

Surgical complications of the transsphenoidal endonasal endoscopic approach to pituitary macroadenomas: single center study

Complicaciones quirúrgicas del abordaje endoscópico endonasal transesfenoidal en macroadenomas hipofisarios no funcionantes: estudio de centro único

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Abstract

Background: Surgical approaches to the sellar region have been a challenge for the neurosurgeon. With the introduction of the endoscopic technique, surgical trauma has been minimized; however, it is not free of complications. **Objective:** To describe our institutional experience in patients undergoing resection of pituitary macroadenomas by endoscopic-assisted microsurgical approach, with emphasis on the resulting complications. **Method:** We reviewed the electronic files of 17 patients who underwent this procedure consecutively between 2017 and 2018, collecting variables such as age, sex, imaging classification, time of diagnosis at the time of surgery, postoperative complications and recurrence. **Results:** The average age of the patients was 45.23 years, with 70.59% women. Radiologically, grade 2 Knosp predominated (47.05%). The main complication was transient diabetes insipidus (23.52%) followed by cerebrospinal fluid fistula (11.76%). **Conclusions:** The endoscopic-assisted microsurgical approach has proven to be a valuable resource for treating pituitary macroadenomas, however it presents variable degrees of complications, which requires the acquisition of skills for the use of the endoscope, adequate preoperative planning, and multidisciplinary joint management in order to avoid them.

Keywords: Endoscopy. Pituitary adenoma. Surgical complications.

Resumen

Antecedentes: Los abordajes quirúrgicos de la región selar han sido un reto para los neurocirujanos. Con la introducción de la técnica endoscópica se ha minimizado el trauma quirúrgico, pero esta técnica no se encuentra exenta de complicaciones. **Objetivo:** Describir nuestra experiencia institucional en pacientes sometidos a resección de macroadenomas hipofisarios por vía microquirúrgica endonasal transesfenoidal asistida por endoscopia con énfasis en las complicaciones resultantes. **Método:** Revisamos los expedientes electrónicos de 17 pacientes sometidos a dicho procedimiento de manera consecutiva entre 2017 y 2018, y recabamos variables como edad, sexo, clasificación imagenológica, tiempo de diagnóstico al momento de la cirugía, complicaciones posoperatorias y recurrencia. **Resultados:** La edad promedio de los pacientes fue de 45.23 años y el 70.59% eran mujeres. Radiológicamente predominó el grado 2 Knosp (47.05%). La complicación principal fue

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diabetes insípida transitoria (23.52%), seguida por la fístula de líquido cefalorraquídeo (11.76%). Conclusiones: El manejo microquirúrgico asistido por endoscopia ha demostrado ser un recurso valioso para tratar macroadenomas hipofisarios, pero presenta grados variables de complicaciones, por lo cual se requiere la adquisición de habilidades para el uso del endoscopio, la planeación preoperatoria adecuada y el manejo conjunto multidisciplinario con el fin de evitarlas.

Palabras clave: Endoscopia. Adenoma hipofisario. Complicaciones quirúrgicas.

Introduction

Surgical approaches to the sellar and parasellar region have represented a challenge for neurosurgeons for many years. The introduction of the endoscopic approach is a reflection of neurosurgery evolution, seeking to avoid broad craniotomies by using increasingly smaller approaches and therefore reducing the complications associated with surgical trauma and thereby obtaining better postoperative results.

The first resection of a sellar region lesion was described by Schloffer in 1907¹. With the advent of surgical microscope, Hardy described in 1962 the trans-sphenoidal microsurgical technique for the resection of these lesions², which was the procedure that was most commonly used during the second half of last century, until the introduction of the trans-sphenoidal endonasal endoscopic technique described by Jankowski in 1992³. Currently, this approach is widely used throughout the world, but it is not free of complications.

In this work, we present the institutional experience in patients who underwent pituitary macroadenomas resection by endoscopy-assisted endonasal trans-sphenoidal microsurgical procedures within 2 consecutive years (2017 and 2018), with an emphasis on immediate and mediate complications associated with this approach.

Method

We created a retrospective cohort, by reviewing the electronic records of all patients who underwent pituitary adenoma resection by endoscopy-assisted endonasal trans-sphenoidal microsurgery in our institution, Licenciado Adolfo López Mateos Medical Center, consecutively from January 2017 to December 2018. We included only patients with complete medical records, whose lesions had pituitary adenoma confirmatory histopathological report, with other types of lesions, lesions larger than 10 mm (macroadenomas) and lesions with previous endocrinology evaluation that classified them as non-functioning being

excluded, with 17 patients meeting these inclusion criteria.

The variables that were collected from patients included age, gender, imaging classification (Hardy-Vezina and Knosp), time since diagnosis at the time of surgery and postoperative complications within the first 2 weeks, as well as 6-month follow-up.

Statistical analysis was carried out by two independent investigators. All the information was collected in a Microsoft Excel spreadsheet (Office 2016, Microsoft) and then analyzed with IBM SPSS (Version 21, IBM).

Results

Preoperative patient characteristics

Seventeen patients were included in this study (Table 1), out of whom 12 were women (70.59%) and 5 were men (29.41%). Average age of all patients was 45.23 years: 46.3 years for women (range: 28-62) and 42.6 years for men (range: 22-55). Average time with pituitary macroadenoma diagnosis prior to surgery was 6.9 months. Concomitant hypothyroidism was documented in 23.52% (5 cases) prior to surgery.

As for the Knosp classification (Table 2), used to assess the degree of invasion of the cavernous sinus, we identified that 47.05% of patients (8) had grade 2, followed by grade 4 in 23.52% (4) and, finally, grades 3 and 2 (17.64% and 11.76%, respectively).

Regarding the degree of local invasion of the sella turcica according to modified Hardy-Vezina classification (Table 2), we observed that 52.94% of the patients (9) had grade III; 29.41% (5), grade IV; and 17.64% (3), grade II. As for extrasellar extension, 41.17% (7) were classified in group C, group D came next in order of frequency with 29.41% (5), subsequently, group B with 23.52% (4), and last place was for group E with only one case (5.88%).

Immediate and mediate complications

We identified a total of seven different complications in our patients (Fig. 1). As for those that occurred

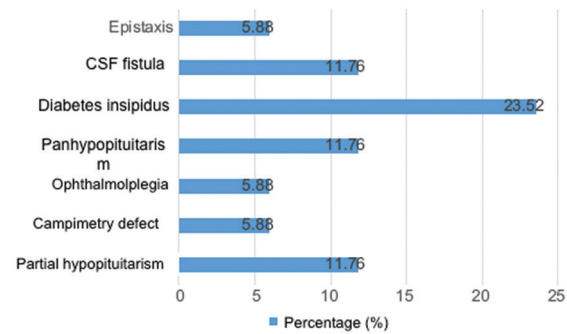
Table 1. Preoperative characteristics of patients with pituitary macroadenomas included in the study

Characteristics (n = 17)	
Gender	
Females, n (%)	12 (70.59)
Males, n (%)	5 (29.41)
Average age (years)	
Females	46.3 (28-62)
Males	42.6 (22-55)

Table 2. Relationship of the number of pituitary macroadenomas surgically intervened in the study period with regard to the assigned imaging classification

Knosp classification		
	n	(%)
1	2	11.76
2	8	47.05
3	3	17.64
4	4	23.52
Modified Hardy-Vezina classification		
Sella turcica	n	(%)
II	3	17.64
III	9	52.94
IV	5	29.41
Extrasellar extension	n	(%)
B	4	23.52
C	7	41.17
D	5	29.41
E	1	5.88

between the time of surgery and up to 2 weeks later, i.e., immediate and mediate complications, the most common was diabetes insipidus in 23.52% (4), with vasopressin requirement. This complication was transient and all patients showed remission in the subsequent medical follow-up evaluation in. After it, cerebrospinal fluid (CSF) fistula was found in 11.76% of cases (2). In these patients, a lumbar subarachnoid catheter was placed for 3 to 5 days, and absolute rest was indicated, with subsequent remission in both cases. Panhypopituitarism and partial hypopituitarism were also present in 11.76% of cases (2), with hormone replacement therapy being required. As less

**Figure 1.** Comparison of postoperative complications in patients who underwent nonfunctioning pituitary macroadenoma endoscopy-assisted endonasal trans-sphenoidal microsurgical resection.

common complications, we found epistaxis (satisfactorily resolved with nasal packing), ophthalmoplegia, and campimetry defects, with one case each (5.88%); the latter two without improvement in subsequent assessments.

Tumor relapse

In 3 patients (17.64%), lesion growth was documented in the following 6 to 12 months, and for this reason, they underwent trans-sphenoidal endoscopic surgical management again, with no postoperative complications being reported.

Discussion

Access to the sellar region has important anatomical and surgical limitations, since it is located above the optic chiasm and the circle of Willis; laterally, it is surrounded by the cavernous sinus and, behind, there are vital structures, such as the basilar artery and its respective branches⁴. Traditionally, microsurgical technique had been used to approach this region, but since two decades ago, the use of endoscopic endonasal trans-sphenoidal surgery for pituitary lesions has been one of the most remarkable advances, since it involves a decrease in the number of complications and avoids procedures with high morbidity, such as craniotomies⁵. Its advantages include proper visualization of anatomy, a wide surgical field, and easiness for the angle of work with the endoscope to be modified.

Adenomas are the most common lesion in the sellar region, and account for 10-15% of all intracranial lesions, which implies a high percentage of neurosurgical pathology⁶. Cavernous sinus lateral wall anatomical factors play an important role in tumor invasion, which

Table 3. Incidence of complications associated with pituitary macroadenomas endoscopic endonasal resection in comparison with those reported in the world literature

Authors	CSF fistula	No. of cases (%)			Epistaxis	Pituitary dysfunction	Nasal septum perforation	Meningitis	Death
		Total	Transient	Permanent					
Shen et al. ¹²	0	2 (5)	2 (5)	0	0	0	NA	0	0
Jho et al. ¹³	10 (8)	11 (9)	6 (5)	5 (4)	0	18 (14)	NA	0	1
Cappabianca et al. ¹⁴	3 (2)	13 (9)	8 (5)	5 (3)	2 (1)	20 (14)	NA	0	0
White et al. ¹⁵	6 (12)	11 (22)	9 (18)	2 (4)	1 (2)	0	0	1 (2)	0
Rudnik et al. ¹¹	0	3 (5)	NA	3 (5)	0	NA	NA	0	1
Caster et al. ¹⁰	4 (27)	3 (20)	3 (20)	0	1 (7)	0	3 (20)	0	0
Kabil et al. ¹⁶	5 (2)	16 (5)	12 (4)	4 (1)	4 (1)	8 (3)	2 (1)	0	0
Current series	2 (11.76)	4 (23.52)	4 (23.52)	0	1 (5.88)	2 (11.76)	0	0	0

CSF: cerebrospinal fluid; NA: not applicable.

is why magnetic resonance imaging is of vital importance for determining the behavior of the lesion to be resected. With this premise in mind, we used the Knosp classification, whereby we found that 47.05% of our patients were classified as grade 2, extending outside the intercarotid line, without surpassing the intrasupracavernous carotid tangent.

Another important factor is to identify the degree of invasion of the sella turcica, which is accomplished with Hardy-Vezina modified classification, whereby we demonstrated that 52.94% of patients had sellar floor-focused perforation (grade III). As for extrasellar extension, the most common variant was group C, which refers to significant displacement of the floor of the third ventricle, with 41.17% of cases.

Endocrine complications

They are with no doubt the most common complications reported all over the world⁷, with diabetes insipidus being the most predominant. It has been attributed to vasopressin-producing neurons dysfunction caused by surgical manipulation. This alteration requires evaluation and subsequent endocrine follow-up, although it usually has a complete recovery in the following 6 months, as it occurred in our 4 cases (23.52%). Another complication in this area is partial (adenohypophysis) or complete hypopituitarism (panhypopituitarism), which usually occurs due to excessive use of aspiration or due to coagulation of the sellar cavity with damage to healthy peri-tumor glandular tissue.

Infectious complications

Meningitis is an uncommon complication, reported in 0-2% of cases⁸. Meningitis goes hand in hand with postsurgical CSF fistula, and its presence is the main risk factor given that it is the route of entry for pathogenic microorganisms into the central nervous system. No patient in our series had this complication.

Structural complications

During the approach, the floor of the sella turcica is removed or drilled in order to have access to the dura mater and subsequently to the adenoma; however, this maneuver can generate a CSF fistula. In our series, we found 2 patients (11.76%) who had this alteration, which was successfully managed with a subarachnoid catheter. The degree of this complication in our institution is within the ranges reported in the world literature⁹. It is usually conservatively treated with a subarachnoid lumbar catheter, and if it does not subside, it requires reoperation.

Nasal complications

The most commonly reported is epistaxis, which is usually secondary to an injury of the sphenopalatine artery, which is why its proper coagulation is of the utmost importance. This complication has been reported in up to 7% of cases¹⁰. We reported one case (5.88%), attributed to surgical manipulation during

macroadenoma resection, which was resolved with nasal tamponing.

Other complications reported in the literature include anosmia and hyposmia in up to 10% of patients⁸; however, in our series we did not observe such alteration. In addition, septal perforation has been documented as a complication in up to 3% of patients⁸. This complication did not occur in our series either.

Vascular complications

One of the complications most feared by the neurosurgeon when using this approach is internal carotid artery injury. However, this complication has considerably decreased after the introduction of neuroendoscopy, and in the world literature it is reported in less than 1% of cases¹¹. Fortunately, none of our patients had such complication.

In general, we can comment that the rate of complications found in our study is similar to that reported in international series (Table 3)¹¹⁻¹⁶.

Conclusion

The best strategy for treating complications is to avoid them. This depends on proper understanding of the disease, detailed knowledge of the surgical anatomy of the sellar and parasellar region, acquisition of skills for endoscope operation, appropriate preoperative planning individualizing each case, use of the right surgical instruments, regular post-surgical follow-up and multidisciplinary coordinated work between the neurosurgeon, endocrinologist, otolaryngologist, radiologist, pathologist and radiation oncologist, and thereby achieve success in the management of our patients. It is virtually impossible to completely eliminate complications owing to the surrounding structures in the sellar and parasellar region, but if these guidelines are followed, said complications can be considerably reduced.

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Conflicts of interest

The authors declare that they have no conflicts of interest.

Ethical disclosures

Protection of human and animal subjects. The authors declare that no experiments have been performed on humans or animals for this research.

Confidentiality of data. The authors declare that they have followed the protocols of their work center on the publication of patient data.

Right to privacy and informed consent. The authors declare that no patient data appear in this article.

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