KUNJAN ACHARYA [1]
YOGESH NEUPANE[1]
NG YUK HUI [2]

Ganesh Man Singh Memorial Academy
of ENT and Head and Neck Studies
TU Teaching Hospital, Kathmandu, Nepal.[1]

Department of ENT Head and Neck Surgery
Singapore General Hospital
Singapore [2]

Corresponding author
Dr Kunajn Acharya
Ganesh Man Singh Memorial Academy
of ENT and Head and Neck Studies
TU Teaching Hospital, Kathmandu, Nepal.
Email: acharyakunjan@gmail.com

RISK FACTOR ANALYSIS FOR INTRAOPERATIVE CSF LEAK DURING ENDOSCOPIC TRANSNASAL HYPOPHYSECTOMY; A RETROSPECTIVE REVIEW.

ABSTRACT

Objective:

To analyze the possible risk factors which may be responsible for intraoperative CSF leak during endoscopic pituitary surgery.

Material and Method:

The study was done in Singapore General Hospital, Singapore. It was a retrospective data extraction and analysis from 2008 to 2011.

Outcome measured: size of tumor, volume of tumor, consistency of the tumor during surgery, attempts for removal which was correlated with Intraoperative CSF leak in eachpatient. The tumor was classified into Micro and Macro adenoma with reference of Craniocaudal Length i.e > 1 cm is Macroadenoma and <1 cm is Microadenoma. The volume of the tumor was calculated using IPLAN CRANIAL VERSION 2.6 provided by the brain lab.

Results:

The total number of patients were 128 and Among 128 patients 68 were male and 60 female. Out of 128 patients, 28 Patients had intraoperative leak which was identified during the time of surgery and were sealed using different technique. Out of leaking 28 patients, 3 patients had post-operative leak even after initial closure on table which were managed successfully with Lumbar puncture. The intra operative leak was not significantly associated with studied variables nevertheless the intraoperative CSF leak significantly increased the hospital stay (p=.009).

Conclusion:

Intraoperative CSF leak is a definitely important morbidity to the patients as it lengthen the hospital stay as shown in our study. In order to shorten the hospital stay we tried to look for possible factors like tumor volume, size, consistency, endocrine status and attempts for surgery, none of these variable shows any statistical significance with intraoperative Leak.

Keywords: CSF leak, Endoscopic approach, Pituitary adenomas.

INTRODUCTION

Pituitary adenomas are nowadays removed by the endoscopic approach. Traditionally it used to be removed by trans cranial approach. Few Neuro Surgeons still prefer removing it by transnasal route using the Microscope. However, with the use of 0 degree and 30 degree endoscope, the field of Rhinology and skull base is expanding day by day. The use of the endoscopes for Trans-sphenoidal surgery has provided improvements in panoramic visualization, the ability to look around using angled lenses. The first documented Trans-sphenoidal approach for resection of a pituitary lesion dates back to 1906 by Schloffer.[2] His efforts were soon followed by Kocher and von Eiselsberg in the early part of the twentieth century. One of the challenge of endoscopic Trans-sphenoidal Hypophysectomy is to avoid CSF leak during the surgery. As we know that rate of complications decreases as the surgeon becomes more skill full over the time. For both microscopic and endoscopic Transsphenoidal surgery, the most common complications are CSF leak, meningitis, and sinusitis as described by Tabaee et al. [3] Recent studies have shown endoscopic techniques to be associated with similar or reduced rates of

complications compared with microsurgical techniques as shown by Jho HD. [5]

The purpose of this paper is to analyze the possible risk factors which may be responsible for intraoperative CSF leak, so that we can predict the etiology of the CSF leak if there are any. After going through the extensive literature review we were able to think of factors like tumor volume, tumor cranio-caudal diameter, tumor consistency during surgery and revision or primary surgery are looked in as the possible causative factor for the intraoperative CSF leak.

Material and Method

The study was done in Singapore General Hospital, Singapore. It was a retrospective data extraction and analysis from 2008 to 2011. We extracted the patient details who had undergone Endoscopic transnasal Pituitary surgery like age, sex, size of tumor, volume of tumor, consistency of the tumor during surgery, attempts for removal and the looked for Intraoperative CSF leak in each patient. The inclusion criteria were those patients who underwent endoscopic trans-sphenoidal Hypophysectomy for pituitary adenoma. In order to make similarity in the study, we excluded those patients whose frozen section or postoperative histopathology came out to be other than pituitary adenoma. There were total of 172 patients operated in this duration, however 45 excluded and only 128 patients were analyzed. Among 45 patients 37 did not undergo immediate per operative MRI so that we were not able to calculate volume of tumor and were excluded. Similarly 3 craniopharyngioma,3 Clival tumor , 2 Rathke cyst and one was converted to open surgery were also excluded.

The size of the tumor was calculated in all three dimensions; Craniocaudal, Anterioposterior and Transverse. It was calculated in T2 weighted MRI which used to be done just before the surgery inside the operation theater. As the vertical diameter of tumor is related to the dura and tuberculum sellae, we have picked the Craniocaudal diameter and analyzed with the intraoperative CSF leak. The tumor was classified into Micro and Macro adenoma with reference of Craniocaudal Length i.e length > 1 cm as Macroadenoma and less than 1 cm as Microadenoma.

The volume of the tumor was calculated using IPLAN CRANIAL VERSION 2.6 provided by the Brain Lab. It represents the three dimensional volumetric calculation. The encrypted preoperaive CD of each patient undergone Endoscopic Trans sphenoid surgery were retrieved form the Operation Theater and brain lab software was used to calculate the volume of the pituitary tumor. While looking for the volume of tumor T2 weighted MR scans were used to compute the volume of the tumor. Since we need intraoperative encrypted CD to determine the volume of the tumor, the patients who did not undergo intraoperative MR scan were excluded from our study as mentioned earlier.

Similarly, other variables like consistency of tumor, attempts for removal and incidence of intraoperative leak were retrived from operative notes from patient data base. While retrieving the detail for consistency of tumor, we found surgeon has mentioned the tumor as soft, fibrous or mixed hence we categorized the nature of tumor as noted in operative notes by the surgeon.

The bio statistician was consulted for the data analysis and the p value less than 0.05 was consider as the level of significance.The ethical approval for the conducting the study was also received.

RESULTS

There were total of 128 patients included for study after exclusion.Among 128 patients, 68 were male and 60 female. (The following figure shows the gender distribution of the study group.) Minimum age of the patient who underwent the Transphenoidal Hypophysectomy was 19 years old and maximum age was 85 years with mean age of 50.34 years.Similarly, among 128 patients, 106 patients were operated for first time and 22 patients had revision surgery. Out of 128 pituitary adenoma, some were found to secrete different hormones like Growth hormones, Prolactin, TSH, LH/FSH, ACTH. However, the most common pituitary adenoma was nonfunctioning 77/128 i.e 60.2%. (Table 1)

Table 1. Showing Varieties of hormone secreted by Pituitary adenoma.

	Frequency	Percent
Non-secretory	77	60.2
Growth Hormone	10	7.8
LH/FSH	10	7.8
Pan hypopituitarism	10	7.8
Prolactin	9	7
ACTH	9	7
TSH	3	2.3
Total	128	100%

Out of 128 patients operated, 28 patients had intraoperative leak which was identified during the time of surgery and were sealed using different technique. However out of those leaking 28 patients, 3 patients had post-operative leak even after initial closing during primary operation, which were managed successfully with Lumbar puncture. When tumor consistency was looked for while operating it endoscopically, most of the tumor were either soft or cystic as shown in Table 2.

Table 2: Different Consistency of pituitary adenoma encountered during the surgery.

Consistency of Tumor	Frequency	Percent
Soft or Cystic	95	74.2
Mixed	25	19.5
Fibrous	8	6.2
Total	128	100

For analysis purpose the pituitary adenoma were broadly classified into secretory and non-secretory adenoma and cross tabulated against presence or absence of intraoperative CSF leak. Similarly, the consistency of tumor, primary or revision surgery were also looked for any possible relation using Chi square Test.

As shown in following Table 3 none of the variable like attempts of surgery, consistency of tumor or endocrinal status have statistical relation with incidence of intraoperative CSF leak while doing trans-nasal Hypophysectomy. P value was calculated using Chi-square test.

Table 3: Cross Tabulation between Intraoperative CSF leak and Studied Variables

Attempts of surgery				P value
		Primary	Revision	
Intraoperative leak	No	81	19	0.304
	Yes	25	3	
Endocrine Status				
		Normal	Abnormal	
Intraoperative leak	No	58	42	0.346
	Yes	19	9	
Intraoperative Consistency of Tumor				
		Soft	Mixed	Fibrous
Intraoperative leak	No	77	19	4
	Yes	18	6	4

In order to see the relation of volume and craniocaudal diameter of tumor, the mean of these two variable was calculated and were divided into 2 groups one above the mean and another below the mean value. These two groups were then analyzed for any possible association with intraoperative CSF leak using Chi- square test.

Table 4: Descriptive analysis of Volume and Craniocaudal diameter of Tumor

	Minimum	Maximum	Mean	S.D.
Craniocaudal Length of Tumor in cm	0.4	4.8	2.49	0.93
Volume of Tumor cm^3	0.05	41.18	7.92	6.84
Hospital stay in days	3	35	5.63	3.97

Table 5: Cross Tabulation between the intraoperative Leak and volume of the tumor

		Below mean volume	Above mean Volume	Total	P value
Intraoperative CSF leak	No	67	33	100	0.334
	Yes	16	12	28	
Total		83	45	128	

Table 6 : Cross Tabulation between the Intraoperative leak and the Craniocaudal Diameter of tumor.

	Intraoperative CSF Leak		Total	P value
	No	Yes		
Micro adenoma	6	1	7	0.617
Macro adenoma	94	27	121	

There was no statistical significant relation of intraoperative CSF leak with volume of tumor. There was also no significant difference between Craniocaudal length of adenoma with intraoperative CSF leak.

Similarly, when the duration of hospital stay was analyzed whether it increased or decreased the hospital stay, using unpaired t test. Stay was significantly (P=0.009) more when the intraoperative leak occurred. Table 7 shows the significant difference in the mean of hospital stay when the intraoperative leak occurred during the surgery.

Table 7: Significant difference in hospital Stay when leaked occurred.

	Intraoperative CSF leak	N	Mean	S.D.	P Value
Hospital stay in days	No	100	5.15	3.28	0.009
	Yes	28	7.36	5.56	

Discussion:

Method of choice for removing pituitary adenoma is Endoscopic guided Navigation assisted Trans-sphenoidal approach as described by Michael Buchfelder and Sven Schlaffer.[8] As we know any kind of surgical intervention to the human body can have complication which varies from minor to major. The technology developing in 21st century is trying to minimize the complication, which hold true in case of Endoscopic Trans-sphenoidal Navigation assisted surgery too. The varieties of complication following the surgeries like CSF leak, meningitis, deterioration of endocrine function and vascular injury can happen as described by Michael Buchfelder and Sven Schlaffer.[8] In our study we tried to look at the one of the common intraoperative complication i.e, intraoperative CSF leak. The main limitation of our study is that it is a retrospective study which has lot of recall bias, but however it is minimized by using Computerized data base of patients available at Singapore General Hospital. All individual data was scrutinized before identifying the variables. Similarly in order to avoid discrepancy between different nature of tumor, we have included only those tumor whose frozen section histopathology was adenoma. Hence the final number of patients for the study was is 128.

The intraoperative CSF leak was noted in 28 of 128 patients which account for 21% in our study. Literatures shows the rate of leak is around 18.1 to 53.2%. [6] This shows the rate of leak is obviously less in our study. We looked for possible preoperative variable like functional status of the tumor, intraoperative variables like consistency of tumor, attempts of tumor, size and vertical diameter of tumor which may influence the intraoperative CSF leak but none of these factor were found to be significantly associated.

Gautam et al [4], showed no statistically significant difference in the rate of intraoperative leakage for cases of repeat surgery (37%) as compared with first-time operations (30%; p = 0.52). Our analysis also shows no statistical difference, (p=0.304).However, Samuel et a in a retrospective study including 217 patients showeda different result, intraoperative leaks occurred in 63.4% of revision procedures (26 of 41) versus only 25.6% (45 of176) of primary operations (P =001).[7] Sameul et al argued that most of the revision surgery were for residual tumor thus the surgeon will be aggressive during the surgery and chance of traumatizing the diaphragm sella is relatively higher resulting in CSF leak.[7] Similarly, distorted anatomy during revision surgery may be also factor for having more rate of intraoperative leak in revision group.

Samuel et al [7] has also studied the postoperative stay at hospital following the surgery. It was significantly longer for patients with CSF leaks (CSF leak group, 5.4 +/- 2.2 d; no-leak group, 3.5 +/- 1.9 d [P _.001]). This finding correlates with our results too. The mean hospital stay in days (CSF leak group: 7.36 versus no leak group 5.15: unpaired t-test p=0.009) in our study. Hence intraoperative leak significantly increases morbidity to the patients.

According to Gautam et al [4] Macro adenomas

with suprasellar extension had a greater rate of leakage (34%) than those that did not extend superiorly (27%). Fewer leaks were observed during surgery for tumors with suprasellar extension when CSF drainage was performed from 57% to 5% ($p < 0.001$). Cerebrospinal fluid using lumbar drainage was effective for tumors without suprasellar extension, as leaks in this group occurred in 29% of cases without drainage and in no cases in which drainage was done ($p = 0.31$). This results may forecast that the Macro adenoma with suprasellar extention has more like hood of have intraoperative CSF leak. However we analyzed in our study that tumor categorized into Micro and macro adenoma using vertical diameter more than 1 cm (Macro adenoma) and below 1 cm (Micro adenoma) did not show any relation with chances of intraoperative leak ($p = 0.617$).

In our study we tried to look for possible correlation between volumes of tumor measured in T2 weighted MRI and chance of intraoperative CSF leak which shows no correlation statistically($p=0.334$). We tried to look for the similar studies in published in literature however no similar research was done previously.

Conclusion and Limitation

Intraoperative CSF leak is a definitely important morbidity to the patients as it lengthens the hospital stay as shown in our study. Tumor volume, size, consistency, endocrine status and attempts for surgery, none of these variable showed any statistically significant correlation with intraoperative CSF leak. Our study is a retrospective study, which has lower scientific evidence, had it been prospective we would have designed similar study in better way.

REFERENCES

1. Jane JA Jr, Han J, Prevedello DM, et al. Perspectives on Endoscopic Transsphenoidal surgery. Neurosurg Focus 2005;19(6):E2.
2. Doglietto F, Prevedello DM, Jane JA Jr, et al. A brief history of endoscopic Transsphenoidal surgery-from Philipp Bozzini to the First World Congress of Endoscopic Skull Base Surgery. Neurosurg Focus 2005;19(6):E3.
3. Tabaee A, Anand VK, Barron Y, et al. Endoscopic pituitary surgery: a systematic review and meta-analysis. J Neurosurg 2009;111(3):545–54.
4. Gautam U, Edward H, Oldfield . Prevention of intraoperative cerebrospinal fluid leaks by lumbar cerebrospinal fluid drainage during surgery for pituitary macroadenomas. J Neurosurg 2012;116:1299-03.
5. Jho HD. Endoscopic Trans-sphenoidal surgery. Neurooncol 2001;54(2):187–95.
6. Seiler RW, Mariani L. Sellar reconstruction with resorbable Vicryl patches, gelatin foam, and fibrin glue in transsphenoidalsurgery: a 10-year experience with 376 patients. J Neurosurg 2000;93:762–765.
7. Samuel G, Shiley FL, Johnny B, Delashaw, Stanley L, Barnwell PH, Peter A, Mark W. Incidence, Etiology and Management of cerebrospinal fluid leak following Trans-sphenoidal surgery. Laryngoscope 2003;113: 1283-1288.
8. Michael Buchfelder , Sven Schlaffer. Surgical treatment of pituitary tumours. Best Practice & Research Clinical Endocrinology & Metabolism. 2009;23:677–692.