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

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Abstract

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

Methods. A prospectively held database documenting endoscopic endonasal repair of cerebrospinal fluid (CSF) leaks in the anterior skull base was reviewed. Post-operative meningitis and antibiotic usage within 30 days of the index procedure were recorded.

Results. A total of 285 consecutive cases were identified with a post-operative meningitis rate of 3.5 per cent. The post-operative confirmed bacterial meningitis rate was 2 per cent. All cases received a single dose of a single agent antibiotic peri-operatively.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 peri-operative antibiotic regimen would appear to be adequate following an endoscopic endonasal approach to repair a CSF leak in the anterior skull base.

Main Article

Paul Nix takes responsibility for the integrity of the content of the paper

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Introduction

Cerebrospinal fluid (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 past 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.

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 database 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 peri-operative nasal preparation, repair type, CSF culture results, peri-operative antibiotic administration and 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 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 peri-operative antibiotic. Patients received 1.2 g of Augmentin, unless they were penicillin allergic where Teicoplanin was used.

There was no specific peri-operative 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 onlay pedicle nasoseptal graft. For small defects a fat plug was utilised. The graft was glued in place using Tisseel® and supported by a small 4 cm 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 six cases, equating to a 2 per cent post operative bacterial meningitis rate. Thirty-two patients underwent a repair for a spontaneous anterior skull base CSF leak with no post operative meningitis; leaks were classified as low flow. Four patients underwent a repair following trauma to the anterior skull base with no post-operative meningitis; leaks were classified as low flow. One hundred and two patients underwent a repair of a low flow leak identified during skull base surgery, of which one patient developed post-operative meningitis. One hundred and forty-seven patients underwent a repair of a high flow leak, of which nine developed post operative meningitis ($p = 0.0214$). This cohort of patients included resection of skull base meningiomas, 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: *Escherichia coli* x2, *Proteus, Klebsiella*, *Enterobacter 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 ($p < 0.00001$).

Two of the patients had resection of a clival chordoma, three for a craniopharyngioma, two for a meningioma, one for a macroadenoma and two 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 peri-operative and post-operative antibiotics in anterior skull base surgery as documented in a survey of the North American Skull Base Society.[3]

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 two doses of a single agent to more commonly prolonged post-operative courses up to 5 days with the use of more than one 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 one meta analysis, published in 2020, of 2275 cases a post-operative meningitis rate of 1.6 per cent was recorded.[5] However, such data combine 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 significantly increased in the presence of active CSF leak into the nasal cavity at the time of the operation. In one systematic review, the post-operative meningitis rate following anterior skull base surgery involving CSF was however 13 per cent.[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 peri-operative decontamination of the nasal cavity before the start of surgery. All patients had a single dose, single agent peri-operative antibiotic. This is in contrast to most reported studies utilising multiple doses in the post-operative period. Augmentin was chosen as the peri-operative 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 onlay 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 onlay free mucosal graft.[9] Defects involving high flow CSF leaks involved an inlay graft with underlay

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support or a gasket type seal if an inlay graft was not possible followed by an onlay 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 overestimation 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 six patients with positive culture results, this equates to a 2 per cent 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 peri-operative 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 per cent 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 per cent meningitis rate cased upon 75 cases.[12] Conger *et al.* report a 2.1 per cent post-operative bacterial meningitis rate in 284 patients receiving a 24 hour to 5 day post-operative antibiotic course.[13]

Of the 10 patients in this series, only 6 had CSF cultures drawn from a lumbar puncture that grew organisms. Three patients had no growth following CSF cultures, and one patient did not have a CSF sample taken for culture. Of the three patients with no growth, two 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.

Conclusion

In the era of increase in antibiotic resistance, antibiotic stewardship needs to be considered. A single dose, single agent peri-operative 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 per cent 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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