



# Cerebrospinal Fluid Leakage During Transsphenoidal Surgery: Postoperative External Lumbar Drainage Reduces the Risk for Meningitis

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**Abstract.** Postoperative meningitis is a well known complication of transsphenoidal surgery (TSS). The objective of this study was to evaluate whether postoperative external cerebrospinal fluid (CSF) drainage in case of intraoperative CSF-leakage, reduces the risk of postoperative meningitis. We retrospectively reviewed a series of 278 consecutive transsphenoidal operations. In all operations with intraoperative CSF leakage, an external lumbar drain (ELD) was inserted directly postoperatively, and removed after at least 5 days.

The incidence of postoperative meningitis was compared with that in a previously studied series of 228 consecutive transsphenoidal operations, without insertion of an ELD in cases with intraoperative CSF leakage.

In the present series, postoperative meningitis occurred in 2/278 (0.7%) operations, compared to 7/228 (3.1%) operations in the previous study period ( $P < 0.05$ ). Intraoperative CSF leakage was noted in 70/278 (25.2%) operations. All these patients received an ELD immediately after surgery for at least 5 days. There were no reported complications of ELD insertion. In the present series, 1 of 70 (1.4%) patients with intraoperative CSF leakage developed meningitis, compared to 3 of 22 (13.6%) patients in the previous study ( $P < 0.05$ ).

The present report on 278 consecutive transsphenoidal operations shows that the routine insertion of an ELD in patients in whom intraoperative CSF leakage is observed significantly reduces the incidence of postoperative meningitis. Possibly, diversion of CSF prevents the formation of a CSF fistula and thereby the risk of infection. The role of prophylactic antibiotic treatment in patients with CSF rhinorrhea after TSS remains to be established.

**Key Words.** cerebrospinal, drainage, leakage, meningitis, transsphenoidal

## Introduction

Transsphenoidal surgery (TSS) is the treatment of choice for most lesions in the sellar region. In experienced hands, it is a safe procedure with low morbidity

and mortality rates. Disadvantages of the transsphenoidal approach are a restricted field of surgery, generally absent visualization of the optic nerves, and the risk of postoperative meningitis [1].

Postoperative meningitis is a well known complication of TSS, with an incidence ranging from 0.4 to 9% [1]. Infection is suggested to occur via a CSF fistula in the postoperative period. When intraoperative CSF leakage is observed, meticulous, watertight reconstruction of the sellar floor should be performed, in order to prevent the formation of a CSF fistula and CSF rhinorrhea [1–5]. In addition, an external lumbar drain (ELD) can be inserted to prevent postoperative rhinorrhea and fistula formation. However, the effect of ELD insertion on the risk of postoperative meningitis, has not been described yet.

In a previous report, we identified risk factors for meningitis after transsphenoidal surgery [6]. In that retrospective study, 228 transsphenoidal operations were reviewed. Postoperative meningitis occurred in 7/228 (3.1%) patients. It was concluded that an abnormal X-ray of the paranasal sinus, indicative of sinusitis, and postoperative CSF rhinorrhea were important risk factors for meningitis after transsphenoidal surgery.

After these findings, our perioperative protocol was changed in two respects, in an attempt to eliminate the previously identified risk factors for meningitis after TSS. First, patients with radiological signs of sinusitis were adequately pre-treated, and only accepted for TSS when the sinus-abnormalities had first been completely resolved. Secondly, when intraoperative CSF leakage was observed, an external lumbar drain (ELD) was

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inserted directly postoperatively, and removed after 5 days, to prevent postoperative CSF-rhinorrhea.

In the present study we reviewed the results of the consecutive 278 further transsphenoidal operations to evaluate whether adequate preoperative treatment of paranasal sinusitis and postoperative external CSF drainage in case of intraoperative CSF-leakage, reduces the risk of postoperative meningitis.

## Patients and Methods

The medical records of all patients who underwent TSS in our hospital between January 1996 and October 2003 were reviewed. All operations were performed by the same three neurosurgeons. The preoperative work-up included a roentgenogram of the paranasal sinuses.

In all operations, the sellar floor was reconstructed by placement of a portion of the bony nasal septum precisely between the dura and bony openings of the sella, after which the sphenoid sinus is filled with tissuecoll to further seal off the sellar floor.

After TSS, a nasal tampon with sterile gauze drenched in a suspension containing 5 mg of oxytetracyclin/ml, 10.000 U of polymyxin B/ml, and 5 mg hydrocortisone/ml (Terra-Cortril, Pfizer) was inserted. The gauzes were removed postoperatively on the 4th or 5th day. The standard perioperative antimicrobial regimen was the same as in the previous study: amoxicillin 750 mg orally every 8 hours during the day before the operation, a single 1000 mg intra-muscular injection on the morning of the operation, and subsequently 750 mg orally every 8 hours until the sixth postoperative day.

Compared to the previous study, the protocol of our perioperative regimen was changed in two respects. First, patients with an abnormal roentgenogram of the paranasal sinus, indicative of sinusitis were adequately pre-treated, and only accepted for TSS when the paranasal sinus X-ray first had been completely normalized. Secondly, when intraoperative CSF leakage was observed, an external lumbar drain (ELD) was inserted directly postoperatively, and removed after at least 5 days, to prevent postoperative CSF-rhinorrhea. Noteworthy, the technique of reconstructing the sellar floor in case of intraoperative CSF leakage was the same in both periods. A portion of the bony nasal septum was placed between the dura and the bony opening of the sella. The sphenoid sinus was then filled with fibrin glue as to further seal the sellar floor.

Postoperative liqorrhea was established by the presence of  $\beta$ -transferrin and/or glucose in the nasal fluid. Onset, duration and management of CSF rhinorrhea were recorded. Cases of meningitis were identified according to the definitions of the Centers for Disease Control and Prevention [7]. Detailed information on clinical presentation, culture and chemistry analysis of CSF, treatment and outcome was recorded.

The incidence of postoperative meningitis was compared with the incidence of meningitis reported in the

previous study. Statistical analysis was performed by using Fisher's exact test.

## Results

### Incidence of meningitis

Over the 7-year period, 278 transsphenoidal operations were performed. The indications of these procedures are listed in Table 1. Cases with other pathology in the sellar region included craniopharyngioma, hypophysitis, Rathke's cleft cyst, meningioma and chordoma. Postoperative meningitis occurred in 2/278 (0.7%) operations, compared to 7/228 (3.1%) operations in the previous study period ( $P < 0.05$ ).

Clinical data of the patients with postoperative meningitis are presented in Table 2. In one patient (patient 1, Table 2), reoperated for a non-functioning pituitary macroadenoma, TSS was complicated by a large CSF-leak, for which an ELD was inserted. On the 5th postoperative day the ELD was removed, according to our perioperative protocol. However, on the 7th postoperative day, CSF rhinorrhea was noted, which was treated conservatively, with strict bed-rest. On the 13th postoperative day, the patient developed headache and subfebrile temperature. After a gram stain of the CSF showed gram-negative cocci, antibiotic treatment was started. CSF culture showed *Serratia marcescens*. Recovery was complete.

The second patient was operated for acromegaly, without intraoperative CSF leakage. She developed rhinorrhea on the 3rd postoperative day, after a period of acute severe coughing. Because of persisting rhinorrhea, an ELD was inserted on the 5th postoperative day. However, on the 7th day she developed symptoms of meningitis, and antibiotic treatment was started. Cultures of CSF and sputum showed *H. influenzae*. The outcome was uneventful.

### Preoperative sinusitis

The preoperative roentgenograms of the paranasal sinuses showed abnormalities indicative of sinusitis in 8/278 (2.9%) cases. All 8 patients were treated before TSS: 2 patients by Caldwell Luc operation, 2 patients by infundibulotomy and 4 patients by sinus-lavage.

**Table 1.** Diagnostic reasons for transsphenoidal surgery during a 7-year period

Diagnosis	No. of cases
Cushing's disease	41
Acromegaly	59
Prolactinoma	7
Nonfunctioning adenoma	154
Other pathology in the sellar region	17
Total	278

*Note:* There were 14 reoperations because of Cushing's disease (2), Prolactinoma (2), Acromegaly (1), Nonfunctioning adenoma (8) and other pathology in the sellar region (1).

**Table 2.** Characteristics of two patients with meningitis after transsphenoidal surgery

Characteristic	Patient no.	
	1	2
Diagnosis	Nonfunctioning adenoma	Acromegaly
Preoperative abnormalities on sinus roentgenogram	–	–
Intraoperative CSF leakage	+	–
Immediate postoperative ELD	+	–
Day of onset of CSF rhinorrhea	7	3
Duration of lumbar drainage (d)	0–5	5–15
Day of onset of symptoms	13	12
CSF findings (at the time of diagnosis)		
WBC count (/mm <sup>3</sup> )	Not done	3800
Gram staining result	Gram-negative cocci	Not done
Culture result	<i>Serratia marcescens</i>	<i>Haemophilus influenzae</i>
Initial therapy	Ceftriaxon, Flucloxacillin	Flucloxacillin
Outcome	Uneventful	Uneventful

After treatment, roentgenograms of the paranasal sinuses were repeated and had normalized in all 8 patients. Only thereafter, patients were accepted for TSS. None of these 8 patients developed postoperative meningitis.

### CSF leakage and External Lumbar Drainage

Transsphenoidal surgery was complicated by clear intraoperative CSF leakage in 70/278 (25.2%) operations, compared to 22/221 (9.6%) in the previous study ( $P < 0.001$ ). All these patients received an ELD immediately after surgery for at least 5 days. There were no reported complications of ELD insertion and there were no drain-related infections. In the present series, 1 of 70 (1.4%) patients with intraoperative CSF leakage developed meningitis, compared to 3 of 22 (13.6%) patients in the previous study ( $P < 0.05$ ).

Postoperative CSF rhinorrhea occurred in three patients (1.1%). Meningitis developed in two of these three patients (66%). None of 275 patients without postoperative CSF rhinorrhea developed meningitis ( $P < 0.0001$ ).

### Discussion

Postoperative meningitis is a well known complication of TSS. Infection is suggested to occur via a CSF leak in the postoperative period rather than intraoperatively, as meningitis developed an average of 12 days after the operation [6]. Previously, we demonstrated that preoperative sinusitis and postoperative rhinorrhea are important risk factors for meningitis after TSS. Two of three patients with an abnormal X-ray of the paranasal sinus, indicative for sinusitis, developed meningitis compared with 5 of 225 patients with a normal paranasal sinus X-ray ( $P < 0.005$ ). Six of seven patients with postoperative cerebrospinal fluid (CSF) rhinorrhea and only one of 221 patients without postoperative CSF rhinorrhea developed meningitis ( $P < .0001$ ). When

intraoperative CSF leakage is observed, an ELD can be inserted to prevent postoperative rhinorrhea and fistula formation.

The present study consisting of a series of 278 consecutive patients undergoing TSS suggests that the routine insertion of an ELD in patients in whom intraoperative CSF leakage is observed, considerably reduces the incidence of postoperative meningitis. The incidence of only 0.7% post-TSS meningitis compares favourably with the 3.1% in our previous study and also with the reported incidence of 0.4–9% in other series [8–13].

Intraoperative CSF leakage occurred more often in the present series (25.2%) compared to our previous report (9.6%). This observation can be (at least partly) explained by the fact that in the present series more than 55% of the operations were cases with non-functioning macro-adenoma's, needing supra-sellar exploration at an increased risk of rupture of the arachnoidea. Also, more awareness of the neurosurgeons on intraoperative CSF leakage might partly explain the increase in intraoperative CSF leakage. Because of the higher incidence of intraoperative CSF leakage in the present series compared to the previous series, a larger proportion of the patients was at risk of developing a CSF-fistula and subsequent meningitis. However, despite this increased risk, we still found a decrease in the incidence of meningitis, showing the benefit of inserting an ELD in case of intraoperative CSF leakage.

In cases of intraoperative CSF leakage, meticulous reconstruction of the sellar floor is indicated, for which several techniques have been described [1–5]. In addition, a lumbar drain can be inserted to divert the CSF and to prevent postoperative rhinorrhea and fistula formation. Lumbar drain insertion has been recommended by some authors for every patient with intraoperative CSF leakage, and by others only in those patients with large CSF leaks or in those patients who have had extended cranial base approach with removal of the tuberculum sellae and part of the planum sphenoidale [2,14–16].

Recently it has been shown that for small CSF leaks, adequate local repair of the defect may obviate the need for lumbar drain placement [3,17]. Similarly, in two series of endoscopic transsphenoidal surgical procedures, a lumbar drain was not routinely necessary for successful, safe closure of CSF-leaks [2,18]. In the present series, the extent of CSF leakage or the size of the dural defect was not well documented in all patients. However, on the basis of the fore-mentioned evidence, insertion of a lumbar drain might be reserved for patients with a large dural defect or patients in which the dural repair is not completely watertight.

In the present series there were no reported complications of ELD insertion and no drain-related infections. In a large series of 530 consecutive transsphenoidal operations with lumbar drainage, no neurologic complications caused by CSF drain placement were observed [16]. Bacterial meningitis secondary to the use of lumbar catheters has been studied scarcely, with reported infection-rates between 3–10% [19–22]. Duration of CSF drainage of more than 5 days has been shown to increase the risk of catheter-related infections [23,24]. According to our preoperative protocol, the ELD was removed on the fifth day in most patients, which may explain why we did not observe any lumbar catheter-related infections. Symptomatic pneumocephalus due to lumbar CSF-drainage is another rare, life-threatening complication, which did not occur in the present series [25,26].

The observation that two of three patients with postoperative rhinorrhea developed meningitis stresses the importance to prevent postoperative CSF leakage. In one patient (patient 1, Table 2) rhinorrhea occurred despite previous lumbar drainage for 5 days. This supports the general belief that in order to prevent meningitis additional surgical therapy is warranted in patients with recurrent or persisting CSF rhinorrhea despite adequate lumbar drainage. From the present data, no conclusions can be drawn on the prophylactic use of antibiotics once CSF rhinorrhea is observed.

Another risk factor for meningitis after TSS identified in our previous study was radiological evidence of sinusitis. In the present series, 8 patients had abnormal roentgenograms, indicative of sinusitis. Noteworthy, none of these patients had clinical signs of sinusitis. All eight patients were treated adequately before TSS, and none of these patients developed meningitis. This finding confirms the importance of a preoperative roentgenogram of the paranasal sinuses followed by local treatment when indicated, even in patients without clinical signs of sinusitis.

In previous series an overrepresentation of patients with Cushing's disease who developed meningitis after TSS was observed, possibly by a lowered immune response [27]. In the present study, none of 35 patients with Cushing's disease developed meningitis. Since several years, patients in our clinic with Cushing's syndrome are preoperatively treated with cortisol-lowering drugs, such as ketoconazole and metyrapone. This might have

(partly) restored immunity, thereby reducing the risk of (postoperative) infectious complications.

In conclusion, after TSS the routine insertion of an ELD in patients in whom intraoperative CSF leakage is observed significantly reduces the incidence of postoperative meningitis. Postoperative rhinorrhea should be treated promptly by adequate lumbar drainage and/or surgical repair. Preoperative roentgenograms of the paranasal sinuses and treatment of cases with signs of sinusitis are mandatory. The role of prophylactic antibiotic treatment in patients with CSF rhinorrhea after TSS remains to be established.

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