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## Case study

# Antibiotic prophylaxis and infection prevention for endoscopic endonasal skull base surgery: Our protocol, results, and review of the literature

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## ABSTRACT

Endoscopic endonasal approaches to the skull base provide minimally invasive corridors to intracranial lesions; however, enthusiasm for this new approach is always tempered by the recognition that this route requires passage through a nonsterile sinonasal corridor. Despite an increasing number of patients undergoing these surgeries, there remains no consensus on the use of perioperative antibiotics. A retrospective review of consecutive patients undergoing endoscopic endonasal skull base surgery (EESBS) at Loyola University Medical Center by the same neurosurgeon and otolaryngologist team between February 2015 and October 2016 was performed. Antibiotic regimens, presence of an intraoperative or postoperative cerebrospinal fluid (CSF) leak, dural reconstruction method, and rates of sinusitis, meningitis, and/or intracranial abscess were analyzed. 39 patients who underwent a total of 41 EESBSs with a mean age of 46 years were identified. A vascularized nasoseptal flap was used for dural reconstruction when high flow CSF leaks were encountered intraoperatively ( $n = 17$ ); otherwise, reconstruction mostly consisted of allografts and/or free mucosal grafts. There were zero postoperative cases of CSF leaks, meningitis, or intracranial infection. Our current antibiotic prophylaxis protocol coupled with the use of variable dural reconstruction techniques dictated by intraoperative findings has led to low rates of postoperative CSF leaks, intracranial infections, and meningitis. A survey was also distributed to Neurological Surgery Residency Programs to gain a better understanding of the EESBS protocols that are being used nationally. The practice of antibiotic prophylaxis for patients undergoing EESBS is quite variable and this study should provide the impetus for multi-institutional comparison studies.

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## 1. Introduction

With the evolution of endoscopic endonasal skull base surgery (EESBS), a team approach involving a neurosurgeon and an otolaryngologist has become a safe and efficient method for performing these surgeries. Endoscopic endonasal approaches to the skull base provide minimally invasive corridors to intracranial lesions. Since the approach corridor passes through nonsterile sinonasal cavities, there has been concern over the potential high risk of intracranial infection. While the concern is merited, the risk of

infection has been shown to be comparable to that of an open craniotomy. Documented occurrences of meningitis after transsphenoidal surgery have ranged from 0.7% to 3.1% [1,2] compared to approximately 1.52% for open craniotomies [3]. A more recent large population review has demonstrated a postoperative infection incidence of 1.8% in EESBS [4].

There has been extensive research in EESBS on the role of prophylactic antibiotics in preventing postoperative infections. Several studies have analyzed the duration of antibiotic prophylaxis, showing the most effective time period for their administration [5]. Other reports have looked into determining the best preventative antibiotics by analyzing the most common pathogens causing postoperative intracranial infections [3,4]. Some of these studies have even demonstrated the superiority of prophylactic antibiotic regimens in infection prevention [5,6]. Despite this research, there

Abbreviations: CSF, cerebrospinal fluid; EESBS, endoscopic endonasal skull base surgery; NSF, nasoseptal flap.

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is currently no universally accepted antibiotic prophylaxis protocol among treating surgeons for preventing infection in EESBS.

Prior research has also focused on the potential risk factors for infection and ways to reduce them in EESBS. Previous studies have shown that postoperative cerebrospinal fluid (CSF) leak following EESBS is an important risk factor for postoperative meningitis [7], providing the impetus to make CSF leak prevention a focused goal during surgery for decreasing postoperative infections. The use of a vascularized nasoseptal flap (NSF) by treating surgeons has significantly reduced the incidence of postoperative CSF leak, and therefore has likely reduced the risk of infection from these approaches.

## 2. Methods

A retrospective review of consecutive patients undergoing EESBS at Loyola University Medical Center by the same neurosurgeon and otolaryngologist between February 2015 and October 2016 was performed. Antibiotic regimens, patient demographics, reason for surgery, presence of an intraoperative or postoperative CSF leak, dural reconstruction method, and rates of sinusitis, meningitis, and/or intracranial abscess were analyzed.

A ten-question survey was also distributed to several Neurological Surgery Residency Programs across the United States to gain a better understanding of the EESBS protocols that are being used nationally. The survey included questions regarding the number of postoperative intracranial infections, infections associated with CSF leaks, dural reconstruction techniques, rate of nasoseptal flap use, and prophylactic antibiotic protocols (Table 1).

## 3. Results

39 patients (25 female) who underwent a total of 41 EESBSs with a mean age of 46 years (range 8–79 years) were identified. The most common pathologies treated were pituitary adenomas ( $n = 15$ , 38.5%), spontaneous CSF leaks ( $n = 11$ , 28.2%), and skull base meningiomas ( $n = 3$ , 7.7%). All patients received intravenous ceftriaxone perioperatively (2 g) and this was continued at a meningitis prophylaxis dose (2 g BID) until discharge (mean 5 days, range 2–14 days). A vascularized nasoseptal flap was used for dural reconstruction when high flow CSF leaks were encountered intraoperatively ( $n = 17$ ); otherwise, reconstruction mostly consisted of allografts and/or free mucosal grafts ( $n = 19$ ). Patients were discharged on oral Augmentin (Amoxicillin-Clavulanic acid) or Keflex (Cephalexin) until nasal packing was removed which averaged 7 days after surgery. There were zero postoperative cases of CSF leaks, meningitis, or intracranial infection. 4 patients (10.2%) had postoperative sinusitis that required a course of oral antibiotics for 10–14 days without any further clinical sequelae.

### 3.1. Survey results

Our survey results are displayed in Table 1. A total of 10 institutions responded. There is significant variability in responses, substantiating the lack of any universally agreed upon protocol.

## 4. Discussion

### 4.1. Risk factors

EESBS has many surgical advantages due to the minimally invasive and direct access it provides to intracranial lesions with little to no brain or neurovascular manipulation. Because of the communication between the sinonasal and intracranial cavities, there initially was a reasonable concern for a higher risk of postoperative infections compared to open craniotomies. Several smaller EESBS

studies have shown a postoperative intracranial infection incidence of 0–1.9% [8–10]. Kono et al. studied 1000 patients undergoing endoscopic endonasal procedures with prophylactic antibiotics and demonstrated an infection incidence of 1.8%, comparable to that of clean open craniotomies and traditional microscopic transsphenoidal surgery [4]. While the postoperative infection rate in EESBS has been shown to be similar to open craniotomies, there have been continued efforts to determine the best approach to further decrease infection rates.

Understanding the risk factors for infection in EESBS is integral to lowering the intracranial infection rate. Postoperative CSF leak has been shown to be a strong risk factor for infection due to the continued exposure of the intracranial space to bacteria. The incidence of a postoperative CSF leak following skull base surgery has ranged from 13% to 29% [11] and the incidence of meningitis in patients with a postoperative CSF leak was shown to be 28.5% [8] and 28.4% [3] in two separate studies. In the study by Kono et al., 13 of the 18 patients who developed postoperative meningitis also had a postoperative CSF leak [4]. Horowitz et al. found that the meningitis risk in skull base patients who experienced a postoperative CSF leak was 66%, compared to a 4.5% risk of meningitis in those without a postoperative CSF leak [7], leading to the overall relative risk of meningitis in patients with a postoperative CSF leak being 14.6.

### 4.2. Dural reconstruction

Since the risk of meningitis and intracranial infection is strongly influenced by the incidence of postoperative CSF leaks, preventing leaks by robust dural reconstruction is important (Fig. 1). With the evolution of skull base surgery, the use of a neurovascular pedicled nasoseptal flap (NSF), also known as the Hadad-Bassagasteguy Flap (HBF), was introduced in 2006 [12]. This flap reconstruction began to gain favor among neurosurgeons in EESBS [13,14]. Several studies found that postoperative CSF leak and intracranial infection rates dropped significantly after a vascularized NSF was used for reconstruction [15]. Kassam et al. found that their CSF leak rate decreased from 58% to 5.56% once the HBF was implemented [10]. Ivan et al. noted a CSF leak rate reduction from 33% to 9% through use of a nasoseptal flap, free flap, or vascularized muscle flap [16]. Kono et al. also began using the pedicled nasoseptal flap for dural reconstruction and noted that the infection rates among their most complicated EESBS cases dropped from 11.5% to 2.4% [4]. A vascularized nasoseptal flap is not always necessary for dural reconstruction. This type of flap is a good option for large dural defects with active CSF leaks; however, for smaller defects with low flow leaks, an avascular or mucosal graft is a reasonable option in order to avoid the small but present morbidity of a NSF such as epistaxis, chronic nasal crusting, and increased risk of olfactory dysfunction [13,17].

We determine our skull base dural reconstruction based on intraoperative findings [18]. Entry into a large CSF cistern or ventricle signifies a high flow leak. A water tight multilayer reconstruction with a vascularized nasoseptal flap, when available, is used when a high flow CSF leak is encountered. Avascular grafts, such as a collagen allograft, acellular human dermal matrix, and/or free mucosal graft, is used in the intraoperative setting of no leak or a very low flow CSF leak. We believe adequate reconstruction is imperative and is dictated by intraoperative findings. This reconstruction protocol has led to low observed rates of postoperative CSF leak, meningitis, and intracranial abscess.

### 4.3. Antibiotic importance

With the understanding of EESBS risk factors and effective means of prevention, the importance of antibiotic prophylaxis in

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