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RESEARCH

A study on the effectiveness of multiple intraoperative disinfections and bacteriological monitoring in reducing postoperative intracranial infection rates in transnasal endoscopic skull base surgery

Duanzheng Cao[1,2] · Danke Shen[1] · Zhenyan Shi[1] · Jie Wu[1] · Shenhao Xie[1] · Hai Luo[1] · Bing Tang[1]

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Abstract

Objective This study aims to evaluate the clinical significance of multiple intraoperative sterilizations and bacteriological surveillance in reducing postoperative intracranial infections during transnasal endoscopic skull base surgery.

Methods This study collected clinical data from 1002 patients undergoing transnasal endoscopic skull base surgery between January 2016 and January 2024. Patients were divided into a routine sterilization group (367 patients) and a multiple sterilization group (635 patients) based on the sterilization method. The rates of intracranial infections were compared between the two groups. Additionally, intraoperative bacteriological monitoring before and after sterilization was performed on some patients in the multiple sterilization group to analyze bacterial colonization and its relationship with intracranial infections.

Results In the routine sterilization group of 367 patients, 21 patients (5.72%) developed intracranial infections. Of these, 20 patient had cerebrospinal fluid leakage during surgery. In the multiple sterilization group of 635 patients, 14 patients (2.20%) developed intracranial infections, all associated with cerebrospinal fluid leakage during surgery. Among the 96 patients who underwent bacteriological monitoring, 59 patients and 11 patients had definitive positive bacterial cultures before and after nasal disinfection, respectively. Additionally, 18 patients and 5 patients had definitive positive bacterial cultures before and after sphenoid sinus disinfection, respectively. One patient developed an intracranial infection caused by the same pathogens cultured from the nasal cavity.

Conclusion Most pathogenic bacteria causing postoperative intracranial infections in patients undergoing transnasal endoscopic skull base surgery originate from nasal colonization. Multiple intraoperative sterilizations can reduce the incidence of intracranial infections in patients with high-risk factors for intraoperative cerebrospinal fluid leakage.

Keywords Transnasal endoscopic surgery · Bacteriologic surveillance · Nasal colonization · Intracranial infection

Introductory

With the advancement of neuroendoscopic technology, transnasal endoscopic surgery has become a crucial procedure in skull base surgery, due to its minimally invasive nature and wide field of view [6]. It is widely used in the surgical treatment of pituitary adenomas, craniopharyngiomas, saddle-node meningiomas, chordomas, trigeminal nerve sheath tumors, and other skull base diseases [9, 18, 23]. Although minimally invasive surgery avoids the

✉ Bing Tang
ndyfy03402@ncu.edu.cn

Duanzheng Cao
1847025674@qq.com

Danke Shen
danke1998@foxmail.com

Zhenyan Shi
2148431974@qq.com

Jie Wu
jiewu@email.edu.cn

Shenhao Xie
ndyfy05078@ncu.edu.com

Hai Luo
916044021@qq.com

[1] Department of Neurosurgery, The First Affiliated Hospital, Jiangxi Medical College, Nanchang University, Nanchang, China

[2] Department of Neurosurgery, Jiande First People's Hospital, Hangzhou, China

trauma of traditional craniotomy, it traverses the nasal and sinus cavities, which are bacterial zones. Instruments and implants must pass through these potentially contaminated areas to reach the surgical site, increasing the risk of postoperative intracranial infections. Intracranial infection is a serious complication after neurosurgery, significantly affecting patient prognosis [7]. Studies have shown that the incidence of intracranial infection after transnasal endoscopy ranges from 0.8% to 7.98% [17, 19–21]. Despite significant improvements in neurosurgical and postoperative care techniques in recent years, the reported incidence of intracranial infection after transnasal endoscopy has not decreased. Currently, the etiologic agents of infection after transnasal endoscopic skull base surgery (TESBS) are primarily nonpathogenic bacteria colonizing the nasopharynx and respiratory tract, such as Streptococcus pneumoniae, Staphylococcus epidermidis, Klebsiella pneumoniae, and Haemophilus influenza [2, 3, 21].The nasopharynx is a crucial part of the respiratory tract. Therefore, effectively eliminating colonizing bacteria in the sinus cavity should theoretically reduce the incidence of postoperative intracranial infections.

In our center, we began multiple disinfections of the sinus cavity at all stages of the procedure for patients undergoing TESBS in 2019. Before this, patients only received routine nasal disinfection, and the effect of these different disinfection methods remains unclear. Therefore, this study will retrospectively analyze the clinical data of patients who underwent TESBS at our center from January 2016 to January 2024. We will compare the effects of the two disinfection methods on the rate of postoperative intracranial infection. We will also perform intraoperative bacteriological monitoring on patients undergoing multiple sterilizations to analyze the relationship between nasal colonizing bacteria and postoperative intracranial infections. The aim of this studyis to provide more standardized treatment protocols for TESBS and generate insights into reducing the incidence of postoperative intracranial infections.

Methods

Data collection

This study included 1002 patients who underwent TESBS at the Department of Neurosurgery, First Affiliated Hospital of Nanchang University. The cohort consisted of 483 males and 519 females, aged 4 to 82 years, with a mean age of 45.62 ± 15.11 years. The spectrum of diagnoses included 613 cases of pituitary tumors, 138 cases of craniopharyngiomas, 74 cases of meningiomas, 53 cases of lacunar cysts, 37 cases of chordomas, 20 cases of nerve sheath tumors, and 67 cases of other pathological types.

The patients were divided into two groups: 367 in the routine disinfection group and 635 in the multiple disinfection group, as shown in Table 1. From January 2016 to December 2018, we performed transnasal endoscopic skull base surgery using a gauge disinfection method. The nasal cavity was disinfected with complex iodine solution only before the procedure, and no intraoperative disinfection was performed. From January 2019, the multiple disinfection group received an improved disinfection method. In addition to regular disinfection, the nasal cavity was disinfected with complex iodine after nasal mucosa contraction with epinephrine cotton pads. The operative area was then disinfected again at the sphenoid sinus stage and when exposing the dura of the skull base.Postoperative intracranial infections were recorded and diagnosed based on the following criteria: ① The patient exhibits unexplained fever, intracranial hypertension, and meningeal irritation symptoms; ② Routine cerebrospinal fluid (CSF) examination shows turbid appearance, protein concentration > 2,200 mg/L, white blood cell count > 10 × 10^6/L, glucose < 2.2 mmol/L, or cerebrospinal fluid glucose/serum glucose ratio ≤ 0.4. ③ A positive microbiological culture from specimen smears, drainage tube tips,

Table 1 Patient characteristics according to the disinfection methods

	Regular disinfection	Multiple disinfection	Total
Sex			
Man	196	287	483
Feman	171	248	519
Age	47.31 ± 13.51	44.64 ± 15.88	45.62 ± 15.11
Pathological type			
Pituitary tumor	210	403	613
Craniopharyngioma	50	88	138
Meningioma	38	36	74
Lacrimal cyst	19	34	53
Chordoma	8	29	37
Nerve sheath tumor	9	11	20
Others	33	34	67

implants, or cerebrospinal fluid. Intracranial infection is confirmed when clinical symptoms were supported by significant chemical and microbiological evidence of bacterial presence in the CSF.

Simultaneously, we conducted intraoperative bacteriological surveillance on some patients who underwent multiple sterilizations and collected bacteriological specimens at various stages of the operation. The sampling process was as follows: before routine nasal complex iodine disinfection, a sterile pharyngeal swab was rotated in the patient's nasal vestibule for sampling. After mucosal contraction and nasal cavity disinfection with complex iodine, a sterile cerebral cotton wool piece was used for sampling in the nasal vestibule. After entering the sphenoid sinus cavity, mucous membranes were sampled. The dura mater at the skull base was exposed, disinfected with iodine, and sampled before and after disinfection. Before rinsing the cavity with saline, an intracranial cotton swab was used for examination. The obtained specimens were subjected to general bacteriological culture, isolation culture, and drug sensitivity tests using a fully automated bacterial identification and drug sensitivity analyzer (VITEK2-compact).

Statistical analysis

The incidence of intracranial infections and bacterial detection rates before and after each stage of two sterilization methods were assessed using the chi-square test or Fisher's exact test. Differences were considered statistically significant when $P < 0.05$. All statistical analyses were conducted using SPSS 24.0.

Result

Intracranial infections under different sterilization methods

Twenty-one (5.72%) of the 367 patients who underwent routine sterilization developed postoperative intracranial infections with a definite pathogenic diagnosis. Fourteen (2.20%) of the 635 patients who underwent TESBS after multiple sterilizations developed postoperative intracranial infections with a definite pathogenic diagnosis, including one patient under bacteriological surveillance. Table 2 shows the distribution of pathogenic bacteria in intracranial infections, indicating the presence of different pathogenic bacteria cultured from the same patient.

Since CSF leakage is a significant risk factor for intracranial infection, we stratified 1002 TESES patients based on the presence of intraoperative CSF leak. These were then divided into two subgroups according to the disinfection methods for statistical analysis. The results showed no significant difference in intracranial infections between the two disinfection methods for patients without intraoperative CSF leak (Fisher's exact test, $P > 0.05$). For patients with intraoperative CSF leak, the rate of intracranial infections was lower in the multiple disinfection group (3.82%) compared to the conventional disinfection group (8.93%, $\chi^2 = 6.664$, $P < 0.05$). For detailed data, see Table 3.

Table 2 Distribution of pathogenic bacteria for intracranial infections

Bacterial type	Disinfection methods	
	Regular disinfection	Multiple disinfection
Gram-positive bacteria	**12**	**1**
Staphylococcus epidermidis	4	
Staphylococcus auricularis	2	
Staphylococcus haemolyticus	1	
Staphylococcus sciuri	1	
Staphylococcus aureus	1	
Streptococcus viridans	1	1
Enterococcus faecalis	1	
Others	1	
Gram-negative bacteria	**11**	**14**
Acinetobacter baumannii		6
Klebsiella pneumoniae	2	2
Escherichia coli	2	
Serratia marcescens	1	
Pseudomonas fluorescens	1	
Indole-positive Proteus	1	
Stenotrophomonas maltophilia	1	1
Pasteurella multocida	1	
Enterobacter aerogenes	1	3
Klebsiella oxytoca		1
Others	1	1
Total	23	15

Bacteriological surveillance

Nasal swabs from 59 (61.46%) of the 96 patients who underwent multiple nasal disinfection were cultured 66 strains of bacteria. After constricting the nasal passages and subsequent nasal disinfection, 12 strains of bacteria were cultured from 11 patients (11.46%) in epinephrine cotton swabs. Bacteriological specimens from the mucosal tissue of the sphenoid sinus before disinfecting the sphenoid sinus cavities in 18 patients (18.75%) were cultured 18 strains of bacteria. 20 strains were cultured from bacteriological specimens, and 6 strains were cultured after sphenoid sinus sterilization in 5 patients (5.21%). The distribution of bacteria is shown in Table 4.

Table 3 Incidence of Intracranial Infection in TESES Patients with and without CSF leak

CSF leak	Sterilization method	Intracranial infection		Total	$\chi 2$	*P*
		(-)	(+)			
No	Regular disinfection	142	1	143	Fisher's exact test	0.347
	Multiple disinfection	269	0	269		
Yes	Regular disinfection	204	20	224	6.664	0.010
	Multiple disinfection	352	14	366		
	Total	967	35	1002		

Table 4 Distribution of bacterial colonies in patients undergoing multiple disinfection

Bacterial type	Nasal disinfection		Sphenoid sinus disinfection	
	Before	After	Before	After
Gram-positive bacteria	**39**	**3**	**11**	**3**
Staphylococcus epidermidis	17		9	2
Staphylococcus aureus	6	3	1	1
Streptococcus pneumoniae	2			
Corynebacterium pseudodiphtheriticum	2			
Corynebacterium jeikeium	2			
Other Gram-positive cocci	5		1	
Other Gram-positive bacilli	5			
Gram-negative bacteria	**27**	**9**	**9**	**3**
Enterobacter aerogenes	8	2	5	1
Klebsiella pneumoniae	6	3	2	
Haemophilus influenzae	2			
Klebsiella oxytoca	1		1	
Klebsiella variicola	1	1	1	1
Citrobacter koseri	1			1
Moraxella catarrhalis	1			
Other Gram-negative bacilli	6	3		
Total	66	12	20	6

In some specimens, there are cases where both Gram-positive and Gram-negative bacteria are simultaneously cultured.

We analyzed the bacterial detection rate before and after disinfection. The positive rate of nasal colonization bacteria detection significantly decreased after two nasal disinfections ($\chi^2 = 51.8$, $P < 0.05$), though some patients (11/96) still had detectable bacteria. After the sphenoid sinus disinfection stage, the colonization rate in the operative area decreased further ($\chi^2 = 14.66$, $P < 0.05$). For detailed data, see Table 5.

Discussion

Since 1992, when French otorhinolaryngology and head and neck surgeons, such as Dr. Jankowski et al. [5, 12], first reported transnasal endoscopic resection of pituitary tumors, endoscopic skull base surgery has continuously advanced, becoming a key technique in skull base surgery [6, 17, 18]. However, because transnasal endoscopic skull base surgery passes through bacteria-rich areas such as the nasal cavity and sphenoid sinus, the risk of postoperative infection increases significantly. If an infection occurs, it can severely affect patient outcomes and even result in death [24]. To reduce the incidence of postoperative intracranial infections following this surgery, we conducted bacterial monitoring on a subset of patients. The findings showed that most postoperative pathogens were detectable in the nasal cavity. Additionally, our use of multiple rounds of disinfection effectively reduced the bacterial detection rate along the surgical pathway. For patients who experienced intraoperative cerebrospinal fluid leakage, those who underwent multiple disinfections also had a lower rate of intracranial infection.

Table 5 Comparison of bacterial culture results before and after sinus disinfection

Disinfection stage		Culture results (%)		$\chi 2$	*P*
		(+)	(-)		
Nasal disinfection	Before	59(61.5)	37(38.5)	51.8	< 0.05
	After	11 (11.5)	85 (88.5)		
Sphenoid sinus disinfection	Before	18 (18.75)	78 (81.25)	14.66	< 0.05
	After	5 (5.21)	91 (94.79)		

Changes in nasal cavity colonizing bacteria after multiple sterilizations

Among the patients who underwent bacteriological monitoring in this study, 66 strains of colonizing bacteria were detected in 59 cases before nasal disinfection. After nasal disinfections two times, only 12 strains were detected in 11 patients, resulting in an 81.36% inactivation rate of nasal colonization. These results were consistent weith the fingdings reported by Xiaohai Liu et al. [16]. Overall, using complex iodine to disinfect the nasal cavity was effective but could not completely eliminate the colonized bacteria. This may be related to the inability of povidone-iodine to completely eliminate all bacteria, as well as the fact that the nasal passage is directly or indirectly connected to the external environment, various paranasal sinuses, and the pharyngeal region. Bacteria were cultured in 18 patients from specimens obtained after entering the sphenoid sinus and before sterilization, an increase from 11 patients in the post-nasal sterilization phase. Consistent with the findings reported by Shibao et al. [22], there was no statistical difference. We speculate this is due to the small sample size and the difference in bacteria colonizing the sphenoid sinus versus the nasal cavity. Nasal complex iodine disinfection alone may not effectively kill bacteria in the sphenoid sinus, possibly due to the physiological structure preventing adequate iodine entry into the sphenoid sinus cavity during nasal disinfection. This also indicates the necessity of re-sterilizing the sphenoid sinus cavity. After re-sterilizing the sphenoid sinus cavity, six strains of bacteria were detected in five patients. One of these patients developed an postoperative intracranial infection, and the pathogenic bacteria were the same as the colonizing bacteria detected in sphenoid sinus cavity. Statistical analysis showed a significant difference in the positive rate of bacterial detection before and after sphenoid sinus disinfection, indicating that complex iodine disinfection of the sphenoid sinus cavity was effective.

In summary, repeated disinfection can kill most colonizing bacteria in the nasal cavity, but bacteria may still be present in the operative area. These bacteria may come from areas that were not fully eradicated by disinfection, surgical instruments and materials that frequently enter and exit the nasal cavity, and the hands of the surgeon and instrumentation nurses. Intraoperative measures such as changing gloves before opening the skull base dura mater and sterilizing surgical instruments that need to be reused can reduce potential contamination [10]. Prophylactic antibiotics are necessary to minimize the risk of intracranial infections caused by these bacteria. For patients at high risk of postoperative intracranial infections, intraoperative samples should be collected and sent for testing. This will guide the treatment of subsequent intracranial infections caused by nasal colonization and help improve the prognosis of intracranial infections in patients.

Relationship between pathogenic bacteria in intracranial infections and nasal colonizing bacteria

The common pathogens reported for postoperative intracranial infections in TESBS patients include Staphylococcus epidermidis, Staphylococcus aureus, Klebsiella pneumoniae, Acinetobacter baumannii, Pseudomonas aeruginosa, Haemophilus influenzae, and Enterobacter aerogenes, with gram-negative bacteria being more prevalent [11, 15]. It remains controversial whether intracranial infections are predominantly caused by gram-negative bacteria [15]. In this study, 38 strains of pathogenic bacteria were isolated from the CSF of 35 patients with intracranial infections. Most were gram-negative bacteria (65.79%), primarily Acinetobacter baumannii (6 strains), Klebsiella pneumoniae (4 strains), Enterobacter aerogenes (4 strains), and Staphylococcus epidermidis (4 strains), consistent with literature reports.

Bacteriologic surveillance of 96 patients in this study revealed that common nasal colonizing bacteria included Staphylococcus epidermidis, Staphylococcus aureus, Enterobacter aerogenes, Klebsiella pneumoniae, and Corynebacterium spp. This aligns with the literature on nasal colonizing bacteria in the general population [3, 16]. One patient developed an intracranial infection, with pathogenic bacteria matching those in the nasal cavity. Comparing intracranial infection pathogens with nasal colonizing bacteria showed that most pathogens were detected in the nasal cavity, but some, notably Acinetobacter baumannii, were not. A. baumannii is a major pathogen in ICU patients, causing lung infections, meningitis, bloodstream infections, and urinary tract infections, with a high rate of multidrug resistance [4, 13]. Intracranial infections from undetected nasal pathogens may result from decreased postoperative immunity or invasive procedures like central line placement or lumbar drainage, allowing bacteria to enter the bloodstream and brain. Thus, most postoperative intracranial infections after TESBS originate from nasal colonizing bacteria, though some are hospital-acquired.

Effect of two sterilization methods on the rate of postoperative intracranial infection

This study compared intracranial infections between two sterilization methods. Results showed the overall intracranial infection rate decreased from 5.72% (21/367) to 2.20% (14/635) after adopting multiple sterilizations. A significant difference was noted in infection rates among patients with intraoperative CSF leak under the two sterilization methods.

This suggests that intraoperative CSF leak is a major risk factor for intracranial infection, consistent with literature findings. Grouping patients by presence of intraoperative CSF leak, results showed only one intracranial infection case in patients without CSF leak under routine sterilization, with no significant difference in infection rates between the two methods. In contrast, among patients with intraoperative CSF leak, the infection rate was 8.93% (20/224) with routine disinfection and 3.83% (14/366) with multiple disinfection (Table 1). Therefore, for TESBS patients, especially those at risk for intraoperative CSF leak, multiple and thorough disinfection during surgery can help reduce postoperative intracranial infection rates. Furthermore, preventing postoperative CSF leakage and ensuring meticulous closure of osteo-dural defects play a vital role in minimizing intracranial infection rates.

The pathogens of postoperative intracranial infections differed between the two disinfection methods. The proportion of gram-positive and gram-negative bacteria was similar in the routine disinfection group, whereas gram-negative bacteria dominated in the multiple disinfection group, as shown in Table 2. Hospital-acquired infections are typically caused by gram-negative bacteria [1, 8, 14].It is hypothesized that multiple disinfection may reduce intracranial infections caused by nasal colonization, resulting in gram-negative bacteria predominance in the multiple disinfection group. Therefore, prophylactic antibiotics targeting gram-negative bacteria should be considered for TESBS patients undergoing multiple disinfections to reduce postoperative intracranial infection rates.

While our findings demonstrate a significant reduction in intracranial infection rates, we fully acknowledge the concerning trend of increasing multidrug resistance among pathogens. This is a critical issue that merits further investigation. Although our multiple disinfection technique has demonstrated efficacy to a certain degree, it remains imperative to investigate alternative or advanced disinfection strategies to further mitigate the risk of infections caused by multidrug-resistant pathogens.

Limitations

This study was conducted at a single center and did not include patients with TESBS from other centers, resulting in selection bias. The small number of cases for bacteriological monitoring and the potential for false-negative results in retained samples limit the precise analysis of bacterial profile changes at different stages of the operation. Reducing the rate of postoperative intracranial infections in patients with TESBS is a complex issue. We have observed a decreasing trend in overall intracranial infection rates through continuous improvements in preoperative assessment, disinfection, intraoperative skull base reconstruction, and postoperative management. However, this study focuses only on disinfection methods, presenting certain limitations.

Conclusions

Most pathogenic bacteria causing postoperative intracranial infections in patients with TESBS originate from nasal colonization. Retaining intraoperative samples for examination guides the treatment of these infections. Multiple intraoperative disinfections can eliminate most colonizing bacteria in the nasal cavity and sphenoid sinus, effectively reducing postoperative intracranial infections in patients with high risk factors for CSF leak.

Author contributions D.C. wrote the main manuscript text. Y.S., D.S., J.W., S.X., and H.L. assisted with data collection and figure preparation. B.T. supervised, reviewed and revised the paper, and provided necessary funding for the research. All authors reviewed the manuscript in the end.

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Data availability No datasets were generated or analysed during the current study.

Declarations

Human ethics and consent to participate All procedures performed in studies involving human participants were in accordance with the ethical standards of the First Affiliated Hospital of Nanchang University,and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Informed consent Informed consent was obtained from all individual participants included in the study.

Conflict of interest The authors declare no competing interests.

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