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What is the risk of meningitis, utilising a single agent, single dose perioperative antibiotic following endonasal endoscopic repair of a CSF leak?

Author: Paul Nix BM BCH MD FRCS(ORL-HNS)

Department of ENT, Leeds

Correspondence

Mr Paul Nix

Department of Otorhinolaryngology

Leeds Teaching Hospitals NHS Trust

Great George Street

Leeds LS1 3EX

Email Paulnix@nhs.net

Abstract

Introduction

Endoscopic endonasal surgery of the skull base carries the risk of meningitis. However no consensus on the prophylactic antibiotic regimen exists.

Methods

Review of a prospectively held data base documenting endoscopic endonasal repair of CSF leaks in the anterior skull base. Post operative meningitis and antibiotic usage within 30 days of the index procedure were recorded.

Results

285 consecutive case were identified with a post operative meningitis rate of 3.5%. The post operative confirmed bacterial meningitis rate was 2%. All cases received a single dose of a single agent antibiotic perioperatively.

The risk of developing post operative meningitis was associated with a post operative CSF leak in cases undergoing tumour resection of the anterior skull base.

Conclusion

A single dose, single agent perioperative antibiotic regimen would appear to be adequate following an endoscopic endonasal approach to repair a CSF leak in the anterior skull base.

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What is the risk of meningitis, utilising a single agent, single dose perioperative antibiotic following endonasal endoscopic repair of a CSF leak?

Introduction

CSF leaks from the anterior skull base have traditionally occurred due to trauma or spontaneous leaks through a weakened anterior skull base. With the advent of the Hopkins rod, endoscopic endonasal surgery has now become the predominant cause of an anterior skull base CSF leak[1]. Over the last 30 years the endonasal corridor has been used to repair spontaneous and traumatic leaks and access more intracranial pathology such as meningiomas and craniopharyngiomas that are based on the anterior central skull base. As such the number of CSF leaks requiring repair has significantly increased over the years. Just as CSF leaks into the sinonasal cavity, a conduit exists for ascending infection and meningitis. Closure of a CSF leak is essential to prevent the patient developing meningitis.

While the endoscopic endonasal approach provides a direct corridor to the central component of the anterior skull base, access occurs through the paranasal sinuses. Unlike other areas of surgery, where the incision site undergoes antiseptic preparation, this is difficult with the honeycomb nature of paranasal sinuses. In order to reduce the risk of a post operative infection, antibiotics are employed in the pre and post operative period. At present no consensus on the length of antibiotic treatment exists. Prolonged prophylactic antibiotic courses have the propensity to create more issues with antibiotic resistance.

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Materials and Methods

A prospectively maintained database of all endonasal CSF repairs performed at Leeds Teaching Hospitals between 2009 and 2023 was used to identify patients.

The database was retrospectively reviewed to identify all patients undergoing an endonasal endoscopic repair of an anterior skull base CSF leak by the author. The patient's electronic hospital record was identified and searched for evidence of post operative meningitis or antibiotic usage within 30 of the operative repair.

The prospectively maintained data base identified the type of CSF leak with regards to location, high or low flow leak and the type of repair. A high flow leak was defined as a CSF leak encompassing a CSF void such as a cistern or ventricle .

A diagnosis of meningitis was based upon positive CSF cultures following the repair or a clinical presumption of post operative meningitis with antibiotic therapy if CSF cultures results were not available.

Data on the reason for the CSF repair, type of perioperative nasal preparation, repair type, CSF culture results, perioperative antibiotic administration, post operative antibiotic prescription were collected.

Fishers Exact test, at a significance of 0.05, was used to compare groups.

Results and Analysis

From the prospectively maintained database, 297 consecutive cases requiring an endoscopic endonasal repair of the anterior skull base were identified, of which 285 were performed by

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the author. Health records detailing post operative care and follow up were available for all cases. All cases received a single dose of a single agent perioperative antibiotic. Patients received 1.2g of Augmentin, unless they were penicillin allergic where Teicoplanin was used.

There was no specific perioperative nasal decontamination in any case. The Endoscopic repair varied depending upon the location and size of the defect in the anterior skull base. The repair in general consisted of an inlay graft, Duragen® or Spongostan™ or fascia lata with a cartilage or Medpor® support for larger defects and an on lay pedicle nasoseptal graft. For small defects a fat plug was utilised. The graft was glued in place using Tisseel® and supported by a small 4cm dissolvable Nasopore® nasal pack. The nasal cavity itself was not formally packed. Lumbar drains to cover the repair were not used.

Of the 285 patients:

In total 10 patients developed presumed post operative meningitis out of the 285 consecutive cohort (3.5%). Bacterial meningitis was confirmed from CSF cultures in 6 cases, equating to a 2% post operative bacterial meningitis rate.

32 patients underwent a repair for a spontaneous anterior skull base CSF leak with no post operative meningitis. Leaks were classified as low flow.

4 patients underwent a repair following trauma to the anterior skull base with no post operative meningitis. Leaks were classified as low flow.

102 patients underwent a repair of a low flow leak identified during skull base surgery, of which 1 patient developed post operative meningitis

147 patients underwent a repair of a high flow leak, of which 9 developed post operative meningitis,(p=0.0214). This cohort of patients included resection of skull base meningiomas,

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craniopharyngiomas, chordomas, olfactory neuroblastomas, skull base tumours and meningoencephaloceles.

Of the 10 patients with presumptive meningitis, positive CSF cultures were obtained for 6 patients. 3 patients had no growth on CSF cultures and 1 patient was treated for presumed meningitis without any CSF cultures. Cultures grew: Ecoli x2, Proteus, Klebsiella, Enterobacteria Aerogenes and Cutibacterium Acnes bacteria.

A post operative CSF leak occurred in 24 of the 285 patients (8.4%). Of the 10 patients that developed meningitis 9 were in the post operative leak group, ($p<0.00001$).

2 of the patients had resection of a clival chordoma, 3 for a craniopharyngioma, 2 for a meningioma, 1 for a macroadenoma and 2 for recurrent large macroadenomas following radiotherapy.

Discussion

Antibiotic resistant pathogens present a significant threat in modern medicine making current antibiotics less effective[2] . As such, antibiotic stewardship is essential as global resistance continues to rise.

At present there is limited evidence based data available evaluating antibiotic usage in patients undergoing anterior skull base surgery involving closure of a CSF leak. Indeed there is a significant variation in practice for the use of perioperative and post operative antibiotics in anterior skull base surgery as documented in a survey of the North American Skull Base Society[3]

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A met-analysis study, published in 2023, regarding antibiotic prophylaxis for endoscopic endonasal skull base tumour surgery demonstrated similar conclusions regarding antibiotic usage. Regimes varied from 2 doses of a single agent to more commonly prolonged post operative courses up to 5 days with the use of more than 1 agent[4].

The endoscopic endonasal approach, through the paranasal sinuses, provides a direct corridor to the central component of the anterior skull base. It is classed as clean contaminated surgery. Unfortunately the honeycomb nature of the sinuses attached to the undersurface of the skull base presents a significant issue for antiseptic preparation. In contrast to traditional surgery, where by the surgical field undergoes antiseptic preparation before the skin is incised, this is really impossible to achieve within the nasal cavity. As the endonasal instruments pass in and out of the nostrils all the sterile surgical instruments eventually become contaminated. These instruments continually pass through the non-sterile endonasal corridor and beyond the dura during the operation. When repairing the anterior skull base defect, graft material will also pass through this non sterile corridor before being placed beyond the dura to effect a CSF repair.

It is therefore not surprising that meningitis can occur following such procedures and that surgeons prescribe prophylactic antibiotics in order to reduce the risk of this serious complication. In searching the literature it is easy to find the overall post operative meningitis rate for endoscopic endonasal anterior skull base surgery, but this overall figure can be misleading. In 1 meta analysis, published in 2020, of 2275 cases a post operative meningitis rate of 1.6% was recorded[5]. However such data combines cases where intraoperative CSF was evident, with surgery where no CSF was encountered and the vast majority of the patients are in the latter group. One would assume that the risk of meningitis would be

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significantly increased in the presence of active CSF leak into the nasal cavity at the time of the operation. In 1 systematic review the post operative meningitis rate following anterior skull base surgery involving CSF was however 13%[6] .

In this current series all repairs were caried out by one surgeon affording some uniformity to surgical technique and post operative care.

At present no consensus exists on the type of repair that should occur in anterior skull base surgery whether CSF is observed intraoperatively or not. This was highlighted in a recent national prospective observational study in the UK[7].

None of the cases in the current study underwent any formal perioperative decontamination of the nasal cavity before the start of surgery. All patients had a single dose, single agent perioperative antibiotic. This is in contrast to most reported studies utilising multiple doses in the post operative period. Augmentin was chosen as the perioperative antibiotic of choice as it probably has the best cover for nasal and sinus bacteria[8]. If the patient has a penicillin allergy then Teicoplanin has been used.

In addition at the end of the surgical procedure all patients have had a small dissolvable nasal pack placed over the repair site, specifically to hold any on lay pedicle grafts in place. Lumbar drains at the time of the repair were not used even if the CSF defect was deemed to be high flow.

The exact type or repair depended upon the defect size and if the CSF flow was deemed to be high or low flow. In general spontaneous low flow leaks have been repaired by a fat plug technique with an on lay free mucosal graft[9]. Defects involving high flow CSF leaks involved

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an inlay graft with underlay support or a gasket type seal if an inlay graft was not possible followed by an on lay pedicled nasoseptal flap[10].

Post operatively patients were advised to use saline nasal rinses twice daily for one month.

In identifying cases of post operative meningitis the patients electronic records and microbiology results were searched for a minimum of 60 days post procedure. In addition all letters pertaining to the procedure were also reviewed to the limit of the electronic record in order to capture any patient that may have developed meningitis and had been admitted to another hospital. Meningitis was defined as having positive culture results or being treated for suspected meningitis. Adopting this wide definition of meningitis without having to have positive culture results may have resulted in overestimated of the rate of post operative meningitis in this current series.

Overall 10 of the 285 patients were treated for suspected meningitis in the post operative period, (3.5%). Of the 6 patients with positive culture results this equates to a 2% post operative bacterial meningitis rate following the repair of a CSF leak in the anterior skull base, utilising a single dose of an antibiotic in the perioperative period. The small number of positive cultures grew diverse organisms allowing no inferences to be made about this.

This rate of post operative meningitis compares favourably with the reported literature, especially in the context of a single agent single dose antibiotic. Kong et al report a 17.4% post operative meningitis rate in 46 patients following repair of a skull base defect with patients receiving a 5 day post operative course of antibiotics[11]. Ivan et al report a 13% meningitis rate cased upon 75 cases[12]. Conger et al report a 2.1% post operative bacterial meningitis rate in 284 patients receiving a 24 hour to 5 day post operative antibiotic course[13].

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Of the 10 patients in this series only 6 had CSF cultures drawn from a lumbar puncture that grew organisms. 3 patients had no growth following CSF cultures and 1 patient did not have a CSF sample taken for culture. Of the 3 patients with no growth, 2 of the patients had resection of a craniopharyngioma and may have developed a chemical meningitis, due to dispersion of the craniopharyngioma contents during resection.

It is noteworthy that 9 of the 10 patients that developed a post operative meningitis had undergone resections of skull base tumours, meningiomas, craniopharyngioma and chordomas and had developed a post operative CSF leak. This reached significance with a Fishers Exact test. As such developing a CSF leak following a repair of the anterior skull base endoscopically is the most significant risk factor for post operative meningitis, an observation previously documented[14]. In contrast no cases of post operative meningitis were observed following repair of a spontaneous or traumatic anterior skull base CSF leak.

Limitations

While being one of the largest studies reporting on meningitis rates following CSF repair of the anterior skull base, this study is still limited by the overall numbers and lack of a comparison group. In this cohort study, potential confounding variables exist but study numbers do not allow any meaningful analysis. In particular the type of skull base repair varies depending upon the defect, with both autologous and synthetic repair materials being used in the repair. Patients' comorbidities such as diabetes, Cushing's disease or chronic rhinosinusitis may also have an effect on post operative infection rates. In addition this data set spans a 15 year period which may encompass a surgical learning curve of the surgeon.

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Summary

- Consensus on Prophylactic antibiotic usage in endoscopic anterior skull base surgery does not exist.
- Meningitis is a serious complication following anterior skull base surgery.
- Single dose single agent antibiotic prophylaxis is an effective regime for endoscopic endonasal skull base surgery involving CSF repairs with bacterial meningitis rate of 2% and an overall meningitis rate of 3.5%.
- Post operative CSF leaks are the most significant risk factor for developing post operative meningitis.

Conclusion

In the era of increase in antibiotic resistance antibiotic stewardship needs to be considered. A single dose, single agent perioperative antibiotic regimen would appear to be adequate following an endoscopic endonasal approach to repair a CSF leak in the anterior skull base.

Post operative bacterial meningitis is just 2% with this single dose antibiotic regime comparable with the best reported rates from published studies utilising longer courses of prophylactic antibiotics.

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Competing Interests

The author declares none

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