

Trans-Sphenoidal Resection of Pituitary Tumours: Therapeutic Outcomes with the Sub-Labial Paraseptal Approach

I Crandon, S Cawich, N McLennon, H Harding, G Gordon-Strachan

Citation

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Abstract

Objective: To determine the therapeutic outcome after trans-sphenoidal resection of pituitary tumours using the sub-labial paraseptal approach at a tertiary institution in a developing Caribbean nation. **Method:** A cross-sectional analytical study using data collected from the hospital records of all patients who had sublabial paraseptal trans-sphenoidal (SPTS) hypophysectomy between January 1989 and June 2005 was undertaken. The data were analyzed using SPSS Version 12. **Results:** There were 119 SPTS hypophysectomies performed over the study period. There were 73 (61.3%) females and 46 (38.7%) males, with a mean age of 45.4 years (SD +/-14.8; Range 10-79; Median 45; Mode 45). These patients presented with visual disturbances (80.7%), non-specific headaches (72.3%), amenorrhoea (21.9%), galactorrhoea (19.3%), cranial nerve palsies (16%) and pituitary apoplexy (5%). Visual failure (80.7%) and endocrinopathies (44.5%) were the main indications for surgery. The operation resulted in adequate resection in 95% of cases, with endocrine cure in 69% and subjective improvement in vision in 41.8% patients. The commoner post-operative complications were transient CSF leaks (5%), with only 1 (0.8%) requiring lumbar drainage, transient diabetes insipidus (10.9%) and permanent diabetes insipidus (0.8%). There was tumour recurrence in 23 (19.3%) patients, nine of them requiring post-operative radiotherapy. There were no surgical deaths. **Conclusions:** The SPTS approach to pituitary tumours is a safe and effective treatment option in this setting. Heightened clinical vigilance, opportunities for earlier investigation and wider availability of adjunctive pharmacotherapy may improve the results of treatment of this common disorder.

INTRODUCTION

Pituitary tumors are relatively common neoplasms, accounting for approximately 10-15% of all primary brain tumours worldwide⁽¹⁻²⁾. The prevalence of pituitary tumours at the University Hospital of the West Indies (UHWI) in Jamaica is comparable to international figures⁽³⁻⁶⁾. Autopsy studies at the UHWI have revealed that asymptomatic pituitary adenomas occur in 10% of unselected subjects⁽³⁾.

Many patients with confirmed pituitary tumours will require surgical intervention for symptoms of local mass effect or endocrinopathies. There are several approaches to hypophysectomy. Trans-sphenoidal hypophysectomy was introduced in Jamaica in 1989. Literature review reveals that this is the first report documenting the outcomes of sub-labial para-septal trans-sphenoidal (SPTS) hypophysectomy from the Caribbean region.

METHODS

The UHWI is a 500-bed tertiary referral center in Kingston, Jamaica with seven operating theatre suites and two eight-bed multidisciplinary Intensive Care Units. This centre serves as an island wide referral centre for patients diagnosed with intra-cranial tumours who require neurosurgical intervention.

We retrospectively examined the medical records of all patients surgically treated for pituitary tumours at the UHWI over a period of 16 years from January 1989 to June 2005. Patients who had trans-sphenoidal surgery using the endoscopic technique, trans-nasal approach and/or craniotomy were excluded from analysis. Only patients who had SPTS hypophysectomy were evaluated in this study. Confirmation of the surgical approach was carried out with skull radiographs, image intensifier or neuronavigation.

Trans-Sphenoidal Resection of Pituitary Tumours: Therapeutic Outcomes with the Sub-Labial Paraseptal Approach

All the patients had post-operative imaging with computed tomography (CT) scans or magnetic resonance imaging (MRI). Complete resection was defined as gross tumour removal without evidence of residual tumour on post-operative imaging. However, a complete resection is not synonymous with cure. The therapeutic goal is to achieve symptomatic control by an adequate tumour resection within the boundaries of safety. Therefore, we defined an adequate resection as debulking of >50% of tumour mass on post-operative imaging and inadequate resections as debulking of <50% of tumour mass.

The information collected from hospital records included patient demographics, presenting clinical features, pre/post-operative visual field testing, pre/post-operative hormonal assays, morbidity and mortality. Data were analyzed using SPSS version 12.0. Comparisons were performed using Chi squared tests and Fisher's exact tests to determine significance. A P value <0.05 was considered statistically significant.

RESULTS

Over the study period there were 119 patients with pituitary tumours who required hypophysectomy using the SPTS approach. All operations were directly performed or supervised by the primary author, utilizing a Codman Hardy nasal speculum.

There was a 1:1.6 male to female ratio, with 73 (61.3%) females and 46 (38.7%) males. The patients presented at a mean age of 45.4 years (SD +/-14.8; Range 10-79; Median 45; Mode 45). At the time of diagnosis, 31 (30.4%) patients had co-morbid illnesses, most commonly hypertension (34.3%) and diabetes mellitus (9.8%).

Nonspecific headaches and disturbances in vision were the commonest complaints in these patients. Table 1 outlines the presenting symptoms.

Figure 1

| Presentation | Number | Percentage |
|---------------------|--------|------------|
| Visual disturbance | 96 | 80.7% |
| Headache | 86 | 72.3% |
| Amenorrhoea | 26 | 21.9% |
| Galactorrhoea | 23 | 19.3% |
| Cranial nerve palsy | 19 | 16.0% |
| Pituitary apoplexy | 6 | 5.0% |

Full details of ophthalmologic examination including results of visual acuity, visual perimetry testing and retinal examination were reported in 67 of 119 patients (Table 2). Sixty (89.6%) tested patients had visual field deficits, most commonly bi-temporal hemianopsia. There were 63 (94.0%) patients with impaired visual acuity and 25 (37.3%) patients were legally blind at presentation with visual acuity of 20/200 or worse (Table 2). Visual failure was the most common indication for operation.

Figure 2

| Visual status (n=67) | Pre-Operation | Post-Operation |
|------------------------------|---------------|----------------|
| Visual Acuity | | |
| • Normal acuity | 5 (7.5%) | 4 (6.0%) |
| • 20/25 - 20/100 | 37 (55.2%) | 53 (79.1%) |
| • 20/200 - NLP | 25 (37.3%) | 10 (14.9%) |
| Visual Field Deficits | 60 (89.6%) | 45 (67.2%) |
| Optic Atrophy | 34 (50.7%) | Unavailable |

Hormonal assays were routinely performed as a part of the pre-surgical work-up and revealed that the majority of pituitary tumours had no endocrine activity (Table 3). The most common endocrine tumour was a prolactinoma, with 12/29 of these patients already commenced on Bromocryptine for endocrine control.

Figure 3

| Endocrine Activity | Number | Percentage |
|--------------------------------|--------|------------|
| Non-functional Tumours | 66 | 55.5% |
| Hormonally Active Tumours | 53 | 44.5% |
| Hormonal Excess | | |
| • Hyper-prolactinemia | 29 | 24.4% |
| • Acromegaly | 7 | 5.9% |
| • Cushing's disease | 5 | 4.2% |
| • Hyper-thyroidism | 1 | 0.8% |
| Hormonal Deficiency | | |
| • Hypo-thyroidism | 9 | 7.6% |
| • Hypo-gonadism (Testosterone) | 2 | 1.6% |
| • Pituitary Apoplexy | 6 | 5.0% |
| • Pan-hypopituitarism | 0 | 0 |

Most patients (55%) had CT scans as the imaging investigation of choice pre-operatively, while MRI was used in 25% of cases, principally in the latter years of the series.

Plain skull radiographs were used for navigation to the sella in the first 23 patients, intra-operative fluoroscopy in 85 and image-guided neuro-navigation in the last 11 cases.

A muscle graft taken from the vastus lateralis was inserted into the sphenoid sinus after tumour resection in the first 66 patients but this practice was abandoned later in the series.

An intra-operative cerebrospinal fluid leak occurred in six (5%) cases and continued into the postoperative period in one case (0.8%). The latter required temporary lumbar diversion for resolution.

Post-operatively, all patients were evaluated radiologically either with CT scans (107) or MRI (12). Post-operative imaging revealed that there was adequate tumour resection in 113 (95%) cases while 6 (5%) patients had inadequate resections. There was complete resection with no evidence of residual tumour on post-operative imaging in 9 (7.6%) cases.

There were 13 cases of diabetes insipidus (10.9%) developing in the post-operative period. Most of these were transient, with only one (0.8%) patient developing persistent diabetes insipidus that required prolonged replacement therapy with Vasopressin analogues: DDAVP® (desmopressin acetate); Pitressin® (8-L-arginine vasopressin).

Visual acuity improved marginally after surgery. Although 28 (41.8%) patients reported subjective improvement in their visual fields, objective improvement in visual fields was only demonstrable in 15 (22.4%) patients after operation (Table 2). Of 42 patients with hormonal excesses, 29 (69%) endocrinopathies were cured by surgery.

Nine patients had postoperative radiotherapy. There was recurrence of the pituitary tumour in 23 (19.3%) cases. Only one death (0.8%) was recorded in a patient with Nelson's syndrome who died from non-surgical causes.

DISCUSSION

Craniotomy was the first surgical treatment for pituitary tumours, introduced by Sir Victor Horsley in 1889⁽⁷⁾. Unfortunately, there is significant morbidity accompanying craniotomy including cortical injury, intra-cranial haematoma, sacrifice of olfactory tracts and epilepsy⁽²⁾.

These potential complications are avoided with the trans-sphenoidal approach to hypophysectomy. The first recorded trans-sphenoidal hypophysectomy was performed by Herman Schloffer of Innsbruck in 1907⁽⁷⁾. In the same year, Harvey Cushing described a modified para-septal approach without the use of a microscope⁽⁷⁾. Despite a low mortality rate (5.6%) in his series of 422 such operations in the late 1920s, Cushing later abandoned the trans-sphenoidal approach in favor of the trans-cranial route⁽⁷⁾.

The trans-sphenoidal approach was preserved by Norman Dott in Edinburgh, who studied under Cushing as a Rockefeller fellow at the Brigham Hospital in the mid 1920's⁽⁸⁾. Despite the introduction of specifically designed instruments⁽⁸⁾, this approach eventually fell out of favour because it was 'blind'. Dott's pupil, Gerard Guiot reintroduced the approach in Paris under fluoroscopic guidance⁽⁸⁾ and Jules Hardy in Montreal developed and publicized the technique in the modern era⁽⁸⁾. The modern operation, using either an endoscopic trans-nasal or a SPTS approach to the sella is now done using an operating microscope, guided by intra-operative fluoroscopy or neuro-navigation.

A SPTS hypophysectomy is generally well tolerated and boasts the advantages of rapid access, minimal morbidity and the absence of a visible scar^(1,2). The SPTS approach to hypophysectomy was introduced in Jamaica in 1989. To the best of our knowledge, this is the first report documenting the outcomes of SPTS hypophysectomy in the Caribbean region.

The majority of lesions in this series were non-functional adenomas, similar to other reports in the medical literature^(1,2,9,10). These hormonally inactive tumours tend to progress silently until hypopituitarism or chiasmal compression develops^(2,4). This accounted for the relatively late presentation, with advanced visual disturbances in over 90% of tested patients. This is not a feature peculiar to developing nations but reflects the anatomy of the sellar region^(1,11).

Hypophysectomy using the SPTS approach has been proven to be effective in this setting. It is important to note that complete gross tumor removal is not synonymous with cure^(11,15). The therapeutic goal is to achieve adequate tumour resection within the boundaries of safety. Therapeutic success is marked by the control of symptoms of mass effect or endocrine over-activity. We achieved adequate resection in 95% of cases. This is comparable to current reports in the medical literature⁽¹¹⁻¹⁴⁾.

Of 42 patients with endocrine over-activity, 69% of endocrinopathies were cured post-operatively. This is comparable to the endocrine cure rates reported in similar small series of less than 110 cases that range from 25%⁽¹¹⁾ to 72%⁽¹²⁾.

There was marginal improvement in visual symptoms, the most common indication for SPTS hypophysectomy. Post-

operation, there was a reduction in the proportion of patients with visual field abnormalities (89.6% vs 67.2%), although it did not attain statistical significance. Although there were trends toward improved visual acuity, there was no increase in the proportion of patients with normal acuity post-operatively (7.3% vs 6.0%; $P > 0.1$). This may be due to the high proportion of patients at presentation having advanced visual disturbances and reinforces the importance of early diagnosis and treatment to prevent severe permanent visual impairment that may result from prolonged duration of untreated disease⁽¹¹⁾.

Diabetes insipidus and CSF leaks are the commonest reported complications of SPTS hypophysectomy^(9,12). CSF leaks are reported to occur after 11%⁽¹³⁾ to 18%⁽¹⁵⁾ of cases in the neurosurgical literature. Our rates of CSF leaks (5%) compare favourably to these reports. We initially employed a vastus lateralis muscle graft in the first 66 cases in our series. In the latter half of our series, we selectively employed muscle grafts only when there was evidence of intra-operative CSF leak. In this group, there was one case in which a persistent post-operative CSF fistula developed that required lumbar drain diversion.

The incidence of diabetes insipidus is reported to be similar after hypophysectomies by the SPTS and the endoscopic endonasal transsphenoidal approaches^(14,15). Small series report 9-14% incidence of diabetes insipidus after SPTS hypophysectomy^(9,12,15). Our incidence of diabetes insipidus (10.9%) compares favourably to these reports. Most cases resolved spontaneously, with only one (0.8%) case of persistent diabetes insipidus requiring prolonged replacement therapy with Vasopressin analogues: DDAVP® (desmopressin acetate); Pitressin® (8-L-arginine vasopressin).

Tumour recurrence has been reported to occur after 21–50% of hypophysectomies, depending on tumour size and histology, completeness of resection and surveillance duration^(9,12). In this series, tumour recurrence rates (19.3%) compared favourably with figures in the international literature^(9,12).

Adjunctive pharmacotherapy or irradiation may be appropriate in some patients with inadequate resection or post-operative tumour recurrence. This modality has a long history in the treatment of pituitary tumors, since the first report in 1909 by Gramegna using horizontally opposed temporal ports⁽¹⁷⁾. In the mid-20th Century stereotactic

insertion of radioactive seeds to produce local brachytherapy was developed⁽¹⁸⁾. More recently, stereotactic radiosurgery became available and was shown to be safe and effective in Cushing's disease⁽¹⁹⁾ and acromegaly⁽²⁰⁾ refractory to trans-sphenoidal surgery, although late hypopituitarism is common.

Radiotherapy is no longer recommended as a routine post-operative adjunct due to the prevalence of radiation morbidity: chiasmal injury; memory disturbance; radionecrosis and induction of secondary malignancies⁽¹⁷⁾. Irradiation is now reserved as an option for recurrences after repeat surgery, patients unsuitable for general anaesthesia, failure to achieve or maintain endocrine cure and malignant tumours^(17,18). In this series, fewer than 10% of our patients had post-operative radiotherapy. In Jamaica, stereotactic radiosurgery is not generally available and its cost is often prohibitive.

CONCLUSIONS

The efficacy of sub-labial para-septal transsphenoidal resection of pituitary tumours has been demonstrated in this setting with acceptably low operative morbidity and mortality. This operation yields adequate tumour resection in 95% of cases, with endocrine cure in 69% of cases and subjective improvement in visual function in 41.8% of patients. Heightened clinical vigilance, opportunities for earlier investigation and wider availability of adjunctive pharmacotherapy may further improve the results of treatment of this common disorder.

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Author Information

Ivor W Crandon, M.B.B.S., F.R.C.S. (Ed)

Department of Surgery, Radiology, Anaesthesia and Intensive Care, The University of the West Indies, Mona Campus

Shamir O. Cawich, M.B.B.S., D.M.

Department of Surgery, Radiology, Anaesthesia and Intensive Care, The University of the West Indies, Mona Campus

Noel McLennon, M.B.B.S.

Department of Surgery, Radiology, Anaesthesia and Intensive Care, The University of the West Indies, Mona Campus

Hyacinth E Harding, M.B.B.S., D.M

Department of Surgery, Radiology, Anaesthesia and Intensive Care, The University of the West Indies, Mona Campus

Georgianna Gordon-Strachan, B.Sc

Department of Surgery, Radiology, Anaesthesia and Intensive Care, The University of the West Indies, Mona Campus