

**THE HYPOTHALAMIC PITUITARY AXIS
PART 2: ANAESTHESIA FOR PITUITARY SURGERY
ANAESTHESIA TUTORIAL OF THE WEEK 189
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QUESTIONS

Before continuing, try to answer the following true/false questions. The answers can be found at the end of the article, together with an explanation.

1. Transsphenoidal surgery carries a 15% risk of venous air embolism
2. Pituitary surgery is often associated with significant blood loss
3. Transsphenoidal surgery is the most commonly used surgical approach for resection of pituitary tumours
4. Carpal tunnel syndrome is more common in Cushingoid patients than acromegalics
5. Acromegaly is a common cause of difficult intubation
6. A lumbar drain for pituitary surgery is usually sited in the epidural space at L3/L4
7. Smooth emergence from anaesthesia is particularly important after pituitary surgery
8. Two thirds of acromegalics have an enlarged thyroid which may cause tracheal compression
9. Cocaine is usually used to provide topical nasal anaesthesia prior to pituitary surgery
10. Development of SIADH is less common than the development of diabetes insipidus after pituitary surgery

INTRODUCTION

In addition to the anaesthetic hurdles presented by all neurosurgical cases, pituitary surgery carries a unique set of challenges for the anaesthetist due to the surgical approach and effect of hormone secretion by pituitary tumours. In the last tutorial we learned about the anatomy and physiology of the pituitary, the classification of pituitary tumours and the clinical conditions resulting from pituitary hormone over-secretion from these tumours. In this tutorial we will cover the anaesthetic management of these patients in the pre-operative, intra-operative and post-operative periods, the surgical and anaesthetic techniques specific to pituitary surgery and the complications which may arise.

PRE-OPERATIVE ASSESSMENT

Common clinical conditions encountered in pituitary surgery include: Cushing's disease, acromegaly, prolactin overproduction and panhypopituitarism. Both hormone overproduction and underproduction due to the mass effect of pituitary tumours can have various implications for anaesthetists. A careful and detailed pre-operative assessment of these patients is therefore very important.

Airway and respiratory system assessment

A Mallampati grade of 1 or 2 may be falsely reassuring of an easy intubation in a patient with acromegaly. The disease is a well known cause of difficult intubation and in some cases bag and mask

ventilation may also be difficult. The excess growth hormone can lead to thickening of pharyngeal and laryngeal soft tissues, macroglossia, reduction in the size of the rima glottidis and hypertrophy of the aryepiglottic folds, soft palate and epiglottis. A hoarse voice or stridor may indicate recurrent laryngeal nerve palsy or laryngeal stenosis and one third of acromegalics have an enlarged thyroid which may cause tracheal compression. Kyphosis and the 'buffalo hump' seen in Cushing's disease may also make airway management difficult in these patients. Spirometry and indirect laryngoscopy may be of additional value.

Obstructive sleep apnoea is common in both acromegalic and Cushingoid patients. Symptoms are snoring, daytime somnolence, headaches, memory and concentration difficulties. It should be identified and adequately treated pre-operatively to reduce the risk of airway obstruction in the peri-operative period.

Cardiovascular system assessment

An ECG should be carried out routinely in all patients. Abnormalities such as inverted T waves and high voltage QRS complexes are common findings in patients with Cushing's disease. Left ventricular hypertrophy, heart failure, arrhythmias and ischaemic heart disease are common in both conditions and cause high peri-operative mortality. Patients with chronic obstructive sleep apnoea may be at increased risk of cor pulmonale. Echocardiogram can be useful tool to assess if there is a degree of cardiac dysfunction. Hypertension affects 30% of patients with acromegaly and 85% of patients with Cushing's syndrome and should be controlled by pharmacological means prior to elective surgery.

Neurological assessment

A thorough cranial nerve examination should be carried out prior to surgery with particular emphasis on assessment of visual acuity and visual fields (CN II). Tumours compressing the optic chiasma by a mass effect can cause a bi-temporal hemianopia. Following anaesthesia, a reassessment of cranial nerve function should be carried out to see if surgery has resulted in an improvement or deterioration. Symptoms of raised intracranial pressure can occur due to larger tumours and should also be identified prior to surgery. All patients need a pituitary MRI scan to assess the position and extent of the tumour. MRI, where available, is the investigation of choice as it is superior to CT in the evaluation and differentiation of soft tissue lesions.

Endocrine assessment

Diabetes mellitus occurs in 25% of acromegalics and 60% of those with Cushing's syndrome. Impaired glucose tolerance is even more common. A sliding scale insulin regime may be useful in the peri-operative period in such patients. It is particularly important to measure T4 and TSH and to normalise thyroid function prior to surgery to avoid cardiovascular instability and arrhythmias. Basal prolactin and serum cortisol are necessary tests as most patients undergoing pituitary surgery will require peri-operative glucocorticoid cover to enable them to mount an effective stress response.

Pharmacological management of hormone imbalance has been discussed in the previous tutorial, but levels should be repeated prior to surgery to assess adequacy of hormone replacement, or response to bromocriptine in acromegaly, for example.

Investigations

Full blood count, urea and electrolytes, calcium, blood glucose and a group and save should be performed pre-operatively. Although major blood loss is rare in pituitary surgery, it may occur if there is accidental injury to the carotid artery or venous sinuses.

Pre-medication

In general, patients should receive their normal antihypertensive, heart failure, bronchodilator and antacid medications, with the exception of angiotensin converting enzyme inhibitors and diuretics. Special consideration should be given to those prone to gastro-oesophageal reflux, with the use of an H₂-receptor antagonist and proton pump inhibitor e.g. ranitidine and omeprazole. Diabetics should have regular blood sugar measurements and started on an insulin sliding scale when appropriate. Steroid cover is considered below.

Benzodiazepines and other sedative pre-medications should be avoided since the aim in pituitary surgery, as with all neurosurgery, is for the patient to have rapid emergence and recovery from anaesthesia in order to allow early neurological assessment.

Peri-operative glucocorticoid cover

All patients with Cushing's disease will require peri-operative glucocorticoid replacement. Most other patients will also require replacement except if the results of basal cortisol (taken at 0800 hrs) and short synacthen tests are normal. Particular regimens will be used at individual hospitals, but commonly 100mg hydrocortisone is given at induction of anaesthesia, followed by 50 mg bd on the first post-operative day, 25 mg bd on the second post-operative day and 20 mg in the morning and 10mg in the evening on the third and subsequent days and discharged on this dose. Patients with Cushing's disease may need to continue with glucocorticoid replacement for several weeks whilst those with non-ACTH secreting tumours may be able to discontinue maintenance therapy after a few days. Close communication between anaesthetic, endocrinology and surgical teams is needed in order to provide the most appropriate regime of glucocorticoid replacement for each individual patient.

Key Points

History

- Remember to ask in particular about symptoms suggestive of ischaemic heart disease, raised intracranial pressure, abnormal thyroid function and obstructive sleep apnoea

Examination

- Airway Assessment
- Assessment of Cranial Nerves

Imaging

- Pituitary MRI (where available)

Laboratory

- U&Es, Calcium, Blood Glucose, FBC, Basal Prolactin
- TSH, T4
- Serum Cortisol – remember glucocorticoid cover!

Other

- ECG
- Echocardiogram
- Indirect Laryngoscopy
- Spirometry

INTRAOPERATIVE MANAGEMENT

Patient monitoring

All patients should have routine monitoring including pulse oximetry, ECG, temperature and capnography. Invasive arterial blood pressure monitoring and large bore IV access is recommended,

Patients with acromegaly, particularly those with carpal tunnel syndrome, may have compromised ulnar blood flow. It is therefore important that blood flow in both radial and ulna arteries is assessed by Allen's test prior to radial artery cannulation (If ulna arterial flow is compromised, consider dorsalis pedis as an alternative). Fragile skin and easy bruising may complicate attempts at venous and arterial cannulation in patients with Cushing's syndrome. Central venous cannulation is usually only needed in cases of severe cardiorespiratory compromise.

Anaesthetic technique

Anaesthesia for pituitary surgery should aim to facilitate surgical exposure, preserve cerebral perfusion, avoid hypertensive surges and facilitate rapid emergence. The exact technique and agents used will depend on the careful pre-operative assessment of the individual patient and a consideration of any co-morbidities present.

It is acceptable to use any anaesthetic technique suitable for intracranial surgery, ideally with short acting agents for rapid emergence. Special consideration should be made in the presence of raised intracranial pressure. Bag mask ventilation may be difficult in acromegalic patients and adjuncts such as fibre optic intubation may be appropriate if difficult intubation is suspected. Reinforced (armoured) endotracheal tubes are used routinely and should be fixed on the side opposite to the side of surgery. A throat pack should be inserted by the anaesthetist and a clear label attached to the patient to ensure that the throat pack is remembered and removed at the end of surgery.

Propofol, sevoflurane or desflurane are most commonly used for maintenance of anaesthesia. These agents are relatively short-acting and allow smooth, rapid emergence from anaesthesia which is important to allow early neurological assessment in the post-operative period. Neuromuscular blockade using atracurium or vecuronium should be maintained and monitored throughout the operation as coughing and patient movement may have deleterious effects on surgery. Remifentanyl and other short acting opioids are particularly valuable in periods of intense surgical stimulation during transsphenoidal surgery. These should be replaced by longer acting opioids towards the end of anaesthesia to avoid pain on return to consciousness. Antiemetics should be used routinely to try to reduce the high incidence of post-operative nausea and vomiting.

Intra-operative positioning

Patients are usually placed supine with the head up and neck extended in the classic 'deck-chair' position which encourages venous drainage. For patients with stiff necks and limited neck movement, the operating table can be tilted laterally towards the surgeon. The patient's head is held in position with a clamp and the pituitary region visualised via image intensifier. All connections in the circuit should be checked prior to the start of surgery as the anaesthetist will not have easy access to the head intra-operatively.

Protection of pressure points is important as surgery may be lengthy. Eyes should be routinely padded. Thin skin and osteoporosis in patients with Cushing's disease makes them particularly prone to bruising, pathological fractures and development of pressure sores and extra care should be taken in these patients. Use of intermittent pneumatic compression devices (such as flowtron boots) is important to reduce the risk of DVT and PE and to prevent venous pooling. Thromboembolic risk is particularly high in patients with Cushing's disease.

Surgical approach to the pituitary region

The most commonly used approach is trans-sphenoidal. The surgeon follows the midline of the nose, removing bone, penetrating the sphenoid air sinuses and removing the floor of the pituitary fossa. The tumour is then removed using an operating microscope. The transsphenoidal approach is safest and is associated with a shorter hospital stay. Mortality is quoted as 0.27% for microadenomas and 0.9% for macroadenomas. Rarely a transcranial approach (bi-frontal craniotomy) may be used for giant pituitary tumours or for cases of failed transsphenoidal surgery.

Optimising the surgical field

Minimisation of bleeding from the nasal mucosa

Infiltration of the nasal mucosa with xylometazoline (a long-acting sympathomimetic amine which acts on α -adrenoceptors) or 1% lignocaine with adrenaline 1:200,000 may be used to cause vasoconstriction and reduce bleeding. An exaggerated hypertensive response or severe tachycardia may be seen in some patients following nasal infiltration, especially in those with Cushing's disease. Such a response should be treated promptly with phentolamine, β -blocker, or short-acting opioid. Topical cocaine anaesthesia is generally avoided due to the risk of precipitating arrhythmias, angina or myocardial infarction secondary to coronary artery spasm.

Insertion of a Lumbar Drain

For pituitary tumours with significant suprasellar extension, the surgeon may ask for a lumbar subarachnoid drain to be sited. The easiest way to achieve this is to use a standard 16g epidural catheter. This is usually inserted at L3/L4 and 10cm of catheter passed in a cephalad direction. Injection through the catheter of 10mls of normal saline (under strict sterile technique) produces a transient increase in CSF pressure and helps to cause downward movement of suprasellar tumour extension into the operating field. A lumbar drain can also be useful post-operatively to treat a CSF leak.

Key Points

- Anticipate difficult intubation and consider whether asleep or awake fibre-optic intubation would be the safest method of securing the airway
- Anaesthesia for pituitary surgery should allow smooth and rapid emergence, therefore use short-acting and easily metabolised drugs for maintenance
- Short-acting opioids are useful for periods of intense stimulation and helps to prevent hypertensive surges
- The transsphenoidal approach is most commonly used to gain access to the pituitary region
- Use of a lumbar drain may help optimise surgical conditions

POST-OPERATIVE MANAGEMENT

Airway

Patients who have undergone pituitary surgery are at an increased risk of airway obstruction in the acute post-operative period. Anaesthetists should ensure that throat packs are removed at the end of surgery and patients should ideally be extubated in an awake state to reduce the likelihood of aspirating blood. Nasal packs will often be left in after surgery has been completed so oropharyngeal airway patency is particularly important. Acromegalics and other patients with a history of obstructive sleep apnoea may have used nocturnal CPAP preoperatively. Postoperatively, nasal CPAP will be ineffective in the presence of nasal packs. Furthermore, there is a risk that it may cause air to enter the cranium (pneumocephalus) via the defect around the base of the pituitary. Although normally this only causes a headache, if the air is under pressure a tension pneumocephalus may occur increasing ICP and reducing level of consciousness. It should only be used as a last resort and in a critical care area. The main risk to these patients is hypoxaemia, and therefore they should be nursed in an area with overnight pulse oximetry monitoring and supplementary oxygen for the few nights postoperatively.

Neurological assessment

Emergence from anaesthesia should ideally be smooth and rapid to allow the surgeon to make early assessment of the integrity of cranial nerves, particularly CN II-VI which are closest in proximity to the surgical site. As discussed above, rapid emergence may be achieved using short acting and rapidly metabolised anaesthetic agents.

Analgesia

Patients usually complain of a frontal headache following surgery. Historically, codeine has been the mainstay of postoperative analgesia, due to its favourable side effect profile. Stronger opiates may be used if required, particularly if a trans-cranial approach has been taken. PONV is common and prophylactic anti-emetics should also be prescribed for all patients.

Key Points

- Patients who have undergone pituitary surgery are at increased risk of airway obstruction in the post-operative period. Consider a period of observation in a high dependency area, particularly for patients with a history of obstructive sleep apnoea
- Strong opiates may be required for the immediate post-operative period, then codeine analgesia as required.
- Don't forget to write up anti-emetics for PONV

COMPLICATIONS OF PITUITARY SURGERY

The transsphenoidal approach to pituitary surgery is associated with only a 3.5% overall complication rate, however the anaesthetist should be alert to the development of the following complications:

1) Bleeding

Bleeding from damage to the internal carotid artery or veins within the wall of the cavernous sinus is a rare occurrence. Larger tumours and those with suprasellar extension are most likely to be complicated by bleeding. Venous bleeding may require packing whilst arterial bleeding should be reduced by pharmacological reduction of blood pressure using doses of IV induction agent or α and β -blockers. If arterial bleeding occurs, further surgery should be postponed and the patient transferred to intensive care as soon as possible for further monitoring, sedation and ventilation.

2) CSF leak

This may only be identified once nasal packs have been taken out. Patients may have a headache, rhinorrhoea or complain of a salty taste in the mouth due to a postnasal drip. Testing of suspected CSF will be positive for glucose. Associated symptoms of pain, neck stiffness, photophobia and fever should alert the clinician to the possibility of meningitis and the need for appropriate antibiotic treatment. A persisting CSF leak can usually be resolved by leaving the lumbar drain in place for 24 – 48 hours to allow continuous CSF drainage.

3) Diabetes insipidus

Neurogenic diabetes insipidus (DI) results from destruction of the ADH-secreting cells in the posterior pituitary or hypothalamus, or from impaired release of ADH from these cells. Since the function of ADH is to cause water retention in the renal distal tubule and collecting ducts, DI is characterised by polyuria, thirst, raised plasma osmolality and hypernatraemia. It is one of the commonest complications of pituitary surgery and may affect up to 50% of patients in the first 24-48 hours post-operatively.

To distinguish DI from other causes of post-operative polyuria, it is recommended that urine specific gravity and urine output be measured routinely. Polyuria with a urine specific gravity of < 1.005 and low osmolality of < 300 mosm are diagnostic features of DI. Once a diagnosis has been made, access to free fluids and close electrolyte and urine monitoring are first line management strategies. In some cases, cautious use of DDAVP (a synthetic ADH analogue) may be required. The condition is usually transient as other cells take over the production and secretion of ADH.

4) Syndrome of inappropriate anti-diuretic hormone production (SIADH)

This condition is less common post-operatively than diabetes insipidus. It is characterised by ADH release from damaged posterior pituitary cells regardless of the plasma osmolality. Clinical signs include low serum sodium and plasma osmolality and high urinary osmolality (greater than plasma osmolality) in a euvoelaemic patient. The diagnosis is one of exclusion and other causes of hyponatraemia such as Cushing's syndrome, hypothyroidism, diabetes mellitus, NSAIDs and narcotic agents should be ruled out first.

SIADH usually occurs approximately one week after surgery which is much later than many of the other causes. The condition can be treated initially by fluid restriction to try to restore serum sodium to normal. Other options include cautious use of hypertonic saline in order to avoid central pontine myelinolysis associated with rapid sodium restoration.

5) Venous air embolism

There is a 10% risk of venous air embolism as the surgical field is higher than the heart. However, clinically significant venous air embolism with morbidity and mortality has not been reported in association with pituitary surgery.

ANSWERS TO QUESTIONS

1. **F** - Transsphenoidal surgery carries a 10% risk of venous air embolism as the surgical field is higher than the heart. Clinically significant venous air embolism has never been reported
2. **F** - Pituitary surgery is rarely associated with significant haemorrhage
3. **T** - The transsphenoidal approach is most common. Occasionally a transfrontal approach is needed for large tumours or previously failed transsphenoidal surgery
4. **F** - Carpal tunnel syndrome is more common in acromegaly
5. **T** - Acromegaly is a common cause of difficult intubation
6. **F** - A lumbar drain is usually sited in the subarachnoid space at L3/L4. Subsequent injection of air or saline through the catheter can help prolapse suprasellar tumour extension into the surgical field of view
7. **T** - Smooth emergence from anaesthesia is particularly important after pituitary surgery to allow early assessment of neurological function
8. **F** - One third of acromegalics have an enlarged thyroid which may cause tracheal compression and therefore a difficult intubation
9. **F** - Cocaine anaesthesia is not commonly used as it can provoke severe arrhythmias. Lignocaine and adrenaline or xylometazoline are more commonly used
10. **T** - SIADH occurs in approximately 20% of patients following pituitary surgery. Diabetes insipidus occurs in approximately 50%

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