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Outcomes of Transnasal Endoscopic Removal of Pituitary Tumors

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Abstract: ***Pituitary adenomas are common benign tumors of the pituitary gland. Endoscopic trans sphenoidal approach for resection of the tumor is widely applied recently. 50 pituitary adenoma cases from January 2015 to January 2016, operated by trans sphenoidal approach endoscopically were included in this study which were assessed clinically for hormonal imbalance and visual symptoms and radiologically for tumor extension. Post operatively patients were assessed at timely intervals for complications. 39 patients out of 50 patients diagnosed with pituitary adenoma got remission with fewer complications. In conclusion, this study demonstrates that endoscopic endonasal surgery for pituitary adenomas has a high imaging total removal rate (64%) while the endocrinological remission rate of functional pituitary adenoma is 78%.***

Keywords: endoscopic approach, pituitary adenomas, trans-sphenoidal

1. Introduction

Pituitary adenomas are common benign tumors of the pituitary gland, accounting for 10% of all intracranial tumors. Their incidence in unselective autopsies is as high as 20-30% . Microscopic transsphenoidal surgery has long been considered the "gold standard" in surgical treatment of pituitary tumors. Many large series have reported the efficacy, safety, and limitations of this approach. Over the last two decades, however, endoscopic endonasal surgery has gradually gained favor as a primary approach for sellar and parasellar lesions, primarily due to the wide panoramic, up-close visualization offered by the endoscope. In the past, the endoscopic transsphenoidal approach or transfrontal basal approach was mainly adopted for its excision. Although several studies explored the pathogenesis of pituitary adenomas in order to seek new treatments, no new molecular targeted therapies were identified**.** In recent years, with the rapid development of the endoscopic technique, endoscopic neurosurgery has become one of the most active fields of neurosurgery, with the transsphenoidal approach through the bilateral nostrils for resection of pituitary adenomas representing perhaps the most mature and widest application of this surgical technique. In this report, we perform an in-depth evaluation of this technique and highlight the operating characteristics and clinical outcomes.

The classification of tumor is based on modifications of the sella turcica on plain x-ray studies and is now adapted to MRI findings. The tumors are divided in four groups as follows.

Grade I tumors, or microadenomas, are lesions up to 10mm in time in diameter.
Grade II tumors arc more than 1 cm in diameter and cause diffuse enlargement of the sella turcica with or without suprasellar extension. These non invasive macroadenomas remain enclosed in the anatomical structures containing the pituitary gland (diaphragma sellar, medial wall of the cavernous sinus, dura of sellar floor and dorsum sellar) that can be displaced but not invaded.

Grade III tumors are adenomas which show signs of local invasion. Some of them can be smaller than 10mm (invasive microadenomas).

Grade IV tumors show extensive and diffuse invasion oi the skull base and/or the intracranial space1.

Radiologic assessment of parasellar invasion presents the problem of distinguishing whether the inner wall of the cavernous sinus has been infiltrated or simply displaced.

From January 2015 to January 2016, with the collaboration of Department of Otorhinolaryngology and Department of Neurosurgery, we operated 50 cases of pituitary adenoma using transsphenoidal endoscopic approach and achieved satisfactory results. In this report, we aim to review in-depth evaluation of the endoscopic technique and highlight the clinical outcomes of the patients.

2. Material and Methods

Total 50 cases of pituitary adenoma were operated by transphenoidal endoscopic approach from January 2015 to January 2016 at the Department of Otorhinolaryngology and Department of Neurosurgery, B.J Medical College and Civil Hospital, Ahmedabad. All sellar and suprasellar pituitary tumors treated by endoscopic transhenoidal approach were included in the study. The exclusion criteria included the patients managed conservatively, cases operated by

transcranial approach and the sellar and suprasellar masses with pathologies other than pituitary adenoma. All patients were assessed clinically for hormonal imbalance signs and symptoms, headaches, visual symptoms (fundoscopy, visual acuity, color vision and field of vision). Pre–operative investigations include visual perimetry, hormonal assay, x-ray skull and Computer Tomography scan and Magnetic Resonance imaging(brain and sellar). Post operative outcome of all patients was recorded on the time scale of immediate postoperative, 3 months, 6 months and 2 years.

3. Results

Table 1: Age and gender distribution

Age(years)	Percentage
11-20	2
21-30	18
31-40	28
41-50	35
51-60	12
61-70	4
71-80	1

Gender	Cases(Percentage)
Male	19(38 %)
Female	31(62 %)

Classification

- Considering the size and extension of the tumour the patients were sorted in 2 groups
- Microadenoma (size < 10 mm) – 5
- Macroadenoma (size <10 mm) – 45
- Out of 50 cases 12 had suprasellar extension.

Table 2: Distribution Of Cases

Type Of Tumor	Cases(Percentage)
Non Functioning Adenoma	31(62 %)
Gh Adenoma	6(12 %)
Tsh Adenoma	0(0 %)
Acth Adenoma	3(6 %)
Gonado Adenoma	0(0%)
Prolactinoma	10(20%)
Total	50

Table 3: Extent of Tumor Removal

Extent of removal	Cases (Percentage)
Total removal	32(64 %)
Near total removal	15(30 %)
Partial removal	3(6 %)
	50

Table 4: Clinical Features

Clinical Feature	Cases (Percentage)
Visual Impairment	33(66 %)
Headache	28(56 %)
Amenorrhea	10(20 %)
Abnormal Lactation	10(20 %)
Acromegaly	4(8 %)
Infertility	2(4 %)

Table 5: Complications

Complications	Cases
Csf Rhinorrhea	4
Diabetes Insipidous	6
Meningitis	0
Haemorrhage	0
Stroke	0
Damage To Pituitary	0
Visual Loss	0

A total of 50 patients who were diagnosed as pituitary adenoma underwent endoscopic trans sphenoidal excision of pituitaryexcision at our institution from January 2015 to January 2016 were incuded in our Retrospective & prospective analysis. Age, gender, clinical features, etiology, radiological features and surgical outcomes were considered for analysis. The result of the study was analysed by appropriate statistical tool. The mean follow up period was 13.1 months.

The results of the study areas follows.

The age of the patient ranged from 18 years to 75 years. Maximum number of patients were between 41 to 50 yrs (35%).
62 % were females & 38% males. There was slight female preponderance seen.

Most common clinical symptom seen in our study series was visual disturbance followed by headache. These symptoms of mass effect are much common than endocrinologic dysfunction of acromegaly and galactorrhea amenorrhea syndrome. Optic nerve involvement is other common clinical finding presenting in form of decreased vision or loss of vision, field defect or fundus changes. Commonest field defect observed was bitemporal hemianopia.

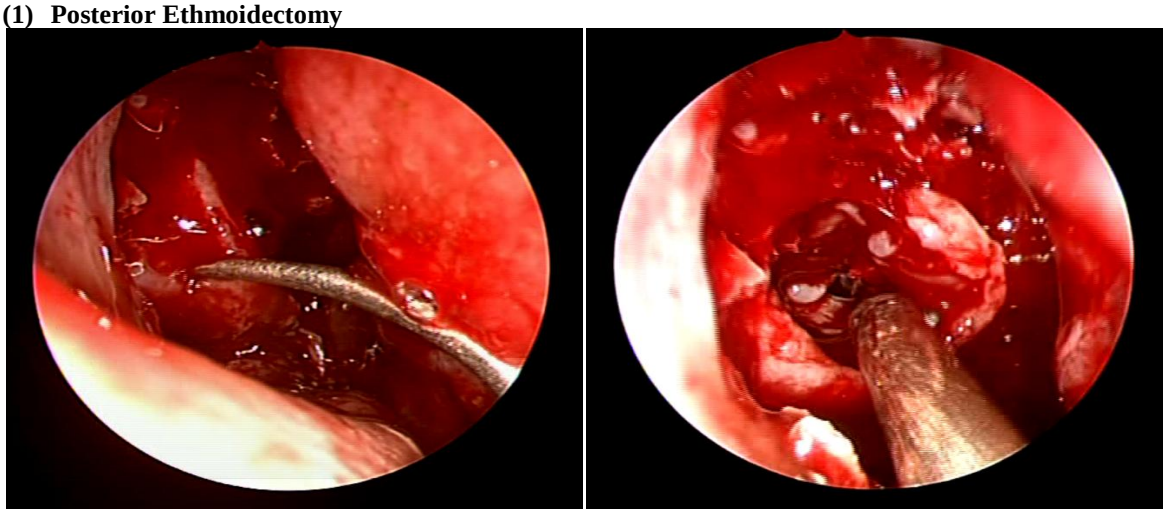
More than half of the patients exhibited normal preoperative pituitary function in form of baseline hormone profile. Among 50 patients 31 were NFPA, 6 were GH adenoma, 3 were ACTH adenoma, 10 were prolactinoma and 2 patients with apoplexy. MRI is the investigation of choice in pituitary tumors to define extent, invasion and relationship to major vessels and nerves.

Total/near total removal was done in 32 patients and subtotal removal done in 18 patients. Adjuvant therapies were given in 5 patients. Two patients were given radiotherapy and 3 were given pharmacotherapy.

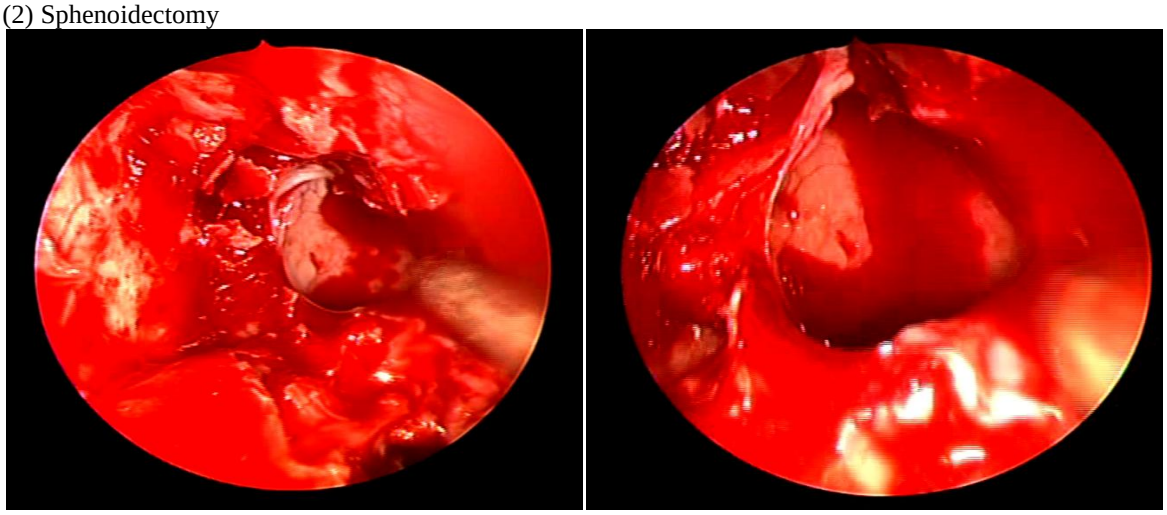
The post operative complications were CSF leak 4 patients, Diabetes insipidus 6 cases. 24 patients out of 31 patients diagnosed with non functioning adenoma got remission, 5 patients out of 6 diagnosed with GH adenoma got remission, 7 patients out of 10 diagnosed with prolactinoma got remission, and all 3 cases diagnosed with ACTH adenoma got remission. Post operatively visual functions improved in 23 patients and it remained stationary in 26 patients. Only one patient complained of worsening of his visual function immediately after surgery which improved in followup period.

Steps of operative procedure:

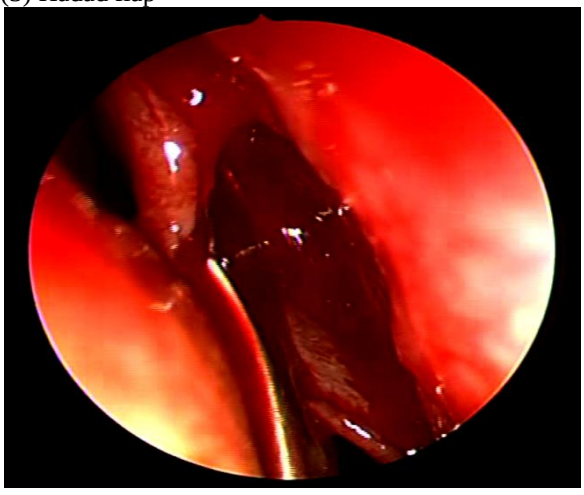
(1) Posterior Ethmoidectomy



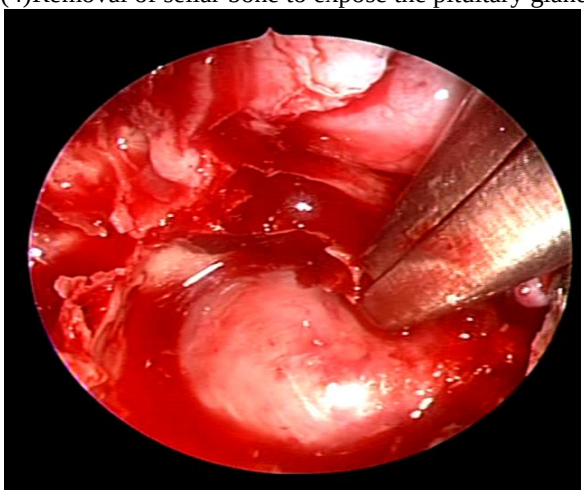
(2) Sphenoidectomy



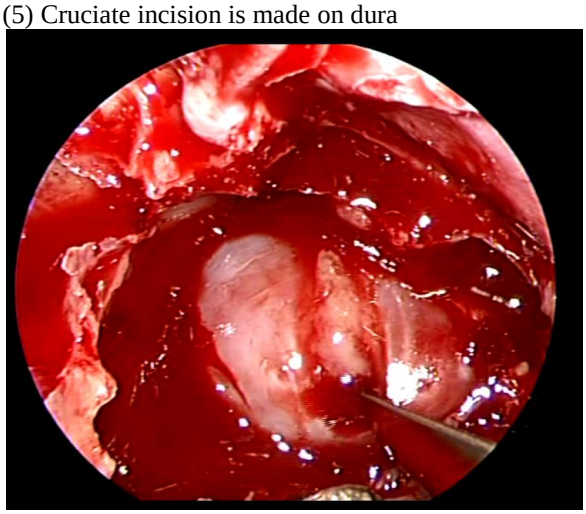
(3) Hadad flap

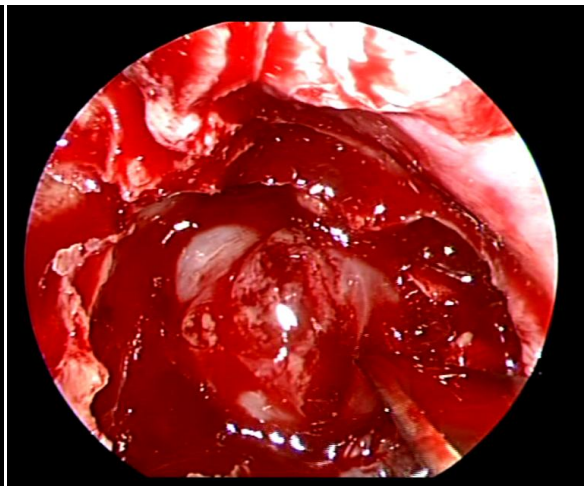


(4)Removal of sellar bone to expose the pituitary gland

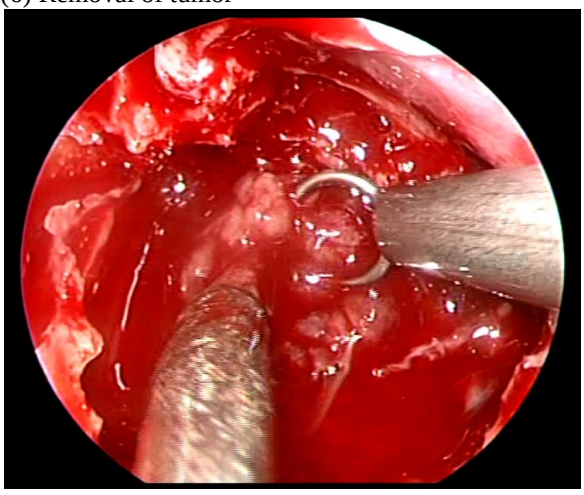


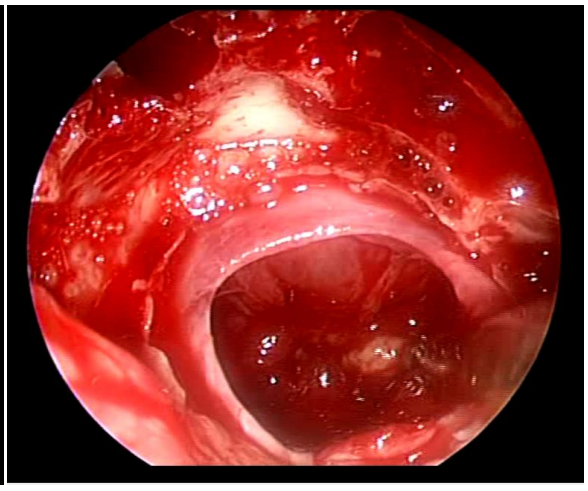
(5) Cruciate incision is made on dura





(6) Removal of tumor





4. Discussion

The age range in present study was from 18 to 75 years. The majority of patients were in the 4th to 6th decade of their life. Similar age distribution pattern were seen in series by Minderman *et al [1]*who found peak incidence between fourth to sixth decade of life. Sex incidence shows female preponderance in our series (M: F- 1:1.6). Similar sex incidence ratios shown in kazumora *et al [2]*(M: F- 3:4) series of 42 patients. Major complain among the patients was visual disturbance (33/50) followed by headache (28/50).

Amenorrhea, abnormal lactation, acromegaly, infertility and vomiting were among the other complains. 10 patients presented with clinical syndrome of amenorrhea and galactorrhea while 4 patients presented with acromegaly features. In series by thaper *et al[3]*. 73% patients presented with mass effect and 86% had endocrinopathy. Many of the patients had presented with signs/symptoms of both mass effect and endocrinopathy and was due to propensity of these tumors to cause multisystem dysfunction and variable combination of mass effect and endocrinal dysfunction. 62% of tumors of pituitary gland in our study were nonfunctioning followed by prolactinoma 20% followed by GH adenoma 12%.

Robert y. osmura *et al[4]* had presented study of 328 cases of pituitary adenomas and have found non functioning adenomas as most common type (31.5%) followed by GH and prolactin producing adenomas. These diagnoses were further confirmed by immunohistochemistry and ultrastructural features in their series. Erfurth *et al[5]*, demonstrated that amongst a cohort of 328 patients of pituitary tumor, 78.8% were non functioning, 21% prolactinomas and remaining others. In past years, MRI has become the procedure of choice in diagnosis of pituitary tumors. While CT scans shows pituitary adenomas as low density lesion in pituitary gland/sellar region. An MRI picture of pituitary differs in different intensity modes. It is of intermediate intensity on T1 weighted image which enhances intensively on gadolinium contrast and hyperintense of T2 weighted image. Multiplanar display of parasellar structures in relation with tumors shows more with MRI. In our series we perform CT and MRI in all cases, MRI is the investigation of choice for these tumors, showing extra sellar extension, mass effects and CT for erosion. Lundin p *et al[6]* in a series diagnosed these tumors solely on MRI basis in 72%. The patients in our study were subjected to surgery as the first and in many cases the only line of definitive treatment. Total/ near total excision of tumors was done in 64% while in remaining 36% a subtotal excision could be done. On analyzing the data subtotal excision was done due to extensive parasellar and suprasellar extension of tumor and the adherence of same to vital neurovascular structures. In study of Xue-feiShou *et al[7]* total resection was done in 84.5% and subtotal/partial resection done in 15.5%. In study of Amin b Kassam *et al* [8]the figure was 93% for total resection and 7% for subtotal resection. We included only the cases operated through the transsphenoidal route in our study and this is the preferred treatment now a day if not contraindicated. Thomas *et al [9]* in a series of 104 cases of pituitary adenomas used the transnasal transsphenoidal route in 84 of patients, while various other transcranial approaches in remaining 20. Similar preference to transnasal routes is preferred by Tyrrnel J Blake *et al[9]*, Sethi DS *et al [11]*and Shimon *et al [12]*. It can be said surgeon's personal preference and experience, availability of infrastructure and tumor extension into neighbouring areas decides the choice of surgical procedure with more and more surgeons favouring endoscopic transsphenoidal techniques if not contraindicated. 70% show improvement in visual function in Salmi *et al[15]* series. 46% of patients in series by Shone *et al[13]* had visual improvement following surgery. The figures were 46% in our series and were in form of increased visual acuity and improvement of field vision as compared to pre operative status. Visual acuity was decreased in 1 patient postoperatively which improved in follow up examination. Visual acuity was improved in totally/near totally resected group and remains stationary/worsened mainly in subtotal/near total resection group. Visual outcomes shown are of immediate postoperative period and initial follow up. We require long follow up for more encouraging results. Overall postoperative remission in our series was achieved in 78% of patients: 83% with GH adenoma and 100% with ACTH adenoma, & 70% for Prolactinoma. Tumor size significantly influence surgical outcome. Patients diagnosed with microadenoma had greater chance for remission after surgery.

Tumor type did not significantly influence surgical outcome. We had 0% mortality and 21% morbidity in our series. Series by Thaper *et al [3]*report mortality rate of 15 and morbidity of 15% while another study by Zervas *et al [14]*reports mortality rate of 0.5% and morbidity of 2.20%. Morbidity was in form of CSF leaks, diabetes insipidus, wound infection etc.DI occurs in 12% of cases which is usually transient in nature. This occurs mainly in the patients in which total/neartotal removal of tumor was done. This may simply reflect the extreme sensitivity of the hypothalamic-neurohypophyseal unit to local alterations in blood flow, edema, and traction on the pituitary stalk. Permanent disturbance of antidiuretic hormone(ADH) secretion is due to direct damage to the neurohypophyseal unit and depends much more on the original size and location of the tumor and the extent of surgical resection. Postoperative CSF leak was seen in 8% of cases, which can be managed by conservative means like lumbar drain. Reexploration required in cases not heals by conservative means. Postoperative CSF leak can be avoided not only by careful surgical technique, but also by the use of lumbar drain for diversion of CSF that helps the cisternal repairing of small CSF leak. Lumbar drain should be kept for minimum duration because it can lead to meningitis by infection due to skin bacteria.

Visual deterioration occurs in 1 patient in our series but it was transient and improved in follow up period. Damage to optic nerves and chiasm can also occur from direct surgical damage, hemorrhage or ischemia. Many patients have preoperative compromise of visual function, making them more vulnerable to further damage. As in our patient vision was already compromised due to apoplexy. Difference in percentage of complications might be due to small sample size in our series. With development of neuroimaging techniques and neuroanaesthesia, along with modern biochemical investigative facilities, aided by newer drugs in management of pituitary cases, overall prognosis of these tumors has became very favourable. Modern microneurosurgery has made the life more comfortable for patients and surgeon alike. No definitive genetic predisposition or aggravating factors in causation of pituitary tumors are established and because nor any preventive solution exist, surgery remains mainstay for neurologically compromised patients and this is well established by available literature and present studies.

5. Conclusion

In conclusion, this study demonstrates that endoscopic endonasal surgery for pituitary adenomas has a high imaging total removal rate (64%) while the endocrinological remission rate of functional pituitary adenoma is 78%. Improvement in surgical skills and familiarity to endoscopic surgery, tumor removal rate and endocrinological remission rate is improved gradually, with the decrease of the complication rate and the length of learning curve. The endoscopic transsphenoidal approach for pituitary adenoma resection has advantages; its main purposes are to reduce surgical trauma, expand tumor exposure, increase the chances of complete tumor excision under erthyphoria, and reduce tumor recurrence. With constantly improved technology and equipment, this technique will surely undergo further development and implementation.

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