Review Article

Anesthetic management of primary hyperparathyroidism: A role rarely noticed and appreciated so far

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ABSTRACT

Endocrine surgeries have been on the rise for the last few years. During surgery, endocrine disorders present unique challenges to the endocrinologist and to the attending anesthesiologist. The endocrine, electrolyte and metabolic disturbances resulting from such disorders can have a profound effect on the normal human physiological milieu. Surgery of parathyroid glands is no exception and is associated with a multiple challenges during pre-, intra-, and post-operative period. Pre-op examination and optimization is essential so as to prevent any intra-op or post-op complications. The most striking electrolyte disturbance during parathyroid surgery is the imbalance of calcium levels in the body and the main emphasis during the entire peri-operative period revolves around the maintenance of normal serum calcium levels. The present article review in depth the various anesthetic considerations and implications during parathyroid surgery with an emphasis on pre-op preparation for elective and emergency surgery.

Key words: Calcitonin, hypercalcaemia, hyperparathyroidism, hypocalcemic tetany, parathyroid

Introduction

Endocrine surgeries and emergencies pose unique challenges to the attending anaesthesiologists and the intensivists.[1-4] The elevation of serum calcium and inappropriate increase in the levels of parathyroid hormones constitute a constellation of symptoms of primary hyperthyroidism.[5] The endocrine, electrolyte and metabolic disturbances resulting from such disorders can have a profound effect on the normal human physiological milieu.[6] The most striking electrolyte disturbance during parathyroid surgery is the imbalance of calcium levels in the body and the main emphasis during the entire peri-operative period revolves around the maintenance of normal serum calcium levels. The classical features of hypercalcemia 'moans, groans and stones' are rarely seen nowadays during the initial clinical presentation owing to the early diagnosis of hypercalcemia and the mainstay of clinical presentation includes asymptomatic features only.[5,7,8]

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The precautionary measures have to be taken during administration of anesthesia as thiopentone and volatile anaesthetic prolong the QTc interval.[9,10] Similarly few drugs like macrolides, quinolones, antifungals like ketoconazole and fluconazole should better be avoided during the peri-operative period as they also have a potential to prolong QTc interval.[9,10] Renal scans and ultrasound are sometimes carried out for diagnosis of renal stones which is very useful for the formulation and planning for peri-operative renal protection strategies when the patient is administered anesthesia.[11,12]

Pre-op Optimization

For any elective and majority of emergency surgeries, pre-op medical management and optimization is extremely

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significant for prevention of various potential peri-op and post-op complications. A large number of geriatric patients that remain undiagnosed and those who are reluctant to seek medical advice, present invariably with advanced stage of the disease process or sometimes malignancy.[13] The clinical symptomatology is diverse and may include moderate to severe dehydration, tachycardia, polyuria, anorexia, vomiting, extreme weakness lethargy, and mental signs and symptoms including psychosis which needs thorough investigations.[14] In untreated cases the condition can deteriorate rapidly and can progress to coma and collapse.[15,16] The emergency therapeutic interventions for optimization of hypercalcaemia include:

1. Infusion of normal saline@ 2.5-3.0 ml/kg/hr with a maximum optimization up to 4-6 liters.
2. Biphosphonates such as Pamidronate 60 mg is the first line of drug for treatment of life threatening hypercalcaemia (Ca^{2+} >4.5 mmol/l)
3. Infusion of phosphate - to lower life threatening hypercalcaemia (>4.5 mmol/l)
4. Calcitonin in doses of 3-4 U/kg - either intravenously (IV) or subcutaneously to lower the calcium levels.
5. Plicamycin and mithramycin administration is done cautiously as these drugs have a very narrow therapeutic index.
6. Frusemide is administered for forced saline diuresis as it inhibits tubular reabsorption of calcium while simultaneously measuring central venous pressure.
7. Although controversial, corticosteroids administered during the acute phase possibly inhibit further absorption of calcium from the gastrointestinal tract.

Anesthetic Management

Regional vs. general anesthesia

The commonest indication for surgery in patient with primary hyperparathyroidism is hyperplasia of functional parathyroid adenoma. Sometimes block dissection of neck is mandatory in cases of locally advanced malignancy of parathyroid gland.[17] There is no specific technique which can be considered absolutely superior. Regional anesthesia such as superficial and deep cervical plexus blockades have been used for parathyroid surgery but such techniques can be extremely hazardous in light of inadequate anesthesia and can cause numerous complications ranging from parasthesia to cardio-respiratory arrest.[18,19] There is a renewed interest in regional anaesthesia with the advent of α-2 agonists such as clonidine and dexmedetomidine which are being extensively used as adjuvants with newer local anaesthetics such as ropivacaine and articaine in neuraxial anaesthesia.[20-22] However, in modern day anesthesia practice, GA with tracheal intubation and muscle relaxants has been widely accepted throughout the globe.

Premedication

Routinely, combination of a benzodiazepine like alprazolam and H2 antagonist ranitidine are good premedication drugs when administered orally a night before and on the morning of the surgery. Sodium citrate is better alternative to H2 antagonists provided it is easily available. Injection glycopyrrolate 0.2 mg ensures drying of oro-pharyngeal secretions, which can be immensely helpful during difficult airway management.

Airway management

Adequate pre-oxygenation with 100% oxygen (O_2) for at least 4-5 minutes is desirable to ensure adequate pulmonary oxygen stores. One can use either armoured ETT or RAE (Ring, Adair and Elwyn) tube but softness of armoured tube makes its negotiation difficult during airway management. In patients presenting for emergency surgery, problems can be compounded by full stomach and an altered mental status due to hypercalcemia that makes the patient vulnerable to risk of aspiration. The difficult airway can further compound the problem and can lead to oesophageal intubation and its associated complications.[23] Patients with tendency for pathological fractures due to prolonged hypercalcemia should be dealt in a meticulous manner during laryngoscopy as the chances for quadriplegia are high due to unstable cervical spine as a result of lytic lesions. Cervical collar and manual in line traction of the neck by an assistant is a better option for preventing any dislocation or possible fracture of the cervical vertebrae. Availability of fibreoptic bronchoscope eases the pressure while in difficult situations laryngeal mask airway (LMA) and combitube can also be used for ventilation.

Anaesthetic techniques and drugs

Short acting opioids such as fentanyl, remifentanyl, and sufentanyl are ideal analgesics as they cause minimal respiratory depression. Propofol is ideal for such procedures in a dose of 2 mg/kg due to its rapid onset of action and recovery due to short context-sensitive half times, minimal side effects, prevention of post-operative nausea and vomiting and dose reduction in combination with opioids due to synergism.[15-17] Etomidate can be used as an alternative if the patient has pre-op cardiac involvement.

Succinylcholine remains the drug of choice especially in cases of anticipated difficult airway management. Rocuronium is being increasingly used for rapid sequence induction and intubation but the limited availability of suggamedex for reversal limits its utility during difficult airway management. Total intravenous anesthesia (TIVA) has become increasingly popular and propofol-fentanyl combination has been extremely useful for such procedures.[24-26]

Positioning

Positioning of neck should be done carefully as there can be potential risk of accidental fractures of cervical vertebrae. Extension of neck is usually done by resting the head on a padded ring thus exposing the parathyroid and thyroid gland to the maximum for ease of surgery. Intravenous access if secured at upper limb should have extension tubing attached as thoraco-cephalic area is occupied by the surgeons and it will be difficult to administer any medicine without disturbing the surgical procedure. Eyes should be moistened by normal saline and must be covered to prevent any corneal dryness and/or abrasion especially in patients with exopthalmos. A head-up position is preferable as it enables the gravitational drainage of blood and decrease the vascularity of gland thus easing the surgical conditions.

Intra-op management and monitoring

Peri-operative monitoring of non-invasive blood pressure, pulse oximetry, ECG with lead II and V5, temperature, end tidal carbon di-oxide ($EtCO_2$) and oesophageal stethoscope are essential. Blood should be arranged or at least a cross match should be done before the commencement of procedure as the risk of hemorrhage is always there due to confluence of so many vessels. Intra-op steroids are definitely helpful in prevention of airway edema and its co-administration with palonosetron reduces the incidence of post-operative nausea and vomiting (PONV).[27] Renal protection strategies should be employed during peri-op period and should continue in post-op period as well.[11] One big concern during parathyroid surgery is the delay caused by frozen section examination for which anesthesia has to be maintained for unduly long periods.

Ambient room temperature has to be maintained throughout the procedure to make surgical conditions comfortable. Pre-op dialysis has a definite role during the surgery for secondary hyperparathyroidism. Platelet count and coagulation studies should be done as dialysis and alfacalcidol administration can cause platelet dysfunction. Methylene blue should be used carefully and the dose should not exceed 5 mg/kg as it can significantly interfere with pulse oximetry. Deranged electrolyte balance especially of calcium can interfere with cardiac conduction disturbances and myocardial contractility. Muscle relaxant should be used in titrated manner as the associated muscle weakness warrants smaller dose of non-depolarizers. Moreover, the degree of muscle blockade should be assured with train of four stimulations during recovery from anesthesia so as to prevent any potential respiratory compromise. However, the elevated calcium level can also antagonize the action of non-depolarizers to some extent.

Post-op anaesthetic management

It is imperative to proceed with smooth process of extubation so as to avoid any stress response and accidental hemorrhage from the operative site.[28] Hypercalcaemia may cause inadequate reversal due to unpredictable augmentation of non-depolarizing neuromuscular blockade, thus possibly leading to post-operative hypoxemia and respiratory obstruction. Use of train of four stimulations can be of immense significance to monitor the degree of neuromuscular blockade not only during the extubation phase but is also helpful in titrating the doses of muscle relaxants during the intra-op period. Dexmedetomidine is commonly used in our set-up in a dose of 1 μg/kg/hr during peri-op period and it allows not only smooth extubation but also decreases the dose of anesthetic and analgesic agents during the peri-op period as well as reduction in the incidence of shivering.[29] Dexmedetomidine is very effective agent in suppression of stress response also before intubation when given in infusion doses of 1 μg/kg, 15-20 minutes before induction of anesthesia.[30] Though extubation in a deeper plane of anesthesia is a more desirable feature but it will not help in elicitation of any vocal cord movement as perceived with indirect laryngoscopy. Extubation should be carried out in a fully awake state and after establishing a regular breathing pattern with adequate tidal volume and muscle strength.

Post-op Complications

1. **Bleeding**: Post-operative episode of bleeding and subsequent development of hematoma can cause respiratory obstruction. Therefore, all the dressings should be checked thoroughly before the patient is shifted to their respective wards from the recovery area.[31,32]
2. **Metabolic abnormalities**: Hypophosphatemia, hypomagnesemia, and hypokalemia can prove catastrophic during post-op period and should be rectified at the earliest. The combined picture projects a constellation of clinical symptomatology such as cardiac failure, dysarrhythmias, neuromuscular irritability hemolysis, platelet dysfunction, and leucocyte dysfunction.[31,32]
3. **Hypocalcemic tetany**: It occurs due to drastic reduction in post-operative serum calcium levels four to five days post-operatively and is clinically manifested by laryngeal spasms, seizures, and presence of Chvostek's and Trousseau's sign.[33,34]
4. **Recurrent laryngeal nerve (RLN) injury:** Unilateral RLN nerve injury is mostly asymptomatic as there occurs compensatory over adduction of the uninvolved cord and is typically characterized by the development

of hoarseness of voice. Unopposed adduction of the cord can occur during bilateral RLN injury and leads to closure of glottis. Endotracheal intubation is a temporary relief measure and tracheostomy is a definite long term preventive measure.[31,32]

5. **Soft tissue trauma and edema**: It can progress to bullous glottic edema involving the glottis and the pharynx. The onset and origin of this complication remains controversial with no definite preventive measures.
6. **Respiratory obstruction**: Respiratory obstruction can occur due to enlarging hematoma from the wound site bleeding, bilateral recurrent laryngeal nerve injury, bullous glottis edema and metabolic abnormalities.[31,32]
7. **Renal complications**: The chances of renal dysfunction are high in patients who already have some renal disease associated with hypercalcemia pre-operatively.[31,32]
8. **Post-op pain**: Numerous techniques and drugs are available nowadays to alleviate even a high intensity pain. Pre-emptive analgesia and patient controlled analgesia are the new dimensions in the pain relief category which are getting very popular at present.

Minimally invasive parathyroidectomy

The Sestamibi scan has a significant role in the accurate parathyroid tumour localization and dissection with excellent results. Minimally invasive radio-guided parathyroidectomy is being performed with a gamma probe in cases of persistent and recurrent hyperparathyroidism.[35,36] The endoscopic dissection with insufflations of gas has also been performed for minimally invasive endoscopic parathyroidectomy.[37,38] A small midline incision at suprasternal notch can be used for gaining access to parathyroid glands for carrying out minimally invasive video-assisted parathyroidectomy. The bilateral neck exploration is an added advantage of this technique and involves the pre-operative localization with sestamibi scan.[39] The anaesthetic techniques are no different than that from other procedures of parathyroid dissection.

Anesthetic management of hypoparathyroidism

Patients with hypoparathyroidism are usually managed conservatively unless they present with some acute surgical emergency. In such situations, patients have to be urgently optimized by laboratory estimation of serum calcium, phosphate and magnesium levels, which have to be measured regularly during the post-op period as well. The symptomatic hypocalcaemia can be treated with either intravenous administration of calcium gluconate or calcium chloride depending upon the degree of hypocalcaemia. Though QTc interval in ECG is a good diagnostic tool of the serum calcium levels but its interpretation is also not a foolproof method of either estimation or treatment of hypocalcaemia. The anesthetic techniques are similar to other parathyroid surgical procedures with an emphasis on prevention of respiratory alkalosis by avoiding hyperventilation and monitoring of $EtCO_2$, as it can precipitate hypocalcemia by decreasing levels of ionized calcium.

Newer drugs have been in experimental stages, such as calcimimetics, which enhance the sensitivity of calcium sensing receptors.[40] Such drugs can hold a future promise in the management of parathyroid disorders and can possibly avoid the risky surgical interventions.

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