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Original Article

OUTCOME OF PITUITARY ADENOMA RESECTION IN PATIENTS WITH HYPERPROLACTINEMIA

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ABSTRACT

Background: Pituitary gland that resides in the sellaturcica is a 60 milligram midline structure. The normal function includes secretion of certain hormones that directly or indirectly regulate the activity of other organs. Some major functions are being controlled by these hormones in the body. Postoperative hypopituitarism and hormonal recovery are well-known consequences of trans-sphenoidal pituitary adenoma removal. The purpose of the study is to assess the post-surgical changes in the levels of pituitary hormones and to determine the outcome of pituitary adenoma resection in patients with mild hyperprolactinemia **Methods**: A total of 39 pituitary tumor patients diagnosed on MRI were included in this study during the period of 24 months from Jan 2013 to December, 2014. Pre and post-operative prolactin levels were recorded on a pre designed questionnaire. Patients who have undergone surgery were kept under observation during the period of stay and were observed in follow-up until the third month after discharge. **Results:** Out of 39 patients, 17(43.58%) were males and 22(56.4%) were females. Satisfactory outcome of pituitary adenoma resection in patients with mild hyperprolactinemia was observed in 82.94%. **Conclusion:** It has been demonstrated that in expert surgical hands, normal anterior pituitary function is usually maintained and often improved following surgery of non-functioning pituitary adenomas. These results strengthen the indication for surgery in patients with hypopituitarism. However, care should be taken as these results are less likely to be reproduced by surgeons with limited experience in pituitary surgery.

Key Words: pituitary adenoma, mild hyperprolactinemia, hypopituitarism

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INTRODUCTION

Pituitary gland that resides in the sellaturcica is a 60 milligram midline structure. The normal function includes secretion of certain hormones that directly or indirectly regulate the activity of other organs. Some major functions are being controlled by these hormones in the body.

Non-functioning adenomas is present with 25-30 % of patients with absence of classical hypersecretory syndromes [1]. Since 70% [1] of adenomas are endocrinologically secreting, the systemic effect obtained is significant to risk the life of patient. The pituitary functions are preserved in 97% of the patients [2]. However, recurrence rate is 13% in ten years [2]. Clinical studies have shown that hypopituitarism develops in approximately 5% of patients undergoing transsphenoidal adenomectomy, whereas 50% of patients have their hormonal functions back to normal [3]. Postoperative hypopituitarism and hormonal recovery are well-known consequences of transsphenoidal pituitary adenoma removal. In most reports, the rate of new long-term pituitary failure is less than 10% [4], with higher rates reported in cases of pituitary apoplexy and reoperations for Cushing's disease [5]. Prevalence of satisfactory outcome was reported in 97% cases [6]

When surgical resection of pituitary tumors is done, there is a change in the levels of hormones secreted from pituitary, as a response to surgical manipulation. Although most trans-sphenoidal surgical series cite rates of new hypopituitarism, there have been no systematic analyses assessing the differences in hormone level before and after pituitary macro adenoma resection in a Pakistani population. Thus, there is a need to determine whether methods used in Pakistan for tumor resection bear the same results so that they may be evaluated in that light, and altered, if necessary. Hence, our study is focused on assessing the post-surgical change in the levels of pituitary hormones and to determine the surgical outcome, by evaluating the functioning of the pituitary gland by assessing the level of hormones in the blood notably prolactin levels, after adenoma resection in patients with mild hyperprolactinemia. Prolactin is a hormone whose main role, is in the production of milk (lactation) in females, which is produced in response to the suckling stimulus, it is also involved in sexual gratification, and the refractory period in males, while an elevated level causes impotence, loss of libido, and decreasein the levels of sex hormones that is estrogen and testosterone in females and males respectively. Hyperprolactinemia typically presents in the females as oligomenorrhia, amenorrhea and infertility, and in men it presents with sexual dysfunction. And if it is due to pituitary adenoma, it presents with visual field disturbances and headaches in addition to the afore mentioned signs and symptoms.

METHODOLOGY

This prospective, case series was conducted for 24 months after approval of Ethical Review Board from Jan 2013 to December 2014. Informed consent was obtained from all study participants. The study participants were all those patients who presented to us within the study period. Patients fulfilling the inclusion criteria were selected from Neurosurgery department at Civil Hospital Karachi. The inclusion criteria included patients of either sex having age of 40 years to 70 years with confirmed diagnosis of pituitary tumor on MRI scan along with both micro and macro adenomas. Furthermore, these patients undergone endonasal transsphenoidal removal of pituitary adenoma and presented with hyperprolactinemia (PCT>18ng/ml). However, patients who received pre-operative cranial or sellar radiotherapy and had post-operative hormonal evaluation for less than 3 months were excluded from the study. The patient population consisted on 39 patients. Adenoma was defined aspresence of circumscribed area of hypo/iso-intense T1 or iso/hyper- intense T2 signals on side of pituitary on MRI. In the present study resolution of hyperprolactinemia was considered as satisfactory outcome. Moreover, Prolactin Levels were considered as normal if they were in the range of 0-18ng/dl. The demographic characteristics of patients along with pre and post-operative prolactin levels were recorded on the pre tested questionnaire. Patients who underwent surgery were kept under observation during the period of stay and were observed in follow-up until the third month after discharge. Data was analyzed using SPSS version 19. Mean and standard deviation were calculated for quantitative variables like age. Frequency/percentages were calculated for categorical variables like the gender and satisfactory outcomes. Stratification with respect to age, micro and macro adenoma and gender was carried out. Post stratification chi-square test was applied and $p \leq 0.05$ was considered significant.

RESULTS

A total of 39 pituitary tumor patients diagnosed on MRI were included in this study. 10 (25.64%) patients were below and equal to 50 years of age, 16 (41.02%) were in the age group of 51 to 60 years and 13 (33.33%) participants were above 60 years of age . The average age of the participants was 56.21±8.22 years, average size of adenoma was 1.04±0.8 cm and average postoperative serum prolactin level of the patients was

TABLE 1
OUTCOME OF PITUITARY ADENOMA RESECTION IN PATIENTS WITH MILD HYPERPROLACTINEMIA WITH RESPECT TO AGE GROUPS

Age Groups (Years)	Resolution of Hyperprolactinemia		Total	P-Values
	Satisfactory	Unsatisfactory		
≤50 Years	8(80%)	2(20%)	10	
51 to 60 Years	11(84.61%)	2(15.38%)	13	0.53
61 to 70 Years	13(81.25%)	3(18.75%)	16	

TABLE 2
OUTCOME OF PITUITARY ADENOMA RESECTION IN PATIENTS WITH MILD HYPERPROLACTINEMIA WITH RESPECT TO GENDER

Gender	Resolution of Hyperprolactinemia		Total	P-Values
	Satisfactory	Unsatisfactory		
Male	16(94.11%)	1(5.88%)	17	0.005
Female	16(72.72%)	6(27.27%)	22	

TABLE 3
OUTCOME OF PITUITARY ADENOMA RESECTION IN PATIENTS WITH MILD HYPERPROLACTINEMIA WITH RESPECT TO SIZE

Adenoma	Resolution of Hyperprolactinemia		Total	P-Values
	Satisfactory	Unsatisfactory		
Micro	20(90.90%)	2(9.09%)	22	0.0005
Macro	12(70.58%)	5(29.41%)	17	

10.9±9 ng/ml. Moreover, out of 39 patients, 17(43.58%) were males and 22(56.4%) were females. Micro adenoma was observed in 56.41% (N=22) cases and macro adenoma was found in 43.58%(N=17) patients.

Satisfactory outcome(improvement in visual field disturbances, resolution of symptoms associated with pituitary adenoma, and diminution in size of the tumor, prolactin levels return to the normal range that is less than 20ng/ml) of pituitary adenoma resection in patients with mild hyperprolactinemia was observed in 82.05% (N=32) cases where as unsatisfactory outcome was observed in only 17.94% (N=7). Satisfactory outcome was high in all age groups but statistically insignificant (p=0.53) as shown in table 1. Furthermore, satisfactory outcome was significantly high in male as compare to female (96.2% vs. 73.3%; p=0.005) as presented in table 2. Similarly, satisfactory outcome was also significantly high in micro adenoma than macro adenoma (93.1% vs. 70.5%; p=0.0005) as shown in table 3.

DISCUSSION

Postoperative pituitary deficiency, particularly pan hypopituitarism, is considered as a significant complication of pituitary surgery because it dramatically affects the patient's quality of life by necessitating hormonal substitution therapy. Following the

introduction of transsphenoidal microsurgery in the management of patients with pituitary tumors, selective adenomectomy has become the main aim in order to preserve as much normal pituitary tissues as possible. Several studies demonstrated that preservation of pituitary tissue was mostly associated with no further loss of pituitary function. However, earlier studies examined only the incidence of deterioration in pituitary function following surgery. It is only recently reported, by several groups, that impaired pituitary function could actually be restored by selective surgical resection of the adenomas [(7)].

Interruption of the pituitary stalk or mechanical compression of the portal vessels would cause diminished hypothalamic control over pituitary hormone secretion, leading to hyperprolactinemia and deficiency in the secretion of all other pituitary hormones. Studies conducted in experimental animals [(8)], as well as in humans [(9)], have demonstrated a classical pattern of change in pituitary hormone secretion when the pituitary stalk is sectioned or compressed by mass lesions such as a large pituitary adenoma [(10)], a carotid artery aneurysm [(9)], a meningioma [(11)], or a craniopharyngioma [(12)]. Patients with pituitary stalk compression demonstrate mild hyperprolactinemia and loss of other pituitary hormone secretion [(13)]. Likewise, patients with large pituitary adenomas often present with similar clinical and biochemical features consisting of hypopituitarism and mild hyperprolactinemia [(10)].

In this study most of the patients that were diagnosed with these tumors n=16 (41.02%) were between 51 to 60 years of age. The findings of our study are consistent with study carried out by Nomikos et al [(11)] where majority of these tumors occurred in middle aged patients, with a maximum between 51 to 60 years of age. In our study out of 39 patients, 17(43.58%) were males and 22(56.4%) were females. Micro adenoma was observed in 56.41% cases and macro adenoma was 43.58%. In men and women, 50%–69% of non secretinggonadotroph adenomas will release FSH, LH, a subunit, or LH b subunit in response to thyrotropin-releasing hormone testing. This suggests that the cells in a gonadtroph adenoma have acquired thyrotropin-releasing hormone receptors, whereas normal gonadotroph cells do not have such receptors [(12)]. Renner et al. [(13)] demonstrated alterations in dopamine D2 receptor subtypes in subjects with nonfunctioning adenomas, which may explain the differential sensitivity of these adenomas to suppression with dopamine agonists.

In present study satisfactory outcome of pituitary adenoma resection in patients with mild hyperprolactinemia was observed in 83.24% which is congruent with work of Nomikos et al study where prevalence of satisfactory outcome was 97% cases [(6)]. Several investigators reported mild hyperprolactinemia accompanying hypopituitarism associated with pituitary macro-adenomas not secreting prolactin as a presenting feature of non-functioning pituitary adenoma. Whilst Marazuela et al. reported 48% of patients with preoperative hyperprolactinemia and Comtois et al. mention a higher incidence of 65% [(14)].

Non secreting adenomas comprise 25%–30% of pituitary adenomas. Refined gonadotropin assays have revealed that 80%–90% of non secreting pituitary adenomas are gonadotroph adenomas. These adenomas often are difficult to diagnose because of the lack of a distinctive clinical phenotype, which usually accompanies secreting pituitary adenomas. Non secreting adenomas usually present with clinical manifestations related to a mass effect, such as headaches, visual changes, and hypopituitarism [(15)].

It is generally accepted that hyperprolactinemia associated with non-functioning pituitary adenomas results from the compression of the pituitary stalk with consequent reduction of prolactin inhibiting factor delivery. Despite hyperprolactinemia, a dopamine agonistic therapy does not reliably induce regression of these adenomas, in contrast to that found with prolactinomas [(16)]. Previous studies indicated preoperative prolactin levels were a useful predictor of postoperative recovery of pituitary function [(17)].

CONCLUSION

It has been demonstrated that in expert surgical hands, normal anterior pituitary function is usually maintained and often improved following surgery of non-functioning pituitary adenomas. These results strengthen the indication for surgery in patients with hypopituitarism without any visual compromise. However, care should be taken not to generalize these results, which are less likely be reproduced by surgeons with limited experience in pituitary surgery.

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Authors contribution:
* Concept and design, ** Write up correction *** Analysis and correction **** Data collection and manuscript writing ***** Data interpretation,Analysis ****** Data interpretation,Analysis ******* Data Collection, ******** Final review and approval

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