The functional evaluation of pituitary in patients with a surgical resection of sellar tumours

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Abstract

Introduction: The aim of this study was to analyse the incidences of hypopituitarism before and after surgical resection of sellar tumours and to find the factors related to the incidences.

Material and methods: From January 2009 to December 2011, 191 patients in the Department of Neurosurgery in Xiangya Hospital, who underwent the surgical resection of sellar tumours, were included in this retrospective analysis. Pre- and postoperative pituitary function assessments were performed by the detection of hormone levels. Tumour size and location were analysed by magnetic resonance imaging (MRI).

Results: In total 152 (79.6%) patients had anterior pituitary hypofunction preoperatively, and 176 (92.1%) patients had anterior pituitary hypofunction postoperatively. The pre- and postoperative adrenal cortex hypofunction incidences were 83 (43.5%) and 103 (53.9%), respectively. Ninety-three (48.7%) patients had thyroid hypofunction preoperatively, and 101 (52.9%) patients had anterior pituitary hypofunction postoperatively. The pre- and postoperative hypogonadism incidences were 131 (68.6%) and 160 (83.8%), respectively. The postoperative incidences of anterior pituitary hypofunction and hypogonadism in patients with craniopharyngioma or pituitary tumours were both significantly higher than the preoperative incidences. Surgery resection methods and tumour sizes were found to be related to the incidence of postoperative hypogonadism.

Conclusions: To sum up, we found that the postoperative incidences of hypopituitarism were higher than the preoperative incidences. Tumour type, surgery resection methods, and tumour sizes were important contributing factors to the incidence of postoperative hypogonadism.

Key words: hypopituitarism, sellar tumours, surgical resection.

Introduction

The sellar region is a complex crossroads where many tissues and cells from many different origins converge; thus, this region can host a numerous and heterogeneous group of tumours including pituitary adenoma, craniopharyngioma, granular cell tumour, pituicytoma, germ cell tumours, gangliocytoma, glioma, chordoma, metastatic carcinoma, and haematopoietic tumours [1]. Tumours arising from the sellar area represent 10–15% of all intracranial neoplasms, and most sellar area tumours are pituitary adenoma [2]. Other than the therapeutic modalities including medical ther-

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apy and radiation [3], the first line of treatment in most cases is surgical resection, which can relieve the pressure on the normal pituitary [4]. However, postoperative hypopituitarism is still a well-known consequence after surgical resection, emphasised by the fact that in patients with pituitary deficits there is a clear tendency towards reduced quality of life and reduced life expectancy [5]. Hypopituitarism may be found at initial work-up of patients harbouring pituitary adenomas (accounting for approximately 10% of all diagnosed intracranial tumours [6]), usually due to compression and destruction of the normal pituitary gland by the expanding mass, and focal necrosis due to compression of the portal circulation is also possible [7]. Hypopituitarism causes a series of hypofunction of endocrine glands, mainly involving the gonads, thyroid, and adrenal cortex. Although hypopituitarism is always reported after the surgical resection of sellar tumours, the systematic comparative analyses between rates preoperatively and postoperatively across different tumour types were few. Here, we analyse 191 consecutive patients who underwent surgical resection of sellar tumours over a two-year period. The incidences of hypopituitarism before and after surgical resection of sellar tumours were recorded respectively, and the factors related to the incidences were analysed.

Material and methods

Subjects

From January 2009 to December 2011, 191 patients in the Department of Neurosurgery in Xiangya Hospital, who underwent the surgical resection of sellar tumours, were included in this retrospective analysis. The characteristic and clinical data were collected, including age, surgical method (transsphenoidal approach [8] and transcranial approach), magnetic resonance imaging (MRI) for tumour size and location, and pre- and postoperative serum levels of pituitary-adrenal hormone (adrenocorticotropic hormone (ACTH) and cortisol (F)), pituitary-gonadal hormone (luteinizing hormone (LH), follicle-stimulating hormone (FSH), testosterone (T), estradiol (E_2), and prolactin (PRL)), and pituitary-thyroid hormone (thyroid-stimulating hormone (TSH), triiodothyronine (FT_3), and thyroxine (FT_4)). Blood samples were collected at 8:00 a.m. from each specimen, and the hormone levels were detected on a Roche Cobas 6000 automatic analyser. Sellar tumour size and location were imaged using a GE Signa HDx3.0T MRI scanner. This study was approved by Xiangya Hospital.

Pre- and postoperative pituitary functional assessment

Pituitary functions (including anterior pituitary, gonadal, thyroid, and adrenal axes) were assessed using strict criteria. Hypopituitarism is a deficiency of one or more pituitary hormones, including pituitary-adrenal hormone (ACTH and F), pituitary-gonadal hormone (LH, FSH, T, E_2, and PRL), and pituitary-thyroid hormone (TSH, FT_3, and FT_4). In our study, hypopituitarism is identified as the deficiency of one pituitary hormone, as previously described [9–12].

Statistical analysis

All data were analysed using statistical software SPSS17.0. The rate was calculated as: ((The postoperative incidence – the preoperative incidence)/the postoperative incidence) × 100%. The rates among different groups were compared by the χ^2 test. Tumour size was expressed as median value ± inter-quartile range and compared using Wilcoxon's test. When the number of data was less than five, Fisher's test was used. $P < 0.05$ was considered statistically significant.

Results

Characteristics of patients

Over a 2-year period 191 patients, including 103 (54%) men and 88 (46%) women, with an age range from 4 to 72 years (average age: 39.37 ±16.82) were enrolled. The median value of their sellar tumour size was 14.85 ±23.28 mm³, with maximum tumour size of 6 × 7 × 5 cm and minimum tumour size of 0.22 × 0.33 × 0.35 cm.

Pre- and postoperative incidences of hypopituitarism

Patients with sellar tumours were evaluated for pituitary, gonadal, thyroidal, and adrenal function preoperatively and postoperatively. As shown in Table I, 152 of 191 patients (79.6%) had anterior pituitary hypofunction preoperatively, and 176 of 191 patients (92.1%) had anterior pituitary hypofunction postoperatively, with a rate of 12.5%. The pre- and postoperative adrenal cortex hypofunction incidences were 83 (43.5%) and 103 (53.9%),

Table I. Pre- and postoperative incidences of hypopituitarism

Parameter	Pre-operative incidence	Post-operative incidence	Rate
Anterior pituitary function	152 (79.6%)	176 (92.1%)	12.5%
Adrenal cortex hypofunction	83 (43.5%)	103 (53.9%)	10.4%
Thyroid hypofunction	93 (48.7%)	101 (52.9%)	4.2%
Hypogonadism	131 (68.6%)	160 (83.8%)	15.2%

respectively, with a rate of 10.4%. Ninety-three (48.7%) patients had thyroid hypofunction pre-operatively, and 101 (52.9%) patients had anterior pituitary hypofunction postoperatively, with a rate of 4.2%. The pre- and postoperative hypogonadism incidences were 131 (68.6%) and 160 (83.8%), respectively, with a rate of 15.2%. These results indicated that the incidence of hypogonadism is most affected by surgical resection.

Pre- and postoperative hypopituitarism incidences of patients with craniopharyngioma and pituitary tumours

We then determine whether different tumour types affect the incidences of hypopituitarism; here, patients with craniopharyngioma and pituitary tumours were selected and the pre- and postoperative incidences were analysed (Table II). Firstly, we found that the tumour size of patients with craniopharyngioma was 28.61 ±44.45 mm^3, while the tumour size of patients with pituitary tumours was 12.50 ±18 mm^3. The preoperative anterior pituitary hypofunction incidences of patients with craniopharyngioma (53 (80.3%)) or pituitary tumours (99 (79.2%)) were both significant lower than the postoperative incidence (62 (93.9%), $p < 0.05$ and 114 (91.2%), $p < 0.05$), with rates of 13.6% and 12.0%, respectively. Thirty-three (50.0%) patients and 38 (57.6%) patients with craniopharyngioma had adrenal cortex hypofunction preoperatively and postoperatively, respectively, with a rate of 7.6%. Fifty (40.0%) patients and 65 (52.0%) patients with pituitary tumours had adrenal cortex hypofunction preoperatively and postoperatively, respectively, with a rate of 12.0%. Thirty-two (48.5%) patients and 41 (62.1%) patients with craniopharyngioma had thyroid hypofunction preoperatively and postoperatively, respectively, with a rate of 13.6%. Sixty (48.0%) patients and 61 (48.8%) patients with pituitary tumours had thyroid hypofunction pre-

operatively and postoperatively, respectively, with a rate of 0.8%. The preoperative hypogonadism incidence of patients with craniopharyngioma (49 (74.2%)) or pituitary tumours (82 (65.6%)) was significant lower than the postoperative incidence (60 (90.9%), $p < 0.05$) and (100 (80.0%), $p < 0.05$), with rates of 16.7% and 14.4%, respectively. In total, it showed that the postoperative incidences of anterior pituitary hypofunction and hypogonadism in patients with craniopharyngioma or pituitary tumours were both significantly higher than the preoperative incidences.

Pre- and postoperative hypopituitarism incidences of patients after different surgery approaches

Afterwards, we determined whether different surgery approaches affected the incidence of hypopituitarism; here, the pre- and postoperative hypopituitarism incidences of patients who had undergone the transsphenoidal approach and transcranial approach were analysed (Table III). We found the tumour size of patients who had undergone the transsphenoidal approach was 10.78 ±18.49 mm^3, while the tumour size of patients who had undergone the transcranial approach was 24.28 ±37.59 mm^3. The preoperative anterior pituitary hypofunction incidence of patients who had undergone transsphenoidal approach (79 (79.8%)) or transcranial approach (67 (80.7%)) were both significantly lower than the postoperative incidence (90 (90.9%), $p < 0.05$ and 77 (92.8%), $p < 0.05$), with rates of 10.1% and 12.1%, respectively. There were no significant differences between the adrenal cortex hypofunction incidences preoperatively and postoperatively both in patients who had undergone transsphenoidal approach (43 (43.4%) and (50 (51.5%)) and transcranial approach (37 (44.6%) and 49 (59.0%)). Also, no significant differences between the thyroid hypofunction incidences preoperatively and

Table II. Pre- and postoperative hypopituitarism incidences of patients with craniopharyngioma and pituitary tumours

Variables	Craniopharyngioma			Pituitary tumours		
	Tumour size 28.61 ±44.45 mm^3			Tumour size 12.50 ±18 mm^3		
	Preoperative incidence	Postoperative incidence	Rate	Preoperative incidence	Postoperative incidence	Rate
Anterior function	53 (80.3%)	62 (93.9%)*	13.6%	99 (79.2%)	114 (91.2%)*	12.0%
Adrenal cortex hypofunction	33 (50.0%)	38 (57.6%)	7.6%	50 (40.0%)	65 (52.0%)	12.0%
Thyroid hypofunction	32 (48.5%)	41 (62.1%)	13.6%	60 (48.0%)	61 (48.8%)	0.8%
Hypogonadism	49 (74.2%)	60 (90.9%)*	16.7%	82 (65.6%)	100 (80.0%)*	14.4%

*$p < 0.05$.

Table III. The pre- and postoperative hypopituitarism incidences of patients underwent different surgery approaches

Variables	Transsphenoidal approach			Transcranial approach		
	Tumour size 10.78 ±18.49 mm³			Tumour size 24.28 ±37.59 mm³		
	Preoperative incidence	Postoperative incidence	Rate	Preoperative incidence	Postoperative incidence	Rate
Anterior pituitary function	79 (79.8%)	90 (90.9%)*	10.1%	67 (80.7%)	77 (92.8%)*	12.1%
Adrenal cortex hypofunction	43 (43.4%)	50 (51.5%)	8.1%	37 (44.6%)	49 (59.0%)	14.4%
Thyroid hypofunction	47 (47.5%)	50 (50.5%)	3.0%	40 (48.2%)	49 (59.0%)	10.8%
Hypogonadism	66 (66.7%)	78 (78.8%)*	12.1%	62 (74.7%)	74 (89.2%)*	14.5%

*$p < 0.05$.

postoperatively both in patients who had undergone transsphenoidal approach (47 (47.5%) and 50 (50.5%)) or transcranial approach (40 (48.2%) and 49 (59.0%)) were found. In contrast, the preoperative hypogonadism incidence of patients who had undergone transsphenoidal approach (66 (66.7%)) or transcranial approach (40 (48.2%)) were both significant lower than the postoperative incidence (78 (78.8%), $p < 0.05$ and 74 (89.2%), $p < 0.05$), with rates of 12.1% and 14.5%, respectively.

Tumour sizes in hypopituitarism and normal groups

The tumour sizes in the anterior pituitary hypofunction, adrenal cortex hypofunction, thyroid hypofunction, and hypogonadism groups, along with the corresponding groups, were detected (Table IV). The tumour sizes in the anterior pituitary hypofunction, adrenal cortex hypofunction, and hypogonadism groups were significantly larger than that in the corresponding groups. The tumour sizes in the thyroid hypofunction group seemed larger than in the normal group; however, no statistically significant difference was found.

Discussion

The incidence of hypopituitarism is estimated to be 4.2 per 100,000 per year, and the prevalence is 45.5 per 100,000, respectively [13]. Although the clinical symptoms of this disorder are usually non-specific, it can cause life-threatening events and lead to increased mortality [10]. Hypopituitarism is a well-accepted consequence after surgical resection of pituitary adenoma and craniopharyngioma. Approximately 70% of cases with pituitary adenoma were reported to have hypersecretory syndrome. If a tumour reaches a sufficiently large size to expand beyond the limits of the sella turcica, it can cause symptoms related to a local mass effect, usually visual disturbances and hypothalamus-based dysfunction [1]. Thus, the comparative analysis concerning the pre- and postoperative hy-

popituitarism incidences in patients with pituitary adenoma or craniopharyngioma was performed in our study. The impact of surgery methods and tumour size on hypopituitarism incidence were also analysed.

Corticotropin-releasing hormone is secreted in the hypothalamus and transported into the anterior pituitary, where it stimulates the release of ACTH from the pituitary gland, which then stimulates the secretion of cortisol at the adrenal glands. These procedures are collectively known as the hypothalamic-pituitary-adrenal (HPA) axis [14]. The hypothalamic-pituitary-thyroid (HPT) axis is controlled by the hypothalamus that synthesises and subsequently releases thyrotropin-releasing hormone (TRH) into the median eminence. TRH

Table IV. The tumour sizes in hypopituitarism and normal groups

Pituitary function	Preoperative		
	Median value	Inter-quartile range	P-value
Anterior pituitary function:			
Hypofunction	15.00	22.17	0.040
Normal	7.61	27.10	
Adrenal cortex function:			
Hypofunction	15.40	21.50	0.041
Normal	12.50	25.25	
Thyroid function:			
Hypofunction	15.12	18.57	0.537
Normal	12.59	29.80	
Gonadal function:			
Hypofunction	16.50	25.07	0.015
Normal	7.27	19.61	

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stimulates the release of thyrotropin (TSH) from the anterior pituitary, and TSH then travels to the thyroid gland to stimulate the synthesis and release of thyroid hormones. The hypothalamic-pituitary-gonadal (HPG) axis mainly refers to the following procedure: gonadotropin-releasing hormone (GnRH) secreted in the hypothalamus can simulate the release of LH and follicle-stimulating hormone FSH from the pituitary, which then exerts effects on the gonads [15]. The HPA axis has been suggested to play a role in HPT-axis regulation, and functional cross-talk between the HPG axis and HPA axis was also discussed previously [16, 17]. Thus, for detection of the incidences of hypopituitarism, we analysed the incidences of anterior pituitary hypofunction, adrenal cortex hypofunction, thyroid hypofunction, and hypogonadism, respectively.

In our study, taking it as a whole, we found that the postoperative incidences of hypopituitarism were higher than the preoperative incidences, indicating the effects of surgical resection on the hypopituitarism incidences. Among them, the incidence of hypogonadism is most affected by the surgical resection. In many cases over the past two decades, improved postoperative pituitary function was seen in 35–50% of patients [18–21]. Research has indicated that even if clear hypofunction is observed at initial work-up, patients should be reassessed after surgery without substitution therapy because practically half the preoperative pituitary hormone deficiencies recover postoperatively, eliminating the need for life-long substitution therapy.

Previous studies also indicated that the variability in rates of new hypopituitarism are probably associated with factors including different surgical strategies with respect to normal gland manipulation and preservation, transsphenoidal surgical experience, and hormonal testing protocols [9]. After determining the pre- and postoperative hypopituitarism incidences of patients with craniopharyngioma and pituitary tumours, we found that the postoperative incidences of anterior pituitary hypofunction and hypogonadism in patients with craniopharyngioma or pituitary tumours were both significantly higher than the preoperative incidences, indicating that the tumour type also affects the hypogonadism incidence. We then also found that different types of surgical resection affect the hypogonadism incidence and tumour size, which is an important contributing factor to the incidence of postoperative hypogonadism, with the exception of thyroid hypofunction. A previous study indicated that transsphenoidal surgery is considered a safe procedure, but it carries the risk of various postoperative complications. The same study also suggested that tumour size or pathology may have

been be contributory factors for their findings [22]. Conclusions have been stated that the transsphenoidal approach in pituitary adenoma surgery is connected with low risk of iatrogenic hypopituitarism [23, 24]. Consistently, in our study, we found that the rate in the transcranial approach group was higher than in the transsphenoidal approach group. Importantly, a previous study indicated that transsphenoidal surgery carries an acceptable risk for sacrificing anterior pituitary function, but the risk is greater in patients with larger tumours and preoperatively compromised pituitary function [19]. Additionally, Fatemi *et al.* suggested that the strongest predictor of new hypopituitarism was tumour size, with a new axis loss occurring in 12% of all patients with adenomas that were 30 mm or greater in diameter [9].

In conclusion, we found that the postoperative incidences of hypopituitarism were higher than the preoperative incidences. Tumour type, surgical resection method, and tumour size were important contributing factors to the incidence of postoperative hypogonadism.

Conflict of interest

The authors declare no conflict of interest.

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