Original Article

Transsphenoidal Pituitary Surgery A Good and Safe Primary Treatment Option for Pituitary Adenomas

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ABSTRACT

Background: Pituitary tumors are the third most common primary intracranial tumors. The microscopic transsphenoidal approaches are the main preferred surgical approaches for surgical management of most cases of pituitary adenomas. The transsphenoidal approaches are gaining many advantages over the microscopic transcranial approaches. The reasons for this is the low morbidity and mortality reported with the transsphenoidal approaches. Patients and Methods: This study has been conducted 40 patients operated upon using the standard microscopic transsphenoidal pituitary adenoma resection. During the period from May/2010 to July/2012, at Department of Neurosurgery, Ain Shams University, Cairo, Egypt, all of the patients in this study had preoperative MRI brain and sella, CT sella and paranasal sinuses. Visual assessment including visual field assessment and visual acuity, hormonal assay for prolactin, growth hormone cortisol level, thyroid hormones level (T3, T4, TSH) and the follow up of these patients was by MRI brain and sella after 3 months, hormonal level, visual field assessment one month postoperative and every 3 months. Results: From our 40 cases we had 4 cases with regrowth of the residual part, 4 cases with C.S.F leak and 2 cases with transient diabetes insipidus and these were the major complications we had and improvement occurred in 83.3% of cases presented by visual field, and in 80% of cases presented by headache, complete hormonal control was achieved in about 44.4% of cases with hormonal disturbance. The follow up period was from 8-24 months (mean 16 months). Conclusion: The present study showed that the microscopic endonasal transsphenoidal surgery can be used in pituitary adenoma excision with avoidance of complications of transcranial route.

INTRODUCTION

Pituitary tumors account for 15% of all primary brain tumors, which can be approached through either transcranial or transsphenoidal routes. The transsphenoidal approach is gaining many advantages over the microscopic transcranial routes. Transsphenoidal surgery is the preferred approach for the surgical management of the majority of pituitary tumors, including macroadenomas. Transsphenoidal approach include the following forms:

a. Sublabial.

b. Transnasal trans-septal approach.

c. Endonasal endoscopic.

Indications for transsphenoidal surgery over transcranial approaches in large pituitary tumors include extension into the sphenoid sinus, associated cerebrospinal cerebrospinal fluid (CSF) rhinorrhea, and invasion and/or destruction of the sphenoid bone with multidirectional intracranial extensions. This approach is also indicated when an intracranial operation would carry excessive risk for a patient (e.g., an elderly person in poor health or a patient with severely compromised vision).

PATIENTS & METHODS

This study has been conducted on 40 patients operated upon using the standard microscopic transsphenoidal pituitary adenoma resection using transnasal transseptal approach during the period from May/2010 to July/2012, at Department of Neurosurgery, Ain Shams University, Cairo, Egypt. The inclusion criteria included:

All patients with pituitary adenoma (functioning and non functioning) showing manifestations of mass effect or hormonal disturbance.

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The exclusion criteria included:
1. Conditions of hormonal disturbance not related to the pituitary adenoma as hyperthyroidism, addison's disease and pheochromocytoma.
2. Recurrent cases.
4. Transsphenoidal surgery is contraindicated when the patient has an infectious process involving the sphenoid sinus, a suprasellar mass associated with a normal sella turcica, or a “bottleneck” constriction between an intrasellar tumor and the suprasellar extension.
All of the patients involved in the study have been subjected to preoperative:

1) **Clinical assessment thorough:**
   - **History taking:**
   - **Systemic examination:** To detect picture of endocrinal disturbance in functioning pituitary adenoma and to detect any systemic risk factor, e.g. Diabetes mellitus, Hypertension and cardiological problems.
   - **Neurological examination:** with special emphasis on cranial nerve examination and cognitive function.

2) **Ophthalmological examination:** Ophthalmological examination; visual acuity, Fundus examination for evidence of papilledema or optic atrophy, and visual field assessment by automated perimetry and confrontation method.

3) **Laboratory Investigations:**
   a. Routine investigations as complete blood count, Prothrombin time activity, random blood sugar, liver and renal function tests.
   b. Hormonal assay: evaluation of endocrine status of the patient through preoperative endocrine evaluation include measurement of serum Prolactin, Growth hormone, TSH, free T3, free T4, serum cortisol 8 AM & 8 PM, ACTH 8AM, FSH and LH levels.

4) **Imaging:**
   - Preoperative imaging is best accomplished using high field strength magnetic resonance imaging (MRI). Coronal and sagittal T1 weighted images with and without gadolinium best define sellar anatomy and the relationship of sellar tumors to surrounding structures, especially the cavernous sinus and optic chiasm.
   - Preoperative computed tomography (CT) scan of brain, sella and sinuses were initial radiographic investigation performed in all cases they gave a very important idea about anatomy of sphenoid sinus and its types sellar, presellar and chonchal, the position of sphenoid sinus septum and these information were very important in planning the decision of surgery.

**Technique:**

**Positioning**

The patient is operated in supine position with slight Trendelenburg position. The head of the patient is turned 10-15°, on the horizontal plane, towards the surgeon, who is on the patient's right side.

**Sterilization:**

About five minutes before the beginning of the procedure the nasal cavities are packed with cottonoids soaked in a diluted solution of Povidone iodine 1/2 strength then vasoconstricting (VC) diluted adrenaline 1mg/ 30 ml saline soaked in cottonoids.

**Transsphenoidal Surgical Procedure:** we use the transnasal trans-septal approach.

After topical treatment with oxymetazoline and injection with lidocaine containing 1:100,000epinephrine, we made an incision in the right nasal septal mucosa approximately 2 to 3 mm behind the mucosal–cutaneous junction.

The incision was continued posteriorly as it descended to keep it behind the nasal sill, and it extended to the lateral portion of the nasal floor. A submucoperichondral plane was developed and the submucosal dissection, which extended onto the nasal floor, was completed on the right side.

Then, we incised the quadrangular cartilage 2 cm posterior to the rostral margin and a similar submucoperichondral and submucoperiosteal dissection of the nasal septum was completed on the left side (dissection of the left nasal floor was not necessary). Then, we remove the posterior portion of the quadrangular cartilage and the perpendicular plate of the ethmoid bone. The keel of the vomer was identified, and the mucosa on the rostrum of the sphenoid bone was elevated laterally on both sides until the sphenoid ostia were clearly visualized. An appropriately sized and shaped bivalve self retaining speculum was then placed and the operating microscope is brought into position.

We opened the sphenoid sinus with a micro-Kerrison punch and the sphenoid inter sinus septum if present was followed posteriorly to the sellar floor. The sella was then opened by fracturing the thin floor using a chisel especially in cases of microadenoma, in cases of macroadenoma where the sellar face is very thin a blunt nerve hook was used. Then, the dura mater was opened. We usually use a cruciate opening for the dura.

Then, we removed piecemeal using cup forceps. Inferiorly using ring curets, and the tumor fragments are removed immediately upon opening the dura. We entered the tumor inferiorly using ring curets, and the tumor fragments are removed piecemeal using cup forceps.

When exploring for a microadenoma, we could usually see the normal gland upon opening the dura. We had visualized the tumor on the preoperative MRI; it can be approached by dissecting through the gland in the appropriate direction with a blunt probe, and then be...
removed with a small ring curet. Hemostasis must be meticulous.

We were careful in the dissection and curettage of the tumor so that minimized the risk of a CSF leak, but intraoperative leakage could be inevitable. In the most cases, CSF leaks from the superior dural margin. Packing the tumor bed with autologous fat was usually sufficient to control the leak. We do not routinely place lumbar drainage for a CSF leak.

The septum then was returned to the midline and mucosa was returned to its position. The nostril was packed using merocel. The packing was removed on the first postoperative morning.

**Follow up protocol:** The follow up period was from 8-24 months (mean 16 months).

The patient is followed up through:

I. In the early postoperative period we excluded the presence of diabetes insipidous (DI) by doing fluid chart, fluid balance and regular Na and K levels in the first 48 hours.

II. Clinical examination which was done preoperative and early postoperative and also was done every 3 months, this clinical examination include:

   a) Systemic examination to detect picture of endocrin disturbance in functioning pituitary adenoma.

   b) Ophthalmological examination include:
      - Visual acuity.
      - Field changes.
      - Fundus examination.
      This is done one month postoperative then every 3 months.

III. Hormonal assay one month postoperative and compare it to the preoperative and then it is done every 3 months.

IV. MRI sella with contrast after 3 months.

**RESULTS**

This study consisted of 40 patients, 18 females (45%) and 22 males (55%) with an average age of 48 years (range 18-60). Tables (1 and 2) demonstrate age and sex.

**Sex distribution:**

Table 1: Sex distribution (Pituitary adenoma was slightly more in males).

<table>
<thead>
<tr>
<th>Sex</th>
<th>Male</th>
<th>Female</th>
</tr>
</thead>
<tbody>
<tr>
<td>No</td>
<td>22</td>
<td>18</td>
</tr>
<tr>
<td>Percent</td>
<td>55%</td>
<td>45%</td>
</tr>
</tbody>
</table>

**Age distribution:**

Table 2: Age distribution (Pituitary adenoma was more common in age between 25-50 years).

<table>
<thead>
<tr>
<th>Age</th>
<th>&lt;20</th>
<th>25-50</th>
<th>&gt;50</th>
</tr>
</thead>
<tbody>
<tr>
<td>No</td>
<td>2</td>
<td>32</td>
<td>6</td>
</tr>
<tr>
<td>Percent</td>
<td>5%</td>
<td>80%</td>
<td>15%</td>
</tr>
</tbody>
</table>
Clinical Presentation:

Table 3: Symptoms/signs
<table>
<thead>
<tr>
<th>Symptoms/signs</th>
<th>No</th>
<th>Incidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Visual deterioration</td>
<td>24</td>
<td>60%</td>
</tr>
<tr>
<td>Headache</td>
<td>20</td>
<td>50%</td>
</tr>
<tr>
<td>Amenorrhea, galactorrhea and infertility</td>
<td>6</td>
<td>15%</td>
</tr>
<tr>
<td>Acromegalic features</td>
<td>12</td>
<td>30%</td>
</tr>
<tr>
<td>Impotence</td>
<td>4</td>
<td>10%</td>
</tr>
</tbody>
</table>

In non functioning macroadenoma visual deterioration was the most common presenting symptoms followed by headache. Acromegally, amenorrhea, galactorrhea and infertility were the most common presenting symptoms and signs in functioning macro adenoma.

Hormonal activity of the pituitary adenomas:

In this study the number of non functioning adenoma (22 cases out of 40) predominate the functioning one (18 cases out of 40).

Table 4: Hormonal activity of the functioning adenomas (prolactin hormone was the main hypersecreted hormone in the cases of functioning adenomas).

<table>
<thead>
<tr>
<th>Hormonal activity</th>
<th>No</th>
<th>Percent</th>
</tr>
</thead>
<tbody>
<tr>
<td>GH-see MA</td>
<td>6</td>
<td>15%</td>
</tr>
<tr>
<td>PRL-see MA</td>
<td>12</td>
<td>30%</td>
</tr>
</tbody>
</table>

Table 5: Hormonal activity of the pituitary adenomas

<table>
<thead>
<tr>
<th>Hormonal activity</th>
<th>No functioning</th>
<th>Functioning</th>
</tr>
</thead>
<tbody>
<tr>
<td>No</td>
<td>22</td>
<td>18</td>
</tr>
<tr>
<td>Percent</td>
<td>55%</td>
<td>45%</td>
</tr>
</tbody>
</table>

Table 6: Tumor extension

<table>
<thead>
<tr>
<th>Tumor extension</th>
<th>No</th>
<th>Percent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intra sellar</td>
<td>34</td>
<td>85%</td>
</tr>
<tr>
<td>Suprasellar</td>
<td>6</td>
<td>15%</td>
</tr>
</tbody>
</table>

Visual Field:

Table 7: Field changes

<table>
<thead>
<tr>
<th>Field changes</th>
<th>No</th>
<th>Percent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Marked affection (Bitemporal hemianopia)</td>
<td>24</td>
<td>60%</td>
</tr>
</tbody>
</table>

Surgical Technique:

Fig. 2: This diagram demonstrates the operation time (hours) in microscopic transphenoidal approach, ranged from 1.5 hours to 3.5 hours.

Table 8: Complications (The most common serious complications were CSF leak and regrowth of the residual part of pituitary adenoma).

<table>
<thead>
<tr>
<th>Complications</th>
<th>No</th>
<th>Incidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>CSF leak</td>
<td>4</td>
<td>10%</td>
</tr>
<tr>
<td>Transient Diabetes Insipidus</td>
<td>2</td>
<td>5%</td>
</tr>
<tr>
<td>Pneumocephalus</td>
<td>2</td>
<td>5%</td>
</tr>
<tr>
<td>Regrowth of the residual part</td>
<td>4</td>
<td>10%</td>
</tr>
</tbody>
</table>

Table 9: Improvement of symptoms postoperative (Improvement occurs mainly in headache, visual affection and radiological cure was in 90% of cases).

<table>
<thead>
<tr>
<th>Symptoms</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Headache</td>
<td>80%</td>
</tr>
<tr>
<td>Visual affection</td>
<td>83.3%</td>
</tr>
<tr>
<td>Complete hormonal control</td>
<td>44%</td>
</tr>
<tr>
<td>Radiological cure</td>
<td>90%</td>
</tr>
</tbody>
</table>

Illustrative cases:

Case 1:

50 years old female presented with headache and visual field affection in form of bitemporal hemianopia. The hormonal study shows GH (0.09 ng/ml) & prolactin (42.3ng/ml). MRI with Gadolinium showed giant pituitary adenoma of homogenous enhancement with suprasellar extension and optic chiasm compression. This patient was operated by microscopic transnasal transphenoidal technique.
Postoperatively, the headache was completely relieved with marked improvement of the visual field. MRI with Gadolinium showed total tumor excision with free optic chiasm.

Case 2:

45 years old male presented with headache and visual field affection in form of bitemporal hemianopia. The hormonal study revealed elevated prolactin (757.8 ng/ml). MRI with Gadolinium showed giant pituitary adenoma with suprasellar extension and optic chiasm compression. This patient was operated by microscopic transnasal transsphenoidal technique.

Postoperatively, headache was relieved with marked improvement of the visual field. MRI with Gadolinium, one month later, showed total tumor excision with free optic chiasm.
DISCUSSION

Transsphenoidal surgery is an extra arachnoid approach, requires no brain retraction, no external scar (aside from where a fat graft is procured, if used). Usually it is the procedure of choice, indicated for microadenomas, macroadenomas without significant extension laterally beyond the confines of the sella turcica, it is also indicated in patients with CSF rhinorrhea, and tumors with extension into sphenoid air sinus.

This approach includes the following forms:
- a. Sublabial.
- b. Transnasal trans septal approach.
- c. Endonasal endoscopic approach.

In our study we used the transnasal transseptal approach.

Transsphenoidal surgery is contraindicated when the patient has an infectious process involving the sphenoid sinus, or a “bottleneck” constriction between an intrasellar tumor and the suprasellar extension. A transcranial approach may also be considered in patients with significant intracranial tumor extension to the subfrontal, or middle fossa regions. A conchal sphenoid sinus is relative contraindication to the transsphenoidal operative approach as the use of a high speed, angled drill allows the pituitary to be exposed safely.

This study included 40 cases of pituitary tumors, operated upon from May 2010 to July 2012, this study included 18 females (45%) and 22 males (55%). Regarding age groups, our patients have been distributed over 3 age groups ranging from 20 to 65 years. The highest age incidence of our cases was during the third and fourth decades of life.

Although this study didn’t include in its cohort any patients from the child age group as the incidence of pituitary adenoma in the pediatric age group is 100/million population, other reports support its feasibility in that age group as in the study of de Divitis. Visual impairment was the commonest presenting symptom in our series 60% followed by rhinorrhea, and tumors with extension into sphenoid air sinus.

Throughout this study, MRI pre and post contrast was performed before surgery in all patients as the main tool used for identification of the soft tissue relations of the tumor especially to the blood vessels of the circle of Willis, cavernous sinus, third ventricle, and the determination of the presence of intratumoral hemorrhage as well as the post-contrast characteristics of the tumor.

In our study 45% of cases (18 out of 40) had tumor volume less than 5 ml in which only 2 cases (11.1%) had residual part. While 55% of cases (22 out of 40) had tumor volume more than 5ml in which complete tumor removal achieved in 20 cases (90.9%) and subtotal removal in 2 cases (9.1%).

In this study, we noticed that as surgeons were more trained on the microscopic transnasal transsphenoidal approach the operative time shortened, furthermore, the mean hospital stay was shorter perhaps because there were fewer surgical complications and patients were more comfortable after the transnasal approach than sublabial.

Serious complications in patients undergoing transsphenoidal procedures are fortunately uncommon. In several large series, the incidence of operative death has been reported as 0.5%. Most fatal cases are associated with additional extenuating circumstances. Likewise, the incidence of nonfatal complications ranges from 1.1 to 13%, with an average of 3.6%. Some complications of transsphenoidal surgery were found as:

CSF Rhinorrhea:

The incidence of postoperative CSF leakage following transsphenoidal surgery depends primarily on the experience of the surgeon and the intrasellar pathologic findings. CSF leakage is common if the diaphragma sellae is disrupted during tumor removal, or in the case of an extensive macro adenoma directly eroding this structure.

Some delayed CSF rhinorrhea possibly occurs as a result of postoperative rupture of the arachnoid where it herniates into the space left by removal of the tumor.

To prevent rhinorrhea, the intrasellar cavity and sphenoid sinus are filled with fat held in place with fibrin glue. The sellar floor may also be reconstructed with septal bone or cartilage, which helps to maintain the position of the fat graft and thus reduce the incidence of CSF leakage. Fat must be packed loosely to avoid producing a mass in itself.

In our study we had 4 cases presented with CSF leak. These patients presented in the second postoperative day with CSF rhinorrhea that has been controlled by complete bed rest, application of lumbar drain for these cases was not needed.

Although that our sample is relatively small, we can conclude that multi-layered reconstruction techniques are relatively superior to a single layered one. This multi-layered reconstruction technique was done by fat harvested from the abdomen and a rigid material to hold this sealing material firmly in place. These materials include septal cartilage and bone. We did this technique in four cases. This conclusion is supported by the results of other studies of Cappabianca et al.
Goudakos et al.\textsuperscript{5} reported CSF leak of 14.4\% as compared to the transcranial pituitary surgery transsphenoidal had lower rate of CSF leak.

**Diabetes insipidus**

This may occur transiently or permanently following transsphenoidal surgery.

In our study we have 2 cases with diabetes insipidous 5\%, in the study of Tab et al. he had reported a rate for permanent DI of 6\%.\textsuperscript{16}

**Visual complications**

Damage to the optic nerves and/or chiasm may occur during removal of tumor from the suprasellar region.

Pressure from a hematoma may damage the optic nerves and/or chiasm and may be reversible following prompt removal of the mass. If vision appears to worsen postoperatively, an immediate computed tomography scan should be performed to identify a possible remediable cause, such as a hematoma or overpacked sella.\textsuperscript{3}

We have no cases of visual complications.

Dekkers et al. reviewed 8 articles on the effects of transsphenoidal surgery in clinically non functioning macro adenoma and showed that visual field defects improved in 87\% of case\textsuperscript{3}. In our study, 24 cases had visual field defect in the form of bitemporal hemianopia. 20 cases of them improved (83.3\%). About 20 cases suffered from headache pre operative; postoperatively, 16 cases improved. According to Fonte, the overall hormonal control was achieved in 71\% (n = 12 out of 17) of hypersecreting tumors while radiological cure was achieved in 81\% of case (n = 26 out of 32).\textsuperscript{4}

In our study 44.4\% of cases (n = 8 out of 18) of hypersecreting tumors returned to normal and 44.4\% (n = 8 out of 18) improved while radiological cure was achieved in 90\% of cases (n = 36 out of 40).

MRI was the main tool used throughout the study to judge the extent of surgical radicality being a more solid and reliable evidence and it was done 3 months postoperative, also we did hormonal level in secretary of adenomas which is very important in the follow up. Also Hardy suggested the use of MRI as the main tool to judge surgical radicality.\textsuperscript{6}

In this study we performed follow up MRI 3 months postoperatively as the early postoperative sella retains its preoperative volume due to graft materials and we can’t differentiate residual tumor from graft materials, however Yoon et al. advocate early postoperative MRI, as they can easily differentiate residual tumor from a normal gland, materials, or postsurgical granulation tissue. In addition, early postoperative MRI can be an excellent baseline if radiation therapy is necessary for treatment of residual tumor or recurrent tumor suspected on follow up MR images.\textsuperscript{7}

We have noticed no evidence of clinical, hormonal nor radiological recurrence in 36 cases during our follow up period that ranged from 8 to 24 months (mean 16 months). We have 4 (10\%) cases with regrowth of the residual part of adenoma after 6-12 months follow up, three of them showed increase in hormonal level and treated medically, one case showed radiological recurrence with visual affection and treated transcranially. In comparison to Mortini, he had recurrence rates of 13.2\%, 7.7\%, 17.8\%, 8.4\%, and 18.7\% in non functioning adenomas, GH secreting adenomas, PRL secreting adenomas, ACTH secreting adenomas, and TSH secreting adenomas respectively in his patients who are followed up after remission for periods more than 1 year.\textsuperscript{8}

**CONCLUSION**

The result of our study confirm the effectiveness of microscopic transspheredal surgery as a golden standard treatment for pituitary adenomas either macro or micro and with improvement of presenting symptoms as headache and visual deterioration and visual field defect. Amenorrhea, galactorhea and infertility were markedly improved postoperative MRI showed residual tumor in 4 cases.

**SUMMARY**

The microscopic transphenoidal approach is safe and effective modality for surgical treatment of pituitary microadenoma and macroadenoma with in apparent of presenting symptoms and little complication rate with short hospital stay.

**REFERENCES**


