Print ISSN: 2321-6379
Online ISSN: 2321-595X

Original Article

Post-operative Cerebrospinal Fluid Leak Following Transsphenoidal Pituitary Surgery: Predictive Factors and Management Options – A Single-Institute Experience

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Abstract

Background: Transsphenoidal route is the principal method for pituitary surgery with cerebrospinal fluid (CSF) leak most feared complication.

Materials and Methods: It is a retrospective analysis of 129 patients undergoing transsphenoidal surgery for pituitary tumors in the Neurosurgery Department of SMS Medical College, Jaipur (Rajasthan), from 2015 to 2018. The objectives were to determine (1) the incidence of CSF leak following transsphenoidal surgery; (2) demographic or intraoperative factors associated with postoperative leaks; and (3) techniques and efficacy of post-operative leak management.

Results: Post-operative CSF leaks occurred in 41.1% (53 of 129) of patients. Leaks were more common in males than females (52.83% vs. 47.1%) and in the age group of 21–40 years (54.72%). The incidence of post-operative CSF leaks was more in macroadenoma (84.9%) in comparison to microadenoma (13.2%). About 49.1% of patients with post-operative CSF leaks had tumors with suprasellar extension. Non-secretory, firm, and moderately vascular tumors were more frequently associated with post-operative CSF leaks. The presence of intraoperative leak was found to be a significant predictor of post-operative CSF leak. Out of 53 post-operative CSF leaks, 45 (84.9%) resolved with conservative measures and remaining six patients were cured with endoscopic reexploration.

Conclusions: CSF leaks following transsphenoidal surgery occurred in 41.1% of cases. The presence of macroadenoma with suprasellar extension on imaging and intraoperative leaks was independent predictors of post-operative leaks. Conservative management for manifested post-operative CSF leaks is a viable first-line option and those failing conservative measures can be tackled with endoscopic reexploration.

Key words: Cerebrospinal fluid leak, Endoscopic, Pituitary adenoma, Post-operative, Transsphenoidal

INTRODUCTION

Cerebrospinal fluid (CSF) leak is a recognized complication of transsphenoidal pituitary surgery. Incidence of post-operative CSF leaks ranges from 6% to 50% who underwent transsphenoidal operations; even higher rates have been reported after an extended transsphenoidal approach. However with newer techniques, the incidence has fallen to 1–10%.[1-4] Potential morbidities associated with post-operative CSF leaks include prolonged hospitalization, additional operations, meningitis, and tension pneumocephalus.[2] To avoid such complications, it would be helpful to identify patients at high risk for post-operative leak. Perhaps, these patients could be managed with more aggressive intraoperative or post-operative measures to prevent a CSF leak.

Factors predictive of post-operative CSF leak remain poorly defined. Black *et al.*[5] reported a higher incidence of

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www.ijss-sn.com

Month of Submission : 11-2020
Month of Peer Review : 11-2020
Month of Acceptance : 12-2020
Month of Publishing : 01-2021

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postoperative leak following resection of macroadenomas versus microadenomas (4.2% vs. 0.9%), whereas Seiler and Mariani[1] noted post-operative leaks to be more common when a visible CSF leak occurred during surgery versus the absence of an intraoperative leak (2.9% vs. 0.0%). Various materials and techniques for closure of the sella turcica have been described to prevent leaks or manage intraoperative leaks, but no studies have directly compared such strategies.

Management of the patients with post-operative CSF leak is controversial. Various strategies have been described, including non-operative management, CSF diversion, and reexploration.[5-7] A growing number of reports have demonstrated success with endoscopic techniques.[6,8,9] However, these reports describe CSF leaks of various origins and sites within the anterior cranial fossa. No study has specifically evaluated the efficacy of endoscopic management of sphenoid leaks following transsphenoidal surgery.

In the present study, we reviewed our experience with CSF leaks in the setting of transsphenoidal pituitary surgery. Various demographic and intraoperative factors were analyzed to elucidate any association with the occurrence of post-operative leaks. We also evaluated our strategies and results in managing post-operative leaks.

MATERIALS AND METHODS

The study was conducted in the Neurosurgery Department of SMS Medical College, Jaipur (Rajasthan). In total, 129 patients who had undergone transsphenoidal surgery for pituitary adenoma from 2015 to 2018 were enrolled in this retrospective observational study. All the necessary and relevant data were obtained from the medical records of patients which included admission sheets, pre-operative, operative and post-operative clinic notes, progress sheets, and discharge summaries. Data collected included patient age, sex, tumor size, extension, tumor characteristics (secretory or non-secretory, consistency, and vascularity), approach performed, intraoperative findings, method of sella turcica closure, and strategies used to manage post-operative CSF leak. Patients without complete documentation of the data were excluded from the study.

Statistical Analysis

Statistical analysis was performed with the MS Excel, SPSS, 23 version for Windows statistical software package (SPSS Inc., Chicago, IL, USA). The categorical data were presented as numbers (percent) and 95% confidence interval, to assess any significant association Chi-square test and odds ratio was used. Binary logistic regression analysis was done to find out significant independent indicators of post-operative leak probability. Multivariate analysis was performed using logistic regression analysis for dichotomous variables. $P < 0.05$ was considered statistically significant.

RESULTS

Between 2015 and 2018, 129 transsphenoidal surgeries were performed for pituitary adenoma. Out of 129 patients, 53 (41.1%) had post-operative CSF leak. There was no significant gender difference seen with respect to post-operative CSF leak; however, the incidence of post-operative CSF leak was significantly more in patients with age group in between 21 and 40 years [Table 1].

Incidence of CSF leaks was significantly higher in patients who had macroadenoma with suprasellar extension. Non-secretory, moderately vascular, and firm tumors had significantly higher post-operative CSF leak in comparison to other [Table 2]. There was no significant difference seen with different approaches (microscopic and endoscopic), extent of resection and the material used for reconstruction of sella [Table 3]. However, the incidence of post-operative CSF was much significant in patients who had intraoperative CSF leak in comparison to who did not. On multivariate logistic regression, age, tumor consistency, and intraoperative CSF leak were observed to be independent risk factors for post-operative CSF leak.

Table 1: Demographic profile of patients who have undergone transsphenoidal pituitary surgery between 2015 and 2018

Parameters	Total patients (*n*=129)		Post-operative leak present (*n*=53)		Post-operative leak absent (*n*=76)		Odds ratio (95% CI)	*P*-value
	*n**	%	*n**	%	*n**	%		
Age ≤20 years	8	6.2	2	3.77	6	7.88	0.667 (0.12–3.58)	9.94
Age 21–40 years	55	42.64	29	54.72	26	34.21	2.231 (1.05–4.65)	0.049
Age 41–60 years	66	51.16	22	41.51	44	57.89		
Male	81	62.79	28	52.83	53	69.74	2.057 (0.99–4.26)	0.077
Female	48	37.21	25	47.17	23	30.26		

*Number of patient out of total patients (*N*), % (*n*/*N*×100)

Table 2: Pituitary tumor characteristics

Parameters	Total patients (*n*=129)		Post-operative leak present (*n*=53)		Post-operative leak absent (*n*=76)		Odds ratio (95% CI)	*P*-value
	*n**	%	*n**	%	*n**	%		
Size								
Microadenoma	13	10.0	7	13.2	6	7.89	2.074 (0.675–6.375)	0.315
Macroadenoma	116	89.9	45	84.9	71	93	3.5 (1.220–10.044)	0.03
Extension								
Sellar	31	24.03	14	26.42	17	22.37	1.246 (0.552–2.814)	0.749
Suprasellar	68	52.71	26	49.1	42	55.26	0.406 (0.188–0.875)	0.033
Parasellar	30	23.26	13	24.53	17	22.37	1.128 (0.494–2.577)	0.941
Nature								
Secretory	61	47.29	20	37.73	41	53.94		
Non-secretory	68	52.71	34	64.15	34	44.73	2.211 1.075–4.545)	0.046
Recurrent	5	3.88	4	7.55	1	1.32	6.122 (90.664–56.412)	0.18
Consistency							Chi-square test (*P*-value)	
Hard	2	1.55	1	1.89	1	1.32	0.586	
Firm	90	69.77	31	58.49	59	77.63	0.034	
Soft	37	28.68	21	39.62	16	28.58		
Vascularity								
Mild	59	45.74	16	30.19	43	56.58		
Moderate	65	50.39	35	66.04	30	39.47	0.0005	
Severe	5	3.88	2	3.77	3	3.95	0.923	
Intraoperative CSF leaks	47	36.43	41	77.36	6	7.89	0.000	

*Number of patient out of total patients (*N*). % (*n*/*N*×100)

Table 3: Operative procedure and extent of resection

Parameters	Total patients (*n*=129)		Post-operative leak present (*n*=53)		Post-operative leak absent (*n*=76)		Chi-square test (p-value)
	*n**	%	*n**	%	*n**	%	
Microscopic	38	29.46	18	23.68	20	37.74	0.459
Endoscopic	91	70.54	35	46.05	56	61.5	
Extent of resection							
Complete	90	69.74	37	69.81	53	69.74	0.85
Partial	39	30.26	16	30.19	23	30.26	

*Number of patient out of total patients (*N*). % (*n*/*N*×100)

There were total 53 cases of post-operative CSF leak, mostly detected within 24 h of surgery and rest were within 5–7 post-operative days. Initially, all the cases were managed with head end elevation and oral acetazolamide. Out of 53 cases, CSF leak stopped in 12 (22.6%) patients within 12–24 h with this measure. Those who continued to have CSF leaks were put on CSF diversion using lumbar drain and with that CSF leaks resolved in 33 (62.3%) patients. Despite conservative measures, CSF leak failed to resolve in 6 (11.32%) patients. These patients were managed by endoscopic repair of the defect, following which all the CSF leak resolved [Table 4].

Out of 129 patients, only two patients developed meningitis and both were successfully managed with intravenous antibiotics. There was no incidence of pneumocephalus and intraoperative mortality. Two patients died in post-operative period due to medical complications.

Table 4: Management of post-operative CSF leaks

Treatment modality	Post-operative leak present *n**	Leak stopped	
		*n**	%
Head end elevation+Acetzolamide	53	12	22.6
Lumbar drain	41	33	80
Endoscopic repair	6	6	100

*Total number of patients

DISCUSSION

Our data suggest that certain factors can predict a greater likelihood of post-operative CSF leak in the setting of transsphenoidal pituitary surgery. Tumor characteristics and intraoperative CSF leaks were the two important factors that were associated with post-operative CSF leaks. In our study, patients between the age group of 21 and 40 years had significantly higher incidence of CSF leaks

in comparison to other age group but there was no sex predilection for CSF leak seen.

Tumor size was one of the important factors that have attracted researchers. Studies have reported a higher incidence of post-operative CSF leaks after resection of macroadenomas compared with microadenomas (3.8–4.2% vs. 0.9–1.3%).[5,10,11] Similarly, in our study, incidence of CSF leaks was more in macroadenomas with suprasellar extension. Most of these tumors were non-secretory in nature because of the late presentation in comparison to the secretory tumor which tends to become symptomatic in early phase due to hormonal factors.

Tumor consistency is also a factor that affects the rate of post-operative CSF leaks. CSF leaks were reported more commonly in firm tumors in comparison to soft tumors.[12,13] In our study, incidence of CSF leaks was more in firm tumor in comparison to soft tumor. One important noticeable thing is that the tumor texture was solely decided by the operating surgeon.

We found that patients with an intraoperative CSF leak had a significantly higher risk of post-operative leak. Intraoperative leaks occurred in 36% of our cases, well within the range of 18.1–53.2% reported in the literature.[1,10] The post-operative leak was seen in 53 (41.1%), out of which 77% had evidence of intraoperative leak while rest had no evidence of intraoperative leak.[1-4] This association was noted by Seiler and Mariani[1] who found post-operative leaks to be nearly 6 times as common when intraoperative leaks occurred. This finding suggests that patients with intraoperative CSF leaks may warrant more aggressive management to prevent post-operative leaks.

Several authors have described strategies for preventing CSF leak after transsphenoidal surgery,[1,2,5,14,15] many proposing more aggressive measures when an intraoperative leak occurs. Ciric *et al.*[2] described a technique of packing the sella with fascia, fat, and fibrin glue when an intraoperative leak is noted. In addition, a fragment of cartilage or bone is used to reconstruct the sellar floor. In our institute, reconstruction of sella was done with fat, fascia, and glue in 65.1% of cases while fat and fascia alone were used in 29.5% and in 6.2% cartilage were used.

There have been various strategies reported in the literature for the management of post-operative CSF leaks. Some authors have favored a trial of non-operative therapy involving lumbar drainage for 3 or more days.[5,6] However, Shiley *et al.*[16] have favored early reexploration without a trial of lumbar drainage. Laws *et al.* cited the ease and efficacy of reexploration as opposed to lumbar drainage, which may be unsuccessful or cause patient anxiety or both. There are no studies comparing the efficacy of non-operative therapy versus reexploration.[5,15]

In our studies, we had 53 cases of post-operative CSF leaks and the conservative approach was tried upfront in all the cases. The post-operative CSF leaks stopped in 45 (84.9%) patients with conservative measures. Out of 45 patients, 12 (22.6%) were managed with oral acetazolamide and head elevation; in the rest, 33 (80%) leaks were resolved with passive lumbar drainage. Our two patients died due to medical condition while they were on conservative measures. Out of total 53 patients, only 6 (11.3%) patients required endoscopic management.

Kelley *et al.*[6] reported successful endoscopic management of 7 out of 8 (87.5%) CSF leaks, most of which were secondary to transsphenoidal surgery. In our study, endoscopic management was successful in all the six patients with no operative or post-operative complication. The technique used by us for endoscopic management was similar to the studies reported in literature.[6,16,17]

CONCLUSIONS

CSF leaks following transsphenoidal surgery occurred in 41.1% of cases. The presence of macroadenoma with suprasellar extension on imaging and intraoperative leaks was independent predictors of post-operative leaks. Conservative management for manifested post-operative CSF leaks is a viable first-line option and those who fail to improve with conservative measures can be tackled with endoscopic reexploration.

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How to cite this article: Phogat V, Meena US, Mishra K, Sharma A. Post-operative Cerebrospinal Fluid Leak Following Transsphenoidal Pituitary Surgery: Predictive Factors and Management Options – A Single-Institute Experience. Int J Sci Stud 2021;8(10):66-70.

Source of Support: Nil, **Conflicts of Interest:** None declared.