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Original Article

A Journey from Endoscopic to Microscopic transsphenoidal surgery

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Abstract

Background: *Endoscopic transsphenoidal surgery was a standard procedure for pituitary adenomas resection in our institution. Since the end of 2016, we have shifted the protocol to microscopic transsphenoidal approach. This paper presented our experience in pituitary surgery using sublabial transsphenoidal approach.*

Methods: *Patients with pituitary tumors who received transsphenoidal surgery during 2003-2022 were included. We compared the extent of resection, re-operation rate, blood loss volume, operative time, and complications mainly postoperative cerebrospinal fluid (CSF) leakage and diabetes insipidus (DI) between microscopic and endoscopic transsphenoidal approaches. Tumors extension to the suprasellar area and cavernous sinus were also analyzed to see their relationship with surgical outcomes.*

Results: *Out of total 210 patients, 122 (58.1%) and 88 (41.9%) patients underwent microscopic transsphenoidal and endoscopic transsphenoidal surgery. There was a significant difference in total removal rate (p=0.01). There was no significant difference in re-operation rate, post-operative CSF leakage rate and blood loss volume. Operative time was significantly (p=0.0001) lower in microscopic surgery. Patients who received endoscopic surgery had a higher rate of DI (p=0.0001). Tumors extension to cavernous sinus was not a significant predictor of near total resection rate (p=0 .08).*

Conclusion: *Our endoscopic and microscopic surgery results are comparable except for the operating time, total removal of tumour and incidence of DI, which are better with microscopic surgery. This report supports our transition from endoscopic to microscopic pituitary surgery.*

Keywords: *Transsphenoidal surgery, Endoscopic, Microscopic, operating time.*

Introduction

As tumors originated from adenohypophysis, pituitary adenomas (PAs) are the third most common intracranial tumors, accounting for 1 0 %-2 5 % (Surawicz et al, 1999)[1]. In the most recent report by CBTRUS, the tumors had incidence rate of 1 7 .9 % of all primary central nervous system (CNS) tumors by histology (Ostrom et al, 2020)[2]. PAs are classified as clinically nonfunctioning pituitary adenomas (NFPAs) or functional pituitary adenomas (FPAs); prolactinomas, adrenocorticotropic hormone (ACTH) secreting, growth hormone (GH) secreting, or thyroid-stimulating hormone (TSH) secreting adenomas are considered as FPAs (Lopes, 2017)[3]. According to size, PAs are described as microadenoma if the size is less than 1 0 mm, while macroadenomas have a size of more than 1 0 mm (Molitch, 2017)[4]. Suprasellar extension of the tumor could compress the optic chiasm and optic nerve, resulting in visual field defect, mainly bitemporal deficit, and blurred vision. Lateral or cavernous sinus extension could lead to diplopia due to compression of the third, fourth and sixth cranial nerve, with sixth nerve compression being the most prevalent because of its medial position in cavernous sinus (Ogra et al, 2014)[5]. In functional adenoma, the presentations depend on the hormone over secretion. Increased prolactin levels in prolactinoma may result in decreased libido and infertility in both sexes, oligomenorrhea or amenorrhea and galactorrhea in women and erectile dysfunction in men. Overproduction of growth hormone results in hand and foot enlargement, alterations in facial features, and gigantism if the excessive hormone develops before the epiphyses closing. Hypercortisolism due to ACTH excessive production causes Cushing syndrome, manifested by weight gain, redistribution of fat resulting in centripetal obesity, diabetes mellitus, hypertension and mood disorders (Molitch, 2017)[4].

Surgery is indicated for patients with visual impairment due to tumor compression and prolactinomas resistant to medical therapy (Russ et al, 2021)[6]. Transsphenoidal approach has been a gold standard for sellar tumor surgery and has evolved significantly over past century (Gandhi et al, 2009)[7]. Horsley performed first operation for PAs using transcranial approach (Choe et al, 2008)[8] and by 1907, Schloffer was the first to resect pituitary tumor with nasal transsphenoidal approach. Cushing then introduced sublabial transsphenoidal approach in 1910 and in1960, Hardy developed Cushing's technique with the introduction of microscope (Liu et al, 2001)[9]. Jankowski et al (1992)[10]demonstrated a fully endoscopic surgery for PAs in 1992, arguing that the approach improved the surgeon's ability to identify vital structures and perform tumor resection with suprasellar and parasellar extension. In recent years, endoscopic transsphenoidal surgery has been a favoured procedure due to its advantages of improved visibility and minimum invasiveness (Gao et al, 2014)[11].

From 2003 to 2015, our institution used endoscopic transsphenoidal surgery which was the standard procedure for PAs resection. Since of 2016, the surgery has shifted to microscopic sublabial approach. This study presented a retrospective study to report our experience in pituitary surgery that had shifted from endoscopic to microscopic approach.

Methods

Selection of Patients

A retrospective analysis was conducted after getting approval from the ethical committee of the hospital. Patients with sellar tumors who received transsphenoidal surgery was done by Dr DK Vatsal, at KK Hospital & ICON Hospital, Lucknow, India during 2003-2022 were included in our study. Exclusion criteria were tumors with histopathology results of non-pituitary adenoma. All patients were clinically examined including visual acuity, visual field, and eye movements. The hormonal analysis and radiological examination of brain magnetic resonance imaging (MRI) were performed to establish the diagnosis.

Surgical Procedure

Endoscopic approach was a standard procedure in our institution for sellar tumor from 2003 to 2015. Since 2016, all patients with PAs who had been indicated for operation had received microscopic transsphenoidal surgery as a standard of treatment. Both surgeries were done under general anesthesia. Consultant neurosurgeons performed microscopic surgery using Zeiss Sensera Microscope through sublabial approach. The head is slightly tilted so that the bridge of the nose is almost kept parallel to the floor and turned fifteen degrees towards the surgeon. The nostrils were decongested using gauze soaked by 1:100,000 epinephrine. Sublabial mucosa was incised using a small blade, then the mucosa was bluntly dissected from the septum to find a junction of nasal septum and rostrum of sphenoid. Hardy's speculum was docked to widen the operating field. After dissecting the septum from the rostrum, the keel bone was removed using Pituitary Rongeurs, and the sphenoidalostium could be identified at 11 and 1 o'clock. Sphenoidotomy was done using chisel and Kerrison Rongeurs to find sphenoidal sinus. Mucosa and septum of sphenoid sinus could be found and removed using Pituitary Rongeurs and forceps. The surgeons identified the sellar floor, clivus posteriorly, planumsphenoidale anteriorly, the bulge of the internal carotid siphon immediately juxtaposed to the sella, and the opticocarotid recess in between the optic nerve and the carotid protuberance. The location of sellar floor was confirmed by fluoroscopy. The sellar floor was opened using a chisel and duralincision was performed in cruciate fashion. Under microscope visualization, the tumor removal was performed from the posterior and then anterior parts. The surgeons resected the tumor in a piecemeal fashion using tumor forceps and curette. Hemostasis was done with bipolar cautery and Surgicel absorbable hemostat. If cerebrospinal fluid (CSF) leakage was encountered, packing of sellar floor was performed with fat and fascia lata. Nasal packing was done by Merosil and the mucosal incision was closed with an absorbable suture. The nasal packing was removed 48 to 72 hours after surgery.

The positioning of the patients were similar to the position of the microscopic approach.

We used Karl Storz Endonasal Skull Base instruments for endoscopic transsphenoidal surgery. We used transostial approaches in the endoscopic endonasal procedure. In transostial approach, after the nasal mucosa was decongested with epinephrine solution, middle turbinate was set aside to ipsilateral under endoscopy guidance to find the sphenoidalostium medial to the superior turbinate. Sphenoethmoidal recess and surrounding mucosa could be coagulated using monopolarcautery to prevent bleeding, and the mucosa was dissected to expose the sphenoidalostium. Keel bone was dissected from nasal septum and removed using Pituitary Rongeurs. Sphenoidotomy was done with chisel, and procedure in sphenoidal phase was similar with microscopic but under endoscopic assistance. The surgeons could use single nostril technique if the size of the nose were sufficient to fit the scope and the surgical instruments. If the nostril size was too small, binostril technique could be used.

We generally performed four-hand techniques in the sellar phase: the first surgeon using both hands held the instruments to dissect or remove the tumor, while the second surgeon held the endoscope and suction. Binostril technique was used to avoid the tools from colliding with each other.

Assessment of Outcomes

We evaluated the extent of resection postoperatively with gross-total removal was defined by no pathological contrast enhancement in head CT immediately (1 –2 days) after surgery. CSF leakage was evaluated clinically by the presence of post-nasal drip and rhinorrhoea postoperatively. We routinely observed fluid output and balance of patients who received sellar tumor surgery. The diagnosis of diabetes insipidus (DI) was established if the urinary production was increased (> 1 5 0 0 mL/8 hour) with the rise of blood sodium level, low urinary sodium value, and diluted urine (< 3 0 0 mOsm/kg). Re-operation was performed if the patients did not gain symptoms improvement or their deficit worsened, with MRI evaluation showing large residue or regrowth of the tumor. Length of operation and blood loss volume of both surgeries were collected for our analysis.

Statistical Evaluation

Statistical analysis was performed using IBM SPSS Statistics 16.0 version (Chicago, Inc., USA). Categorical data is indicated by the number and percentage, while its mean and standard deviation indicates numerical data. The two groups, namely endoscopic and microscopic, were then compared based on sex, age, total resection, leakage, re-operation, DI, blood loss, and duration of operation using the Chi-Square test or Fisher's exact test for categorical data. Independent samples T-test or Mann-Whitney test were used for numerical data.

Results

Profile of Patients

There were 122 (58.1%) and 88 (41.9%) patients who underwent microscopic transsphenoidal approach and endoscopic transsphenoidal surgery, total of 210 patients from 2003-2022. Female patients were predominant (55.5 %), with mean age was 48 years. There was no statistical difference between microscopic dan endoscopic approaches regarding patients' gender and age (p=0.94 and p=0.08).Forty two (20%) patients had functioning pituitary adenoma and 168 (80%) patients were nonfunctioning adenoma. Of 42 functioning tumor cases, 3 patients (7.1%) had gigantism, and the rest were prolactinoma. The most common manifestations were visual field defect and low vision.

Outcome Assessment

Gross total removal was achieved in 79 (64.8%) patients of microscopic approach, and none of the endoscopic surgery patients had total removal. Surgical approach was not a significant factor related to extent of resection with P value of 0.23 (Table-1). Total resection could not done in patients with cavernous sinus extension, and no tumor that had extended to parasella could be removed totally.

The re-operation rate was in 10.7% patients who received microscopic surgery and 19.3% in endoscopic patients. All repeated surgeries were performed due to regrowth of the tumor. Out of re-operation cases, one endoscopic case was re-operated with microscopic technique because it was in the transition from endoscopic to microscopic surgery. The correlation between the surgical technique and re-operation rate was not significant (p=0.08).

Operative Time and Blood Loss

The mean operative length for microscopic approach was 80.40±41.20 minutes, shorter than endoscopic surgery length that was 240.55±45.36 minutes, the difference was significant (p=0.0001). Microscopic transsphenoidal approach had mean blood loss volume of 100.14±88.96 ml, while mean volume of endoscopic surgery was 150.20±100.26 ml. Although the amount of bleeding in endoscopic surgery was higher, the correlation of surgical approach and blood loss was not significant (p=0.07, Table-1).

Complication Rate

Post-operative CSF leakage was reported in 12 (9.8%) microscopic cases and 7 (8%) endoscopic patients. Microscopic and endoscopic surgery did not differ significantly in post-operative CSF leakage risk (p=0.63)(Table-3).

Diabetes insipidus was found in 40 (45.5) and 12 (9.8%) endoscopic and microscopic surgery patients. All patients who met DI insipidus criteria were treated with desmopressin nasal spray or tablet. The analysis showed that patients who received microscopic transsphenoidal surgery had significantly lower incidence of DI (p= 0.0001) than the endoscopic approach (Table-3).

Table-1: Distribution of Profile of patients and comparison of outcomes between Endoscopic and Microscopic surgery

Factors	**Endoscopic surgery (n=88)**	**Microscopic surgery (n=122)**	**p-value**
Male gender, no. (%)	40 (45.5)	56 (45.9)	0.94[a]
Age in years, mean±SD	46.00±14.24	49.07±11.40	0.08[b]
Total removal, no. (%)	0 (0.0)	79 (64.8)	0.01[a]*
Re-operation, no. (%)	17 (19.3)	13 (10.7)	0.08[a]
Blood loss in ml, mean±SD	150.20±100.26	100.14±88.96	0.07[c]
Operating time in minutes	240.55±45.36	80.40±41.20	0.0001[c]*

[a]Chi-square test, [b]Unpaired t-test, [c]Mann-Whitney U test, *Significant

Table-2: Comparison between tumor with and without cavernous sinus extension regarding outcome

Factors	With cavernous sinus extension (n=65)		Without cavernous sinus extension (n=145)		p-value[1]
	No.	%	No.	%	
Total removal	0	0.0	65	44.8	0.82
Re-operation	38	58.5	0	0.0	0.08
Post-operative CSF leakage	4	6.2	15	10.3	0.32

[1]Chi-square test

Table-3: Comparison between Endoscopic and Microscopic surgery

Factors	Endoscopic surgery (n=88)		Microscopic surgery (n=122)		p-value[1]
	No.	%	No.	%	
Post-operative CSF leakage	7	8.0	12	9.8	0.63
Diabetes insipidus	40	45.5	12	9.8	0.0001*

[1]Chi-square test, *Significant

Discussion

Several studies have compared outcomes and complications between endoscopic and microscopic endonasal surgery in treating pituitary tumor. Endoscopic approach was reported to have technical superiority of panoramic visualization (Dhandapani et al, 2018)[12].

Our study showed that surgical approach did not have significant relation with extent of resection. The result is not in accordance with previous studies that reported endoscopic transsphenoidal surgery significantly increased incidence of gross total removal compared to microscopic surgery (Dhandapani et al, 2021; Møller et al, 2020)[13,14]. However, more studies showed that the endoscopic transsphenoidal approach did not significantly correlate with extent of resection (Little et al, 2020; Ahmad et al, 2020)[15,16] similar with our result, though a meta-analysis of 18 papers showed endoscopic approach was superior (Li et al, 2017)[17]. Our research also showed that none of the patients who underwent endoscopic surgery had gross total removal, 79 (64.8%) patients of microscopic surgery had total tumor resection. Besides higher grade of Knosp in endoscopic patients, this phenomenon could also be explained by the lack of experience in handling endoscopy instruments. A study by Zaidi et al (2016)[18] showed that microscopic surgeries performed by more experienced neurosurgeons produced more gross total tumor resection than endoscopic surgery. However, the result was not statistically significant.

Besides surgical technique, tumor size and extension should be considered when setting total gross removal as a goal of surgery. Tumors with higher Knosp grade and larger size significantly had lower rate of complete resection, according to a study by Ahmad et al (2020)[16]. Those findings are consistent with the result of our research; tumor extension to cavernous sinus was inversely related to gross total resection, while suprasellar extension did not significantly correlate with the extent of resection. The findings are understandable given that the transsphenoidal approach could not reach the lateral side of the sella, and aggressive resection of tumor at cavernous sinus could lead to massive intraoperative bleeding and cranial nerve palsies. It should be noted that endoscopic patients in this study had higher grade of Knosp, but the resection rate was not significantly lower than the microscopic patients. Suprasellar extension is not a barrier to total resection because it can be resected through an extended endoscopic transsphenoidal approach.

Persistent CSF leaking is the major cause of morbidity following transsphenoidal surgery for pituitary tumor (Yang et al, 2019)[19]. Previous studies comparison of leakage rates between endoscopic and microscopic transsphenoidal surgery showed different results. In one retrospective study, CSF leakage was significantly higher in endoscopic patients (Azad et al, 2017)[20]. However, many other papers concluded that surgical approach did not significantly affect the incidence of CSF leakage (Little et al, 2020; Dhandapani et al, 2021)[15,13] including a meta-analysis of fifteen studies (Gao et al, 2014)[11]. In our series, CSF keal was higher in microscopic group but there was no significant difference. It also appeared that tumor extension to suprasellar region or cavernous sinus did not affect the incidence of postoperative leakage.

The rate of DI after surgery was various in previous reports. Some studies reported no significant difference in DI rate between endoscopic and microscopic surgery (Dhandapani et al, 2021; Ahmad et al, 2020)[13,16] while reports by Zaidi et al (2016)[18]and Razak et al (2013)[21]favoured endoscopic over microscopic approach. These contrast with a study by Azad et al that favoured a microscopic approach (Azad et al, 2017)[20], consistent with our finding. Unfortunately, our research did not track whether the patients had temporary or permanent DI. With its enhanced visualization, the surgeons may perform more aggressive resections that could lead to stalk manipulation; this phenomenon may explain our result that showed higher incidence of DI in endoscopic patients. However, though the operators tended to be aggressive with an endoscope, the rate of postoperative CSF leakage was not different between the two approaches; this could be elaborated that the intraoperative leakage correction was easier and treated more precisely using endoscopy assistance. This led to successful closure, so clinical CSF leakage did not appear postoperatively.

In our study, the endoscopic approach's blood loss and operative length were higher and longer than the microscopic one, although blood loss was not statistically significant and operating time was statistically significant. It appeared that the operator's skill is an essential factor determining the result. A study by Guo-Dong et al (2016)[22] suggested that duration of surgery affected intraoperative bleeding. Some factors could cause the operative time of endoscopic surgery longer, such as preparation of both nostrils, manipulations that caused bleeding which obscured the lens and required saline irrigation, and inappropriate irrigation. Control of bleeding in the endoscopic approach is challenging, which could prolong surgical time. With years of experience in transsphenoidal surgery using a microscope, it takes time for our neurosurgeons to become accustomed to handling endoscopic instruments effectively.

There are some limitations to this study. First, the design of this report is retrospective. Second, we think the number of endoscopic patients in our institution is still small.

Conclusion

The results of our microscopic surgery are better than the endoscopic approach in terms of total removal, time of surgery and incidence of DI. There is a significant less time of surgery, more percentage of gross total removal and decreased DI in microscopic sublabial technique. These data support shift to microscopic surgery from endoscopic surgery.

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