Introduction

This overview has been prepared to assist members of the Interventional Procedures Advisory Committee in making recommendations about the safety and efficacy of an interventional procedure. It is based on a rapid review of the medical literature and opinion of Specialist Advisors. It should not be regarded as a definitive assessment of the procedure.

Date prepared
This overview was prepared in April 2003

Procedure name
Endoscopic transsphenoidal pituitary adenoma resection

Specialty society
British Association of Otorhinolaryngologists, Head and Neck Surgeons
Society of Neurological Surgeons

Description

Indications:
The pituitary gland is a small structure attached to the base of the brain (behind the nose), where it is protected by a part of the skull called the sphenoid bone.

Pituitary adenomas are benign slow growing tumours that arise within the pituitary gland.

The manifestations of a pituitary tumour depend on the hormone secreted by the tumour as well as the pattern of growth of the tumour within the space in which the pituitary gland is lodged (sella turcica). For example larger tumours can result in individuals experiencing visual problems and headache as the tumour may press on adjoining structures such as the optic nerves.

Pituitary adenomas can also cause hormonal imbalances by producing either too many or too few hormones. In general adenomas are classified as being "non-functional" (non secreting) or functional (secreting) tumours.

Current Treatments and Alternatives:
The treatment options for pituitary adenomas include surgery, pharmacological therapy or radiotherapy.

The transsphenoidal surgical approach has been the preferred procedure for removal of tumours.

However surgery via the endonasal route has become increasingly popular as a means to reduce morbidity. As the endonasal technique has a narrower surgical field the use of an endoscope has been added to this procedure as a visualisation tool.
What the procedure involves:
The patient is given an anaesthetic. An endoscope inserted into the nose towards the base of the tumour at the skull base. Surgical instruments are then inserted and the tumour is removed.

Patients usually undergo the procedure via the right nostril, however surgery is sometimes done via the left nostril, depending on the location of the tumour.

There are also various endonasal approaches that can be used for endoscopic pituitary surgery such as the paraseptal approach.

The use of the endoscope in transsphenoidal surgery for pituitary adenomas has primarily been popularised by the work by Jho \(^1\). Articles on endoscopic transsphenoidal pituitary adenoma resection often refer to this body of work or note that the procedure undertaken is an adaptation of the Jho technique.

More recently the use of flexible endoscopes \(^2\) and computer aided image guided techniques \(^3\) \(^4\) have also been included as part of this procedure.

Efficacy:

- From the evidence presented it would appear that endoscopic transsphenoidal pituitary adenoma resection resulted in comparable surgical outcomes to conventional surgery.

- The procedure may also shorten operation time. The length of hospital stay was also shorter with the endonasal procedure: 2–5 days compared with 4–10 days for conventional surgery.

- The majority of Specialist Advisors considered that this procedure was a minor variation of an existing procedure and was unlikely to alter the efficacy of the procedure. Two Advisors however did note that incomplete tumour removal may be a potential concern with this procedure.

Safety:

- From the evidence presented it would appear that the complication rate of endoscopic transsphenoidal pituitary adenoma resection is less than that of conventional surgery. Major morbidity (cerebrospinal fluid leak, meningitis, stroke, intracranial haemorrhage, and visual loss) occurs in a small number of cases. Less serious complications (sinus disease and nasal septal perforations) occur in less than 7% of patients.

- The most serious reported complication of the procedure was meningitis. This occurred in two patients in the largest case series studies which included 310 patients.

- Specialist Advisors did not report any particular safety concerns, though bleeding, optic nerve damage, cerebrospinal fluid leakage and carotid artery injury were noted as potential complications of endoscopic transsphenoidal pituitary adenoma resection.
Literature review
Rapid Review of Literature

The medical literature was searched to identify studies and reviews relevant to endoscopic transsphenoidal pituitary adenoma resection. Searches were conducted via the following databases from commencement to February 2003: MEDLINE, PREMEDLINE, EMBASE, Cochrane Library and Science Citation Index. Trial registries and the Internet were also searched. No language restriction was applied to the searches.

The following selection criteria (Table 1) was applied to the abstracts identified by the literature search. Where these criteria could not be determined from the abstracts the full paper was retrieved.

Table 1  Inclusion/criteria for identification of relevant studies

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Criteria</th>
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</thead>
<tbody>
<tr>
<td>Publication type</td>
<td>Clinical studies included. Emphasis was placed on identifying good quality comparative studies. Abstracts were excluded where no clinical outcomes were reported; the paper was a review, editorial, technical or animal study</td>
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<tr>
<td>Patient</td>
<td>Patients with pituitary adenoma (any cause)</td>
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<tr>
<td>Intervention/test</td>
<td>Endoscopic transsphenoidal resection. NB this excludes endonasal resection done by microscope</td>
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<td>Outcome</td>
<td>Articles were retrieved if the abstract contained information relevant to the safety and/or efficacy</td>
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<tr>
<td>Language</td>
<td>Non-english language articles will be excluded unless they are thought to add substantively to the English language evidence base.</td>
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<tr>
<td>Authors, location, date, number of patients</td>
<td>Key efficacy findings</td>
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<td>--------------------------------------------</td>
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</table>
| **Cho and Liau (2002)**<sup>a</sup>        | Endonasal endoscopic surgery | Transseptal operation | Endonasal endoscopic surgery | Transseptal operation | Method of randomisation unclear  
Methodology unclear  
Hospital stay in the endonasal group was significantly shorter  
However at the beginning of the study the operative time and the hospital stay were the same for both procedures - learning curve  
Control approach: sublabial incision |
| Chinese Randomised Controlled Trial 1996-2000 | Normal prolactin level 66%  
Prolactin levels <100ng/ml 93%  
Visual field improvement 5/8 63% (macroadenoma) | Normal prolactin level 75%  
Prolactin levels <100ng/ml 85%  
Visual field improvement 6/10 60% (macroadenoma) | 1 patient sinusitis  
Complication rate: 4.5% | 2 patients sinusitis  
1 patient hypopituitism  
1 patient nasal septum perforation  
1 wound disruption  
1 massive nasal bleeding  
Complication rate: 27% |
| 44 patients  
22 patients endonasal surgery  
22 patients transseptal surgery | Prolapineomas | Microadenomas Complete Response 7/7  
Partial Response 0/7  
Macroadenomas Complete Response 5/9  
Partial Response 4/9 | Microadenomas Complete Response 6/6  
Partial Response 0/6  
Macroadenomas Complete Response 11/12  
Partial Response 1/12 | 2 patients cerebrospinal (CNS) fluid fistula  
1 patient meningitis  
Complication rate: 15% | 4 patients cerebrospinal (CNS) fluid fistula  
1 patient cranial nerve injury  
Complication rate: 24% |
| Prolactinomas | Mean follow-up 3.5 years  
1 patient sinusitis  
1 patient hypopituitism  
1 patient nasal septum perforation  
1 wound disruption  
1 massive nasal bleeding  
Complication rate: 27% |
| **Badie, Nguyen, & Preston (2000)**<sup>a</sup> |未指定 | Microadenomas  
Complete Response 7/7  
Partial Response 0/7  
Macroadenomas  
Complete Response 5/9  
Partial Response 4/9 | Microadenomas  
Complete Response 6/6  
Partial Response 0/6  
Macroadenomas  
Complete Response 11/12  
Partial Response 1/12 | 2 patients cerebrospinal (CNS) fluid fistula  
1 patient meningitis  
Complication rate: 15% | 4 patients cerebrospinal (CNS) fluid fistula  
1 patient cranial nerve injury  
Complication rate: 24% |
| Non randomised comparative study (historical controls) | University of Wisconsin  
1996 – 1999  
41 patients  
34/41 procedures were done for resection of pituitary adenomas  
Endonasal  
7 microadenomas  
9 macroadenomas  
4 other sella | 2 patients cerebrospinal (CNS) fluid fistula  
1 patient meningitis  
Complication rate: 15% | Historical cohort follow-up in endonasal group was shorter  
Hospital stay and operative time in the endoscopic group shorter  
Surgeon unfamiliar with the use of the endoscope  
Control approach: sublabial or columellar incision |
| 7 microadenomas  
9 macroadenomas  
4 other sella  
Transseptal  
6 microadenomas  
12 macroadenomas  
3 other sella | Mean follow-up: unclear |
<p>| <strong>Sheehan, Atkinson,</strong> | Complete resection | Complete resection 15/36 | 3 patients with | 7 patients with cerebrospinal |
| Complete resection | Historical cohort follow-up in endonasal endoscopic surgery |</p>
<table>
<thead>
<tr>
<th>Authors, location, date, number of patients</th>
<th>Key efficacy findings</th>
<th>Safety</th>
<th>Comments</th>
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<tbody>
<tr>
<td>Kasperbauser, Erickson, &amp; Nippoldt (1999)</td>
<td>7/16 44% Visual field improvement 11/16 92%</td>
<td>46% Visual field improvement 27/36 87%</td>
<td>bleeding &gt;500ml 3 patients with cerebrospinal fluid leakage</td>
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<tr>
<td>Non randomised comparative study 1995 –1997</td>
<td>70 patients 26 endonasal 44 Sublabial</td>
<td>Non-functioning pituitary macroadenomas</td>
<td>Complication rate: 24%</td>
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<td>Kawamata, Iseki, Ishizaki &amp; Hori (2002a)</td>
<td>Acromegaly Post operative remission rate 28/43 65.1%</td>
<td>Acromegaly Post operative remission rate 40/67 59.7%</td>
<td>3 patients cerebrospinal (CNS) fluid leakage</td>
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<td>Non randomised comparative study (historical controls) 215 consecutive patients with pituitary tumours Tokyo 1996-2001</td>
<td>Prolactinoma Post operative remission rate 15/34 44.1%</td>
<td>Prolactinoma Post operative remission rate 25/53 47.1%</td>
<td>Complication rate 1.4%</td>
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<td>Nasseri, Kasperbauer, Strome, McCaffrey, Atkinson, &amp; Meyer (2001)</td>
<td>Microadenomas 29/35 (83%) without recurrence</td>
<td>Macroadenomas 31/102 no recurrence 32/102 debulked 11/102 treated irradiation 27 revision operation</td>
<td>2 patients epistaxis</td>
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<tr>
<td>Case series 164 patients pituitary adenomas</td>
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<td>7 patients cerebrospinal (CNS) fluid leakage</td>
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<td>Mean follow-up 10.28</td>
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<td>4 patients alar laceration</td>
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<td>1 patient meningitis</td>
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<td>Complication rate: 12%</td>
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<td>Months</td>
<td>Length of hospital data was also shorter compared with historical data</td>
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<tr>
<td>35 microadenomas</td>
<td>129 macroadenomas</td>
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<tr>
<td>16 other sella</td>
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Cappabianca, Cavallo, Colao, & De Divitis (2002)

**Case series**
**January 1997 and July 2001**
146 consecutive patients with pituitary adenomas
125 individuals has a pituitary macroadenoma, whereas 21 had a microadenoma

Follow-up 3 months to 4 years after the procedure

Not reported (not aim of the study)

2 patients epistaxis
3 patients sphenoid sinusitis
3 patients cerebrospinal (CNS) fluid leakage
1 patient residual lesion
1 patient meningitis
1 patient IS haematoma
1 patient internal injury
1 patient cranial nerve palsy

Complication rate: 9%

Complications divided into groups according to anatomical structures.

* The rate may not be an accurate reflection as some patients may have had more than one complication
Validity and generalisability of the studies

- Studies included patients with a range of pituitary adenomas, for example secreting and non-secreting tumours. This has potential implications for the generalisability of the results to all patients with pituitary adenomas.

- In the studies identified, no information is reported on the experience of surgeons in performing the endoscopic endonasal procedure. This is despite acknowledgment by many of the groups that a learning curve exists in relation to this procedure, and is evident from reported operation times. It is therefore unclear what impact the learning curve may have on safety and or efficacy outcomes.

- The endoscopic procedure often slightly varied among papers. This is also true for the comparative technique in the studies with a control group. It is hard to know how significant these variations are in relation to the overall generalisability of results.

- Outcome measures also varied between the studies. Not all studies reported that the primary aim was resection of tumours.

Specialist advisor’s opinion / advisors’ opinions

Expert advice was sought from the British Association of Otorhinolaryngologists, Head and Neck Surgeons, and the Society of Neurological Surgeons

- Procedure is considered a minor variation on an existing procedure.

- The main issue regarding efficacy is the adequate removal of tumours.

- Potential adverse events were listed as CSF fistula and carotid artery injury.

- Specialist Centre and training were also mentioned.

Issues for consideration by IPAC

- There would appear to be a learning curve associated with this procedure.

References


