

A COMPARATIVE STUDY BETWEEN ENDONASAL ENDOSCOPIC AND MICROSCOPIC TRANSSPHENOIDAL APPROACHES IN MANAGEMENT OF PITUITARY ADENOMAS

By

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ABSTRACT

Background: Advances in the era of modern micro-neurosurgery enabled a reduction of surgical invasiveness and brain retraction which has been defined as minimally invasive or keyhole surgery. Sinonasal endoscopy has brought radical changes in the concepts of pathophysiology and treatment of sinonasal diseases as well as surgical techniques.

Objective: Assessment of patient outcomes regarding transsphenoidal endoscopic and microscopic approaches of pituitary adenomas.

Patients and methods: Our study included 40 cases of pituitary adenomas, operated upon during 2 years, half of them (group A; 20 cases) underwent endoscopic endonasal transsphenoidal pituitary adenoma resection, while the remaining (group B; 20 cases) operated upon using the standard microscopic transsphenoidal pituitary adenoma resection.

Results: The highest age incidence of our cases was during the third and fourth decades of life, with a male to female ratio of nearly 1:1. Headache was the commonest presenting symptom in our series both in endoscopic and microscopic groups; (60% & 70%) respectively followed by visual impairment; (55% & 60%). Although, loss of libido was the most common endocrinopathies; (75% & 60%) respectively. In our study CT-sella with coronal cuts was the initial radiographic investigation, performed in all our cases. It gave an idea about bony anatomy of the sella, sphenoid sinus, and particularly was important in showing the position of the sphenoid sinus septum, which was crucial in planning the decision of operation. In our study, improvement in out-come was higher in endoscopic group opposed to microscopic group (100% vs. 71% improved headache, 82% vs. 58% visual improvement and 80% vs. 55% total tumor removal).

Conclusion: Endoscopy offers a very special and wide visualization, close to the target and inside the anatomy. The panoramic view provided by the endoscope, allowing the identification of all the landmarks around the sella during the entire procedure, minimizes the chance of an inaccurate orientation.

Keywords: Endonasal Endoscopic, Microscopic Transsphenoidal Approaches, Management of Pituitary Adenomas.

INTRODUCTION

Among all the intracranial tumors, pituitary adenomas represent the third most common lesion, with a prevalence of

16.9% in autopsy studies (*Ezzat et al., 2014*). The management of these lesions can become particularly challenging especially in those classified as large or

giant and with wide intracranial extension or prevalent inferior involvement down into the nasal and paranasal cavities (Cappabianca *et al.*, 2012).

The operative microscope soon became the standard for transsphenoidal pituitary tumor resections. The mid 1990's saw the emergence of rigid endoscopes for resection of pituitary tumors (Gamea *et al.*, 2010). Shortly after its introduction, several institutions began to transition to endoscopic techniques due to the improved visualization provided by the endoscope's wider and angled views (Zaidi *et al.*, 2016).

Proponents of the endoscopic approach believe that the improved visualization and additional lighting allows for better differentiation between tumor and normal gland, which may improve preservation of pituitary function and increase extent of tumor resection (EOR) (Cavallo *et al.*, 2012).

Immediately following its introduction, expanded endonasal approaches to intracranial lesions faced substantial criticism due to their high risk of postoperative cerebrospinal fluid (CSF) leak and the perceived risk of intracranial infection with sinonasal flora. Progressive development of the technique, led by multiple pioneering centers around the world, reduced these pertinent concerns. We are approaching the 10th anniversary of the pedicled nasoseptal flap, which was quickly adopted worldwide and dramatically reduced postoperative CSF leak rates, making the technique reliable and reproducible. Furthermore, the apprehension regarding high rates of postoperative infection proved to be unfounded. Consequently, endoscopic

endonasal approaches (EEAs) to address intracranial diseases became a viable alternative to traditional approaches (Sinha *et al.*, 2010).

The conventional transcranial approach has been traditionally the first choice for the removal of large intracranial adenomas, because of limited visualization beyond the sella provided by microscopic transsphenoidal approaches (Sinha *et al.*, 2010).

The improved visualization gained with the introduction of the endoscope, adopted over the past two decades for the treatment of pituitary adenomas and other sellar lesions, has opened the possibility of removing lesions that grow considerably beyond the sella, thus greatly increasing the number of tumors being approached via the transsphenoidal route (Cappabianca *et al.*, 2012).

In many neurosurgical centers worldwide, endoscopic approaches are routinely used in clinical practice (Di Maio *et al.*, 2011).

The aim of the present work was assessment of patient outcomes regarding transsphenoidal endoscopic and microscopic approaches of pituitary adenomas.

PATIENTS AND METHODS

This present work was a comparative study between 2 different transsphenoidal approaches to pituitary adenomas; endoscopic and microscopic. Data were collected retrospectively mainly but also prospectively for all patients who underwent either microscopic or endoscopic transsphenoidal resection of pituitary tumors over period of 2 years.

Total 40 adult patients were included in our study, divided into 2 equal groups: group A underwent microscopic surgery, while group B underwent endoscopic one.

Patient inclusion criteria included adult patients, having macroadenoma with mass effect, prolactinomas with prolactin level > 150 ng/dl not responding to medical treatment, other functioning adenomas like acromegaly and Cushing's disease. Also, at least 6 months follow up after surgery was required.

Exclusion criteria was children, nonfunction adenoma with no mass effect and deemed more suitable for conservative management, prolactinomas responding to medical treatment and patients with less than 6 months follow up after surgery.

Preoperatively, all patients had full endocrinology assessment including prolactin, IGF-1, GH, ACTH, fasting 8 am cortisol level, TSH, free T3 and T4, LH and FSH. Other tests were done if needed including oral glucose suppression test and overnight dexamethasone suppression test in cases of acromegaly and Cushing's disease respectively.

Full visual assessment also was done including visual field, visual acuity and fundus examination.

All patients had preoperative MRI pituitary gland with T1, T2, and T1 post

contrast sequences and CT nasal sinuses to aid the preoperative planning.

Postoperatively, all patients underwent endocrinological evaluation at 2 weeks, 6 weeks and 6 months. MRI was repeated after 6 months. Regarding secreting tumors, relevant endocrinological tests were done. Hospital stay, operative time, extends on intraoperative exposure, post-operative complications.

The microscopic approach was performed by a neurosurgeon experienced in the transseptal route, whereas the endoscopic approach, employed the 2 nostril, 4 hand technique performed by a neurosurgeon and an otolaryngologist.

Statistical analysis:

Recorded data were analyzed using the statistical package for the social sciences, version 20.0 (SPSS Inc., Chicago, Illinois, USA). Quantitative data were expressed as range. Qualitative data were expressed as frequency and percentage. Chi-square (x2) test or Fisher's exact test of significance was used in order to compare proportions between two qualitative parameters. The confidence interval was set to 95% and the margin of error accepted was set to 5%. P-value <0.05 was considered significant.

RESULTS

No statistically significant difference could be detected between both studied groups as regard presenting symptoms. Headache was the commonest presenting symptom in both endoscopic and

microscopic groups (60% & 70% respectively) followed by visual impairment (55% & 60% respectively). Although, loss of libido was the most common endocrinopathies (75% & 60%

respectively). The most common type of sphenoid sinus in both groups was the sellar type, followed by the conchal and presellar types. The sphenoid sinus septa could be easily described from CT images whether single or multiple. The sellar floor was intact in 40% of endoscopic cases and in 60% of microscopic cases.

No statistically significant difference could be detected between both studied groups as regard preoperative CT findings. Endocrinopathies were the most common indication followed by failure of previous management then visual or cranial nerve affection, while hydrocephalus came in the last (**Table 1**).

Table (1): Age, sex range, previous management, endocrinopathies, preoperative CT findings and indication for surgery in both studied groups

Parameters \ Groups		Endoscopic group (N=20)	Microscopic group (N=20)
Age		24 years -65 years	28 years- 60 years
Sex		10 male -10 female	12 male -8 female
Previous management	Medical	3 (15%)	4 (20%)
	Surgical	6 (30%)	4 (20%)
	G- knife	2 (10%)	3 (15%)
	Non	9(45%)	9 (45%)
Endocrinopathies	Headache	12 (60%)	14 (70%)
	Field	10(50%)	11(55%)
	Fundus	4 (20%)	5 (25%)
	Visual	11 (55%)	12 (60%)
	Acromegaly	4 (20%)	3 (15%)
	Cushing	2 (10%)	2 (10%)
	Loss of lipido	15 (75%)	12 (60%)
	Amen/ galact syndrome	7 (35%)	6 (30%)
	Hypopituitarism	4(20%)	5(25%)
Preoperative CT findings	Type of sphenoid sinus		
	Sellar	13(65%)	14(70%)
	Presellar	3(15%)	2(10%)
	Conchal	4 (20%)	4 (20%)
	Sellar floor		
	Intact	8 (40%)	12 (60%)
Indication for surgery	Not intact	12 (60%)	8 (40%)
	Sphenoid sinus septum		
	Single	10(50%)	11 (55%)
	multiple	10 (50%)	9 (45%)
	Failure of previous management	8 (40%)	11 (55%)
	Visual or Cranial nerve affection	10 (50%)	13 (65%)
	Hydrocephalus	1 (5%)	2 (10%)
	Endocrinopathies	16 80%)	15(75%)

Nasal complications were more common among microscopic group compared to endoscopic group with significant difference in between by chi-square test. CSF leak occurred in 3 microscopic cases versus 4 endoscopic cases. Yet, meningitis was not recognized

as one of postoperative sequelae in this study. Headache was the most common symptom to improve postoperative both in microscopic and endoscopic groups; 71 and 100% with a significant difference in between by chi-square test (**Table 2**).

Table (2): Postoperative complications and postoperative improvement

Parameters		Groups	Endoscopic, N=20	Microscopic, N=20	P
Postoperative complications	Diabetes insipidus		4 (20%)	3(15%)	>0.05
	CSF leak		4 (20%)	3(15%)	>0.05
	Nasal		4 (20%)	15 (75%)	<0.001
	Hypopituitarism		3(15%)	3(15%)	>0.05
	Deterioration of consciousness		0(0%)	0(0%)	>0.05
	Meningitis		0(0%)	0(0%)	>0.05
	Visual deterioration		0(0%)	2 (10%)	>0.05
Postoperative improvement	Visual		9/11 (82%)	7/12 (58%)	>0.05
	Fundus		3/4 (75%)	1/5 (20%)	>0.05
	Field		6/10(60%)	3/11(27%)	>0.05
	Headache		12/12 (100%)	10/14 (71%)	>0.05

Hormonal control was better achieved with endoscopic approach with best results seen with prolactinomas (**Table 3**).

Table (3): Post-operative hormonal improvement

Hormonal Level		Groups	Endoscopic	Microscopic
Improved to normal	Prolactin		5/5 (100%)	5/6 (84%)
	ACTH		4/5 (80%)	4/6 (66%)
	GH		4/5 (80%)	5/6 (84%)
Improved	Prolactin		0/5 (0%)	1/6 (16%)
	ACTH		1/5 (20%)	2/6 (33%)
	GH		1/5 (20%)	1/6 (16%)
	TSH		1/5 (20%)	0%

Concerning postoperative radiological (MRI) follow-up, tumor resection was divided into either total (refers to a complete gross total removal) or subtotal (anything less). Comparing both study

groups exposes 80% total resection in endoscopic group versus 55% in microscopic group with significant difference in between by chi-square test (**Table 4**).

Table (4): Postoperative radiological improvement

Improvement (Radiological)	Groups	Endoscopic, N=20	Microscopic, N= 20	P
Subtotal resection		4/20(20%)	9/20 (45%)	>0.05
Total resection		16/20(80%)	11/20 (55%)	>0.05

DISCUSSION

Our study included 40 cases of pituitary adenomas, operated upon during 2 years, half of them (group A; 20 cases) underwent endoscopic endonasal transsphenoidal pituitary adenoma resection, while the remaining (group B; 20 cases) operated upon using the standard microscopic transseptal transsphenoidal pituitary adenoma resection.

Selection between both groups (group A& B) and choice of the surgical approach was in a random order according to surgeon preference and expertise. The highest age incidence of our cases was during the third and fourth decades of life, with a male to female ratio of nearly 1:1 and this coincides with the findings of (Greenberg, 2011).

Headache was the commonest presenting symptom in our series both in endoscopic and microscopic groups; (60%& 70%) respectively followed by visual impairment; (55%& 60%). Although, loss of libido was the most common endocrinopathies; (75%& 60%) respectively. This coincides with the findings of (Blevins *et al.*, 2010 and Cavallo, 2012).

In our study, visual complaints were encountered in the form of diminution of vision, which was bilateral in all cases and was accompanied with bitemporal hemianopia in almost all cases presenting

with diminution of vision. While all hormonally active adenomas presented with endocrinal manifestations in the form of acromegaly, amenorrhea/ galactorrhea syndrome in female, loss of libido and impotence in male, and Cushing syndrome. This coincides with the findings of (Blevins *et al.*, 2010).

In our study, CT-sella with coronal cuts was the initial radiographic investigation, performed in all our cases. It gave an idea about bony anatomy of the sella, sphenoid sinus, and particularly was important in showing the position of the sphenoid sinus septum, which was crucial in planning the decision of operation. Throughout the study, MRI brain with and without contrast was performed before surgery in all patients as the main tool used for identification of the soft tissue relations of the tumor. MRI was also the main tool used throughout the study to judge the extent of surgical radicality being a more solid and reliable evidence. Also, Blevins *et al.* (2010) suggested the use of MRI as the main tool to judge surgical radicality. There was no constant relationship between tumor size and preoperative hormone levels, however, the larger tumors showed a higher level of preoperative prolactin especially in cases with cavernous sinus invasion for prolactin secreting adenomas. Also, there was no relationship between the MRI findings and the pathological nature of the. We performed follow-up MRI 3

months postoperatively. However; *Yoon et al. (2011)* advocates early postoperative MR imaging; as it is useful in the detection of residual tumor. Since the early postoperative sella retains its preoperative volume, one can easily differentiate residual tumor from a normal gland, implanted materials, or postsurgical granulation tissue. In addition, early postoperative MR images can be an excellent baseline if radiation therapy is necessary for treatment of residual tumor or recurrent tumor suspected on follow-up MR images.

In our study, prolactin level improved significantly in all cases of. Analysis of the hormonal profile results showed better results in endoscopic than microscopic group.

We found that the endoscope enabled better differentiation between tumor and normal pituitary tissue than the operating microscope, also better sight of residual cavity after tumor removal and these coincide with *Gamea et al. (2010)* who emphasized that the endoscope was helpful for tumor micro-dissection with excellent panoramic vision. *Batay et al. (2012)* performed a comparative study of an outlook obtained from an extended transsphenoid approach on 10 cadavers using both endoscope and microscope, a larger exposure was provided by the endoscope than by the operating microscope while measuring the horizontal and vertical extent. *Spencer et al. (2010)* had contributed through quantifying and comparing the “volumes of view” of the endoscope and microscope in the setting of pituitary surgery. In their anatomical study of surgical approaches to the pituitary gland, they were able to

objectively demonstrate with statistical significance that the 0° endoscope afforded more comprehensive views of the sella turcica than the microscope. Also, the longer operative distance was the main disadvantage in using the microscope. A surgeon inexperienced with the technique may become frustrated by the small operating space.

Complications in the fully endoscopic procedure can be almost completely avoided with careful technique. Incidence of morbidity is related to injuries to the normal gland or to surrounding neurovascular structures.

Throughout this study, complications associated with endoscopic surgery were, in general, fewer than with microsurgery as there was less wound trauma with the endoscopic approach resulted in less nasal complications. No patients with nasal septum perforation, sinusitis, and gum wound disruption or massive nasal bleeding. *Batay et al. (2012)* reported that 85% of patients with endoscopic hypophysectomy were satisfied with their nasal airways postoperatively, they had no operative infections. Improved visualization allowed the surgeon to identify and avoid injury to the normal pituitary, carotid prominences, hypothalamus and optic chiasm leading to fewer complications with better out-come. The incidence of sinusitis was higher in microscopic group, because the trauma to the sphenoid sinus and nasal cavity are greater. Visual deterioration was more common among microscopic group compared to endoscopic group. We distinguished four cases with diabetes insipidus in endoscopic group vs. three cases in microsurgery, also four cases

with CSF leak comparing to three for microscopic group, and this does not equivalent to what *Koren et al. (2011)*. *Louis et al. (2014)* reported the incidence of various complications in both groups was recorded, and the results were compared to those from a national survey by *Ciric et al. (2010)*. Our results were nearly parallel in the microscopic group, with reduction in the incidence of sinonasal complications in endoscopic group.

In our study, improvement in out-come was higher in endoscopic group opposed to microscopic group. *Sheehan et al. (2011)* compared a group of patients who underwent the sublabial approach with a group who were operated endoscopically and found no differences in out-come regarding vision and anterior pituitary function. *Cappabianca et al. (2012)* found improved out-come of endoscopic group against microscopic one regarding tumor excision and hormone imbalance. *Jho and Carrau (2010)* reported similar results. Preliminary evidence suggests that complication rates and surgical outcomes of our microscopic group were nearly parallel to those that have been reported in large series of transsphenoidal microscopic pituitary surgeries.

CONCLUSION

Endoscopy offers a very special and wide visualization, close to the target and inside the anatomy. The panoramic view provided by the endoscope, allowing the identification of all the landmarks around the sella during the entire procedure, minimizes the chance of an inaccurate orientation.

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دراسة مقارنة بين طرق التنظير الداخلي الأنفي والميكروسكوبية عبر العقد في علاج أورام الغدة النخامية

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خلفية البحث: أدى التقدم الكبير في مجال جراحات المخ الميكروسكوبية إلى الحد من مقدار التداخل وأيضاً مقدار الشد على نسيج المخ أثناء إجراء الجراحة ليظهر مفهوم جديد يعرف باسم الجراحات ذات التداخل البسيط أو جراحات ثقب المفتاح. وقد أدى تطور المنظار الجراحي في مجال الأنف والجيوب الأنفية إلى تغييرات جذرية في فهم طبيعة وعلاج أمراض الأنف والجيوب الأنفية وأيضاً في تقنيات الجراحة.

الهدف من البحث: تقييم نتائج المرضى فيما يتعلق بكلا النهجين: التنظير الداخلي الأنفي والميكروسكوبية عبر العقد في علاج أورام الغدة النخامية.

المرضى وطرق البحث: تضمنت دراستنا 40 حالة من أورام الغدة النخامية تم إجراء العملية عليها خلال عامين، وخضع نصفهم (المجموعة أ؛ 20 حالة) لاستئصال الورم الحميد عبر الأنف بالمنظار، بينما خضع الباقي (المجموعة ب، 20 حالة) لعملية استئصال الورم الحميد عبر الحاجز المعيارى عبر الحاجز المعيارى.

نتائج البحث: كانت أعلى نسبة عمرية لحالاتنا خلال العقدين الثالث والرابع من العمر، وكانت نسبة الذكور إلى الإناث 1:1 تقريباً. كان الصداع أكثر الأعراض شيوعاً في سلسلتنا في كل من المجموعات التنظيرية والمجهريّة؛ (60% و 70%) على التوالي يليها ضعف البصر؛ (55% و 60%). على الرغم من أن فقدان الرغبة الجنسية كان أكثر اعتلالات الغدد الصماء شيوعاً؛ (75% و 60%) على التوالي. كان التصوير المقطعي المحوسب للتخفيضات التاجية هو الفحص الشعاعى الأولي الذي تم إجراؤه في جميع حالاتنا، وأعطت فكرة عن التشريح العظمي لسليلا، الجيب الوتدي، وكان مهماً بشكل خاص في إظهار موضع الحاجز

الجيوب الوتدي، والذي كان حاسماً في التخطيط لقرار العملية. في دراستنا، وكان التحسن في النتيجة أعلى في مجموعة التنظير الداخلي مقارنة بالمجموعة المجهرية (تحسن الصداغ بنسبة 100% مقابل 71%، وتحسن الرؤية 82% مقابل 58%، و 80% مقابل إزالة الورم الكلي بنسبة 55%).

الاستنتاج: يعطي المنظار صورة أوضح وأوسع وأقرب للمجال الجراحي والتشريحي. والصورة البانورامية التي يعطيها المنظار الجراحي تتيح التعرف على كل نقاط الاستدلال في المجال الجراحي أثناء إجراء الجراحة ما يقلل من احتمالية التوجيه الغير دقيق.

الكلمات الدالة : التنظير الداخلي الأنفى – الالتظير الميكروسكوبى – علاج أورام الغدة النخامية .