utilized antibiotics by pituitary surgeons.¹³ However, based on our results, ampicillin had an extremely high resistance rate; therefore, it is not effective.

The current study had several limitations. The bacterial flora might have been affected by factors such as the race of the patient and antibiotics used before admission. Although caution was taken to ensure that the collection device and sample did not come into contact with the nasal cavity upon collecting sphenoid sinus mucosal samples, the risk of intranasal contamination was undeniable.

In conclusion, there was a difference in bacterial flora in the sphenoid sinus mucosa samples collected

before and after intraoperative antibiotic administration. This study proposed that first- or second-generation cephalosporins might be an effective prophylactic antibiotic for ETSS. Further, in high-risk patients or those with CSF leakage, switching to broad-spectrum antibiotics, such as third-generation cephalosporins, may be a useful option.

Conflicts of Interest Disclosure

All authors have no conflict of interest to declare.

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