International Journal of Research in Medical Sciences
Nanjundaswamy NH et al. Int J Res Med Sci. 2018 Feb;6(2):515-520
www.msjonline.org
pISSN 2320-6071 | eISSN 2320-6012
DOI: http://dx.doi.org/10.18203/2320-6012.ijrms20180290

Original Research Article

Perioperative management of patients with acromegaly-a retrospective analysis

Nethra H. Nanjundaswamy, Raghavendra Biligiri Sridhara*

Department of Anesthesiology, Bangalore Medical College and Research Institute, Bangalore, Karnataka, India

Received: 11 January 2018
Accepted: 15 January 2018

***Correspondence:**
Dr. Raghavendra Biligiri Sridhara,
E-mail: bsrags@gmail.com

ABSTRACT

Background: Acromegaly poses several challenges to the anesthetists, neurosurgeons, endocrinologists and intensivists, mandating a careful, coordinated multidisciplinary approach for a successful surgical outcome. An emphasis is required on a thorough preoperative evaluation of airway, neurological and endocrine and metabolic status so as to formulate a suitable perioperative management plan.
Methods: The rates of various perioperative complications, both surgical and anesthesia related, during pituitary surgeries in acromegaly patients were studied. Data collected included demographics, patient's medical history and any associated comorbid conditions, diagnosis, procedure performed, anesthetic management, intraoperative and postoperative complications.
Results: This is a retrospective analysis of 22 patients of acromegaly who underwent excision of a growth hormone (GH) secreting pituitary adenoma from October 2012 to December 2017. Male: female, 14:8 with a mean age of 32±9.5 years. The common presenting symptoms were somatic dysmorphism, headache, visual field defects and menstrual irregularities. Preoperative associated co-morbidities were hypertension (4), diabetes mellitus (6), Ischemic Heart Disease (1), hypothyroidism (3), situs solitus (1), lumbar and cervical disc prolapse (1), nephropathy (1) and poliomyelitis (1). One patient had difficult tracheal intubation with repeated attempts at direct laryngoscopy and surgery was deferred to a later date where awake fibreoptic bronchoscopic intubation was done. Two more patients with anticipated difficult airway, trachea was intubated using a fibreoptic bronchoscope. Out of 22 Transsphenoidal surgical approach (transnasal or sublabial) and pterional craniotomy was done in 18 and 4. Inhalational anaesthetic was used in the majority of patients (isoflurane, 18 and sevoflurane, 03) propofol infusion was used in 1 patient. Intraoperative cardiac complications like hypertension, ventricular ectopics was seen. Postoperatively metabolic, water and electrolyte imbalance were common occurance. CSF rhinorrhoea was seen in 4 patients and one developed meningitis.
Conclusions: The present data shows that patients undergoing pituitary surgery for acromegaly have many airway issues, cardiac and metabolic risk factors.

INTRODUCTION

Pituitary tumours usually occur in adults and represent 10% of all intracranial neoplasms out of which accounts 2.8 to 13.7 cases per 100000 people.[1] Pituitary tumours may be classified according to their size into microadenomas (<10mm) or macroadenomas (>10mm) and, according to function, they may be classified as functioning or nonfunctioning. Functioning tumours often present with symptoms of hormonal hypersecretion as acromegaly, galactorrhoea, excessive weight gain with cushingoid features, menstrual irregularities and water imbalances and also the proximity of pituitary to many

critical anatomical structures from various physiological systems confluence in sellar and parasellar region results in pressure and mass effect on these neurovascular components leading to variety of signs and symptoms like visual loss, headache, convulsions and panhypopituitarism.[2]

Acromegaly is functional pituitary tumour with excess growth hormone secretions leading to physical manifestations, Prognathism, malocclusion of teeth, coarsening of facial features and bony proliferation are pathognomonic of acromegaly. There can be thickening of the pharyngeal and laryngeal tissues, hypertrophy of the periepiglottic region, calcinosis of the larynx leading to narrowing of the glottic opening and even injury to the recurrent laryngeal nerve. A history of hoarseness of voice and obstructive sleep apnoea (OSA) should alert the anaesthesiologist of possible laryngeal involvement.[3-9]

Several retrospective cohort studies suggest that perioperative mortality in acromegaly is at least twice of that in the general population.[4] The incidence of OSA in patients with pituitary disease has been reported to be 60-80% in patients with acromegaly and 18-32% with Cushing's disease when compared to general populations where prevalence is 2-25%.[4-7]

The main surgical approach for pituitary surgery is transsphenoidal as it is minimally invasive with better outcome either alone or in combination with medical treatment, conventional radiotherapy and/or radiosurgery.[10] The advent of minimally invasive surgery along with neuroimaging has considerably decreased perioperative morbidity and mortality following pituitary surgery This retrospective analysis was to determine the perioperative complications in patients with acromegaly.

METHODS

This is a retrospective review of case records of 22 Acromegalic patients who underwent pituitary tumour excision (Transsphenoidal or Transcranial) between October 2012 and December 2017.

Data collected included demographics, patient's medical history and any associated comorbid conditions, diagnosis and procedure performed, anesthetic management, preoperative investigations, intraoperative and postoperative complications. Permission was obtained from the institute.

Intraoperative and postoperative records of the patients were recovered to collect the information on perioperative events during the hospital stay. Various intraoperative and postoperative events recorded included: Difficult mask ventilation, Difficult to intubate, tachycardia (sudden increase in heart rate by 20% of baseline value), bradycardia (fall in heart rate by 20% or more), hypertension and hypotension (rise or fall in blood pressure by more than 20%, respectively), preoperative airway assessment, preoperative investigations including hormonal assay (Growth Hormone, ACTH, TSH, T3, T4, Cortisol, Prolactin) were extracted. Hypothermia (fall in core temperature below 35.5°C), electrolyte disturbances (hyponatremia or hypernatremia), nausea and vomiting, fever (temperature above 99°F), increased ICP (suggested by the signs like nausea and vomiting, bradycardia, drowsiness or altered sensorium and CT findings), arrhythmias (like premature ventricular contractions, bigemini and asystole), hemorrhage, delayed awakening, meningitis, diabetes insipidus, shivering, convulsion, respiratory complications (stridor, wheezing, postoperative mechanical ventilation). Data are presented as mean (SD), median (range), or number (percentage).

RESULTS

This is a retrospective analysis of 22 patients of acromegaly who underwent excision of a growth hormone (GH) secreting pituitary adenoma from October 2012 to December 2017. Out of the 22 patients who had pituitary surgery for acromegaly (male: female, 14:8) with an age range from 22-59 years and a mean (±SD) age of 32±9.5 years. The main presenting symptoms of the patients were related to the effects of the hormone secretion by the tumor. The common presenting symptoms were somatic dysmorphism, headache, visual field defects and menstrual irregularities (Table 1).

Table 1: Incidence of presenting symptoms.

Symptom	No. of patients	% total no. of patients
Headache	14	63.63
Increase in body size	20	90
Diminision of vision	12	54.54
Menstrual irregularities	6	27.27
Vomiting	1	4.54
Lethargy	1	4.54
Milk discharge from nipple	2	9.09
Drooping eyelids	2	9.09
GTCS	2	9.09
Giddiness	1	4.54
Erectile dysfunction	1	4.54
Polyphagia, polydypsia, polyuria	1	4.54
Pain in the ear	1	4.54
Low back ache	1	4.54
Neck pain % quadriparesia	1	4.54

The mean Growth Hormone level was 69.8±11.2ng/mL (Normal value: <2ng/mL). TSH, T3, T4, and cortisol levels were in the normal range (Table 2).

Preoperative associated co-morbidities were hypertension (4), diabetes mellitus (6), Ischemic Heart Disease (1), hypothyroidism (3), situs solitus (1), lumbar and cervical

disc prolapse (1), nephropathy (1) and poliomyelitis (1) (Table 3).

Table 2: Preoperative hormonal assays of acromegalic patients.

Hormone	Hormone level
Growth hormone	69.8 ±11.2ng/ml
ACTH	36.5±14.1pg/mcl
TSH	1.4 ± 1.2µiu/ml
T3	11.9 ± 35.6ng/ml
T4	17.5±33.5µg/dl
Cortisol	17±18.5µg/dl
Prolactin	51.4 ±76.1µg/dl

Table 3: Associated comorbidities in acromegalic patients.

Comorbidities	No. of patients	% total no. of patients
Diabetis mellitus	6	27.27
Hypertension	4	18.18
Ischemic heart disease	1	4.54
Nephropathy grade 2	1	4.54
Hypothyroid	3	13.63
Cervical intervertebral disc prolapse	1	4.54
Poliomyelitis	1	4.54
L4-l5 canal stenosis	1	4.54
Congenital H D, mild AR, situs solitus, bicuspid aortic valve	1	4.54

Airway grading was Mallampati class I and II in 20 patients and class III and IV in 2 patients. One patient had difficult tracheal intubation with repeated attempts at direct laryngoscopy and surgery was deferred to a later date where awake fibreoptic bronchoscopic intubation was done. Two more patients with anticipated difficult airway, trachea was intubated using a fibreoptic bronchoscope.

Out of 22 acromegalic patients who underwent transsphenoidal surgical approach (transnasal or sublabial) and pterional craniotomy in 18 and 4 cases respectively. Preoperative lumbar drain was inserted in 3 patients to facilitate descent of the suprasellar part of the tumor or to facilitate CSF drainage postoperatively. Inhalational anaesthetic was used in the majority of patients (isoflurane, 18 and sevoflurane, 03) propofol infusion was used in 1 patient (Table 4).

Table 4: Characteristics of the patients.

Characteristic	No. of patients
Total	22
Male/female	14/8
Mean age in years	32 ± 9.5
Mallampatti I and 2 / 3 and 4	18/4
Transsphenoidal/ transcranial	18/4
Isoflurane/sevoflurane/propofol	18/3/1

Intraoperative complications encountered were hypertension in 6 patients, with 2 patients requiring pharmacological therapy. Hypotension in one patient, tachycardia (HR>130 bpm) in one patient, bradycardia in 2 with one patient requiring atropine 0.6mg and a patient with frequent ventricular ectopics managed by IV lignocaine. One patients had postintubation bronchospasm treated with inj. deriphylline. One patient required higher doses of neuromuscular blocking agents. Mean blood loss was 124±115ml.

Postoperatively, one patient had apnoea and oxygen desaturation that was managed with bag-mask ventilation. Five patients had uncontrolled hyperglycemia. Delayed postoperative complications included, diabetes insipidus in 3 patients, which was treated with fluid intake and Inj. vasopressin and hyponatremia in two patients which was treated with 3% hypertonic saline and tab fludrocortisone.

Four patients had CSF rhinorrhoea of which one developed acute bacterial meningitis requiring treatment in ICU with appropriate antibiotics. There was no mortality in the current series. Two patients had significant residual tumor or a recurrence that required a repeat surgery.

DISCUSSION

The real estimation of incidence of complications associated with pituitary surgery for acromegaly patient is difficult because not all complications are reported and there is a lack of clear definition of what should be considered a complication.[11,12] The reported complication rates for pituitary surgeries varied from 6 to 20%.[12,13] with acromegaly patients rate of complications are much higher.

In the current analysis one patient tracheal intubation was difficult with repeated attempts at direct laryngoscopy and the surgery was deferred to a later date where awake fibreoptic bronchoscopic intubation was done. In two more patients with anticipated difficult airway, trachea was intubated awake using a fibreoptic bronchoscope.

Airway management in patients with acromegaly can pose difficulties both during mask ventilation as well as during tracheal intubation. Mask ventilation can be difficult due to thickening of the soft tissues of the nose, mouth, lips and tongue.

The incidence of difficult intubation in patients with acromegaly is about four to five times higher than the rates of about 2.5% in those without acromegaly.[14] These difficulties have been managed by various measures from tracheostomy to awake fibreoptic intubation both Messick et al and Schmitt et al propose that the incidence of difficult intubation in these patients to be 13% which is higher than the normal population.[13,15,16]

It has also been found that patients who were initially assessed to be Mallampati class 1 and 2 had actually a difficult airway.[16,17] Thus, a reassuring preoperative airway examination could be misleading and the anaesthesiologists should be prepared to manage a difficult airway in these patients and various airway devices to aid intubation should be readily available. Use of intubating laryngeal mask airway has met with limited success for unparalysed acromegalic patients because of upper airway abnormalities, especially, a large tongue.[18] Similarly, flexible fibreoptic intubation also may be difficult in these patients.[19] Awake intubation could thus be a safe option in patients with anticipated difficult airway

The frequency of various cardiovascular changes found in our series was similar to the observations made in other series.[13,20,21] Hypertension was more prevalent perioperatively which was treated using meatprolol and labetalol. Other haemodynamic side effects include bradycardia counteracted by boluses of injection Atropine. Ventricular ectopics was transient, tachycardia and hypotension which were treated by boluses of fluids and injection mephentermine (Table 5). Chowdhury T et al in their study observed 6% of hypertensive episodes and 1% incidence of intraoperative bradycardia.[21]

Long standing Growth hormone secretion will have systemic effects on heart making it susceptible to many haemodynamic events. Hypertension is present in 40% of patients leading to left ventricular hypertrophy (LVH).[22,23] Acromegalic cardiomyopathy is characterised by diastolic dysfunction and a poorly compliant left ventricle, with a need for higher ventricular filling pressures.[24,25] It is due to interstitial myocardial fibrosis and may not return to normal after treatment.

Table 5: Incidence of encountered complications.

Complications	No. of patients (%)
Hypertension/hypotension/ ventricular ectopics	6(27%)/1(4.54%)/2(%)
Tachycardia/bradycardia	1(4.54%) /2(9%)
Post-operative bronchospasm	1
Prolonged apnoea and desaturation	1
Hyperglycemia	5
Hypernatremia/diabetis insipidus	3
Hyponatremia	2
CSF rhinorrhoea	4
Meningitis	1

Immediate postextubation one patient had bronchospasm and was relieved by Salbutamol inhalational puff and injection deriphylline. One patient had prolonged apnoea and desaturation and was supported by mask assisted breaths (Table 5). Right ventricular dysfunction secondary to pulmonary hypertension due to long standing Obstructive Sleep Apnoea(OSA) may also be present.[26] Five patients had metabolic derangements seen as uncontrolled hyperglycemia.

Electrolyte and Fluid disorders are common in the immediate postoperative period as a result of damage to posterior pituitary stalk and hypothalamus leading to diabetis insipidus and hypothermia. Hypernatremia was seen in 3 patients was treated by infusing free water and good hydration. One patient of hypotention needed 3% hypertonic saline infusion. The incidence of endocrinological complications was found to be 17.9%.[13]

The incidence of diabetis insipidus (DI) is comparatively higher after transcranial resection as compared to transsphenoidal surgery. It can be either transient or permanent. The incidence of permanent DI after transsphenoidal surgery in one study has been found to be 2% and that of transient DI 16.6%.[17,27,28]

It usually manifests as hypernatremia, polyuria, thirst and polydipsia and a strict watch on intake, output and serum sodium levels is necessary. Fluid losses are replaced initially with isotonic saline and later with hypotonic fluids depending on serum sodium levels.

Since transient DI is encountered most commonly (>95% of times), a single dose of desmopressin (DDAVP) is usually sufficient. In a series of over 800 patients who underwent transsphenoidal surgery, Nemergut et al found that 12.4% of patients required to be administered DDAVP in the postoperative period.[17] Transient polyuria is frequently noted during the 1st postoperative day, and usually only 20% of patients require treatment with desmopressin.[29] Early transient DI is thought to be caused by temporary dysfunction of vasopressin-producing neurons as a result of surgical trauma.[29]

We had 4 patients with CSF rhinorrhoea of which 1 developed acute bacterial meningitis (Pseudomonas) requiring treatment in ICU with appropriate antibiotics. Continuous lumbar CSF drainage usually promotes resolution of the leak postoperatively which was used in 2 of our patients. Choudhary et al noted CSF leak had highest incidence in acromegalics (64%), followed by 46% in prolactinomas and 33% in non-functioning pituitary adenoma.[21]

Gondim et al in a retrospective review of 301 patients who underwent endoscopic pituitary resection found the incidence of anatomic complications to be 8.97%.[13] A CSF leak may occur intra- or postoperatively and entails the risk of meningitis, which is a potentially fatal complication.[7,12] The reported incidence of CSF fistulas after transsphenoidal surgery is 1 to 4% and the incidence of meningitis is 0.8 to 2%. Meningitis may also occur without a postoperative CSF leak. Prophylactic antibiotic drugs are used by most surgeons in an attempt to prevent meningitis, but the effectiveness of these prophylactic medications has never been proven.[30]

CONCLUSION

The present data shows that patients undergoing pituitary surgery for acromegaly have many airway issues, cardiac and metabolic risk factors. They are also vulnerable for a number of intraoperative and postoperative complications like CSF rhinorrhoea and meningitis. With effective identification of patients at risk and careful clinical, radiological and laboratory monitoring in the perioperative period, they can be managed with very low morbidity. With the advent of minimally invasive transsphenoidal approach resulted in improved outcome with fewer complications, more complete resections and shorter hospital stay

The retrospective nature of our study has its limitation. We did not monitor ICP in our patients, so the reasons provided for hemodynamic changes secondary to change in intracranial pressures can be considered hypothetical. Follow up and long-term outcome of our patients is also not known as it was beyond the scope of our study.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: The study was approved by the Institutional Ethics Committee

REFERENCES

1. Aiketerini L, Alessandro P, John A, Wass H, Niki K. Pituitary. 2017;20(1):4-9.
2. Abraham M. Perioperative management of patients with pituitary tumours. J Neuroanaesthesiol Crit Care. 2016;3:211-8.
3. Marulasiddappa V, Raghavendra. Anaesthetic management of a patient with extreme Gigantism for endoscopic transsphenoidal removal of pituitary adenoma. Int J Res Health Sci. 2015;3(1):62-5.
4. Vasu TS, Grewal R, Doghramji K. Obstructive sleep apnea syndrome and perioperative complications: A systematic review of the literature. J Clin Sleep Med. 2012;8:199-207.
5. Bottini P, Tantucci C. Sleep apnea syndrome in endocrine diseases. Respiration. 2003;70:320-7.
6. Colao A, Ferone D, Marzullo P, Lombardi G. Systemic complications of acromegaly: Epidemiology, pathogenesis, and management. Endocr Rev. 2004;25:102-52.
7. Sze L, Schmid C, Bloch KE, Bernays R, Brändle M. Effect of transsphenoidal surgery on sleep apnoea in acromegaly. Eur J Endocrinol. 2007;156:321-9.
8. Adesanya AO, Lee W, Greilich NB, Joshi GP. Perioperative management of obstructive sleep apnea. Chest. 2010;138:1489-98.
9. Rahimi E, Mariappan R, Tharmaradinam S, Manninen P, Venkatraghavan L. Perioperative management and complications in patients with obstructive sleep apnea undergoing transsphenoidal surgery: Our institutional experience. J Anaesthesiol Clin Pharmacol. 2014;30:351-4.
10. Melmed S, Casanueva FF, Cavagnini F, Chanson P, Frohman L, Grossman A, et al. Guidelines for acromegaly management. J Clin Endocrinol Meta. 2002;87:4054-8.
11. Han ZL, He DS, Mao ZG, Wang HJ. Cerebrospinal fluid rhinorrhea following trans-sphenoidal pituitary macroadenoma surgery: Experience from 592 patients. Clin Neurol Neurosurg. 2008;110:570-9.
12. Shiley SG, Limonadi F, Delashaw JB, Barnwell SL, Andersen PE, Hwang PH, et al. Incidence, etiology, and management of cerebrospinal fluid leaks following transsphenoidal surgery. Laryngoscope. 2003;113:1283-8.
13. Gondim JA, Almeida JP, Albuquerque LA, Schops M, Gomes E, Ferraz T, et al. Endoscopic endonasal approach for pituitary adenoma: surgical complications in 301 patients. Pituitary. 2011;14:174-83.
14. Ali Z, Bithal PK, Prabhakar H, Rath GP, Dash HH. An assessment of the predictors of difficult intubation in patients with acromegaly. J Clin Neurosci. 2009;16:1043-45.
15. Messick JM Jr, Cucchiara RF, Faust RJ. Airway management in patients with acromegaly. Anesthesiol. 1982;56:157.
16. Schmitt H, Buchfelder M, Radespiel-Troger M, Fahlbusch R. Difficult intubation in acromegalic patients: incidence and predictability. Anesthesiol. 2000;93:110-4.
17. Nemergut EC, Zuo Z. Airway management in patients with pituitary disease: A review of 746 patients. J Neurosurg Anesthesiol. 2006;18:73-7.
18. Law-Koune JD, Liu N, Szekely B, Fischler M. Using the intubating laryngeal mask airway for ventilation and endotracheal intubation in anesthetized and unparalyzed acromegalic patients. J Neurosurg Anesthesiol. 2004;16:11-3.
19. Hakala P, Randell T, Valli H. Laryngoscopy and fibreoptic intubation in acromegalic patients. Br J Anaesth. 1998;80:345-7.
20. Fabregas N, Lopez A, Valero R, Carrero E, Caral L, Ferrer E. Anesthetic management of surgical neuroendoscopies: Usefulness of monitoring the pressure inside the neuroendoscope. J Neurosurg Anesthesiol. 2000;12:21-8.
21. Chowdhury T, Prabhakar H, Bithal PK, Schaller B, Dash HH. Immediate postoperative complications in transsphenoidal pituitary surgery: A prospective study. Saudi J Anaesth. 2014;8:335-41.
22. Lie JT, Grossman SJ. Pathology of the heart in acromegaly: Anatomic findings in 27 autopsied patients. Am Heart J. 1980;100:41-51.
23. Rajasoorya C, Holdaway IM, Wrightson P, Scott DJ, Ibbertson HK. Determinants of clinical outcome and survival in acromegaly. Clin Endocrinol (Oxf). 1994;41:95-102.
24. Lopez-Velasco R, Escobar-Morreale HF, Vega B, Villa E, Sancho JM, Moya-Mur JL, et al. Cardiac involvement in acromegaly: specific myocardiopathy or consequence of systemic

hypertension? J Clin Endocrinol Metab. 1997;82:1047-53.
25. Herrmann BL, Bruch C, Saller B, Bartel T, Ferdin S, Erbel R, et al. Acromegaly: Evidence for a direct relation between disease activity and cardiac dysfunction in patients without ventricular hypertrophy. Clin Endocrinol (Oxf). 2002;56:595-602.
26. Fazio S, Cittadini A, Sabatini D, Merola B, Colao AM, Biondi B, et al. Evidence for biventricular involvement in acromegaly: a doppler echocardiographic study. Eur Heart J. 1993;14:26-33.
27. Dunn LK, Nemergut EC. Anesthesia for transsphenoidal pituitary surgery. Curr Opin Anaesthesiol. 2013;26:549-54.
28. Singer PA, Sevilla LJ. Postoperative endocrine management of pituitary tumors. Neurosurg Clin N Am. 2003;14:123-38.
29. Hensen J, Buchfelder M, Henig A, Fahlbusch R. Disturbances of osmoregulation in the neurosurgical setting-with special emphasis on the situation after surgery for pituitary adenomas. Werder K, Fahlbusch R: Pituitary adenomas-from basic research to diagnosis and therapy. Elsevier Excerpta Medica, Amsterdam. 1996:255-68.
30. Van Aken MO, de Marie S, van der Lely AJ, Singh R, de Marie S, van den Berge JH, et al. Risk factors for meningitis after transsphenoidal surgery. Clinical infectious diseases. 1997;25(4):852-6.

Cite this article as: Nanjundaswamy NH, Sridhara RB. Perioperative management of patients with acromegaly-a retrospective analysis. Int J Res Med Sci 2018;6:515-20.