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Intravenous calcitriol: a critical intervention for severe postoperative hypoparathyroidism when oral administration is not feasible

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Abstract

Iatrogenic hypoparathyroidism is a serious complication that can arise from neck surgery, predominantly during thyroidectomy, parathyroidectomy, and laryngectomy; it can be transient or permanent, requiring lifelong treatment. Early detection and treatment are crucial to prevent severe hypocalcemia, which is potentially fatal. This case report describes a 59-year-old male with a history of well-differentiated squamous cell carcinoma of the vocal cords who developed severe postoperative hypoparathyroidism following total laryngectomy with right hemithyroidectomy. Despite initial treatment with cholecalciferol by nasogastric tube, the patient experienced recurrent severe hypocalcemia, requiring intravenous administration of calcitriol due to his inability to swallow. This case highlights the risk factors for triggering postoperative hypoparathyroidism, such as previous surgery or radiotherapy in the cervical region, underlines the importance of careful monitoring of postoperative hypoparathyroidism and proposes the use of intravenous calcitriol as an effective strategy in acute treatment when oral administration is not feasible.

Keywords

Hypoparathyroidism, iatrogenic, intravenous calcitriol, laryngectomy, hypocalcemia, vitamin D

Introduction

Iatrogenic hypoparathyroidism is a potentially serious complication in patients undergoing neck surgery. It has been described mainly in thyroidectomy, parathyroidectomy and laryngectomy [1]. In most cases, it is transient and remits spontaneously in the first weeks after surgery [2, 3]. However, a percentage of patients develop permanent hypoparathyroidism, which requires lifelong treatment [4].

In any case, early detection and management are essential, given the potential severity of severe hypocalcemia [5]. Special attention should be paid to the signs and symptoms of hypocalcemia in these patients: tetany, paresthesias, muscle cramps, nausea, vomiting, confusion, seizures, signs of Chvostek (fasciculations of the facial muscles upon striking the preauricular region over the facial nerve) and Trousseau (flexion of the wrist, the thumb and metacarpophalangeal joints and hyperextension of the fingers, after occlusion of the brachial artery by inflation of a blood pressure cuff above the systolic blood pressure) and lengthening of the QT interval among others [6].

To prevent parathyroid damage in neck surgeries, it is essential to recognize parathyroid tissue based on the use of surgical landmarks. This anticipatory approach in the hands of a skilled surgeon has been shown to decrease the incidence of hypoparathyroidism [7].

However, there are circumstances in which preserving the integrity of the parathyroid glands is really complex, especially in invasive carcinomas of the cervical region [8] or in case of previous surgeries.

Currently, there are no guidelines on the management of the thyroid gland during laryngectomies [9]. Preservation of the thyroid gland can prevent hypothyroidism and hypoparathyroidism, with consequent improvement in quality of life. However, it is essential that this does not compromise the evolution and prognosis from the oncologic point of view.

In this case, we present a patient who presented post-surgical hypoparathyroidism with swallowing alteration secondary to surgery, requiring nasogastric tube placement and intravenous 1,25-OH-vitamin D replacement to normalize calcium levels.

Case report

We present the case of a 59-year-old male with relevant medical history of arterial hypertension, dyslipidemia and well-differentiated squamous cell carcinoma T1aN0M0 [tumor stage classification (tumor size, lymph nodes, metastasis)] of the right vocal cord treated in 2018 in Cuba by endoscopic surgery and radiotherapy (35 fractions with daily dose of 2 Gy), ending in January 2019.

In April 2023, he presents a laryngocutaneous fistula, performing a surgical tracheostomy under local anesthesia.

In October 2023, there was evidence of tumor recurrence, so he was admitted to the Otorhinolaryngology department for total laryngectomy extended to the skin with reconstruction with pectoralis major and selective emptying of the submental area. During the operation, a total thyroidectomy was performed. The day after the operation, a nasogastric tube was placed, given the impossibility of swallowing after surgery, and enteral nutrition was started.

On the sixth day after surgery, the patient began to have bilateral paresthesias in the upper and lower limbs. No blood tests with ions had been taken after the operation. Urgent blood tests were drawn and showed severe hypocalcemia of 4.9 mg/dL (8.3–10.2 mg/dL), hyperphosphatemia of 6.6 mg/dL (2.5–4.5 mg/dL), parathyroid hormone (PTH) < 3 ng/L (15–68 ng/L) and 25-hydroxy-vitamin D of 17.6 µg/L (15–70). An electrocardiogram was performed showing QT segment elongation. The Intensive Care Unit (ICU) was contacted and the patient was admitted under their care for monitoring and intravenous calcium replacement.

The patient remained in the ICU with intravenous calcium gluconate replacement for 6 days, with calcium levels of 8.7 mg/dL at discharge to the ward, suspending perfusion and initiating calcium carbonate and cholecalciferol by gavage. After 48 hours, the patient presented a new hypocalcemia of 7 mg/dL, so the Endocrinology service was contacted for evaluation.

Calcium gluconate perfusion was restarted until calcemia normalized. After this, intravenous calcium supplementation was suspended and calcium carbonate was started by nasogastric tube at a dose of one gram every 8 hours. In addition, cholecalciferol was suspended and intravenous calcitriol was started at 1.5 µg 3 days a week alternately. Calcium remained stable at around 7.5–8 mg/dL, and intravenous calcitriol

was increased to 2 µg 3 days a week and subsequently to 2.5 µg 3 days a week, without modifying the calcium dose, achieving normalization of calcemia.

Subsequently, the nasogastric tube was withdrawn, given the possibility of swallowing, maintaining calcium carbonate 1 gram every 8 hours and introducing oral calcitriol 0.5 µg per day, suspending intravenous calcium supplementation.

One month after discharge, he was evaluated in Endocrinology consultations, with calcium levels of 9.2 mg/dL, phosphate 4.4 mg/dL, corrected calcium 8.7 mg/dL (8.35–10.25), ionic calcium 0.85 mmol/L (0.9–1.25), PTH 26 ng/L (15–68), 25-hydroxy-vitamin D 25.3 µg/L. The calcium dose was decreased to 1 gram every 12 hours. In addition, the patient developed hypothyroidism and remained stable with doses of levothyroxine 150 mcg in successive controls.

Discussion

In neck interventions involving the thyroid area, the risk of postoperative hypoparathyroidism needs to be assessed [10]. The predictive values of hypoparathyroidism include the fact that the surgeon is not able to identify at least 2 parathyroid glands [7, 11], low intraoperative PTH, as well as preoperative levels of serum calcium and 25-hydroxy-vitamin D [12]. The postoperative predictive parameters described are decreased levels of calcium and/or PTH on the first day after surgery [13]. However, normal values on the day after surgery do not rule out the possibility that hypoparathyroidism may develop in the following days, so special attention should be paid to symptoms of hypocalcemia, as well as monitoring of calcium and PTH levels [14].

The patient described presented multiple conditions that made the surgery particularly complex and that favored the appearance of postoperative complications: it was a tumor recurrence, with previous surgery and radiotherapy of the area, with a laryngocutaneous fistula and a surgical tracheostomy. Radiation therapy of the cervical area has been postulated as one of the factors that by itself increases the incidence of hypofunction of the thyroid and parathyroid glands [15]. All this made it especially complex to avoid the development of post-surgical hypoparathyroidism. Furthermore, in the case of laryngectomies, hypocalcemia has been reported in a significant proportion of patients in different series [16]. Table 1 shows the risk factors for long-term and transient hypoparathyroidism in laryngectomies.

Table 1. Risk factors for long-term and transient hypoparathyroidism in laryngectomy [17]

Long-term risk factors for hypoparathyroidism	Risk factors for transient hypoparathyroidism
Total thyroidectomy	Total thyroidectomy
Central neck dissection	Oesophagectomy
Oesophagectomy	Female sex
Pharyngectomy	No additional risk factors
Female sex	

In this patient cholecalciferol was initially administered by nasogastric tube, despite which he again presented hypocalcemia. This is due to the fact that for hydroxylation to occur in the kidney to reach 1,25-dihydroxyvitamin D3, which is the active metabolite, PTH is required [18, 19]. The fundamental problem was that the patient in the acute phase was unable to swallow, and while cholecalciferol can be administered by nasogastric tube, calcitriol in capsule form is contraindicated, since it is an oily solution that can cause obstruction of the tube. Today, recombinant PTH could be an alternative to help maintain calcium within normality in this patient, as it has been shown to decrease calcium and calcitriol doses in patients with hypoparathyroidism, as well as to avoid hypocalcemia [20, 21].

Intravenous calcitriol has been used fundamentally in hyperparathyroidism secondary to advanced renal disease [22], since, in the presence of renal insufficiency, hydroxylation in position 1 to obtain the active metabolite of vitamin D is diminished [23]. Table 2 shows the indications for which intravenous administration of calcitriol should be considered.

Table 2. List of indications in which it is important to consider intravenous calcitriol administration [18, 24–27]

Dysphagia	Malabsorption	Hyperparathyroidism secondary to advanced chronic kidney disease
Neurological disorders: stroke, multiple sclerosis, Parkinson's disease or amyotrophic lateral sclerosis, etc.	Gastrointestinal disorders: celiac disease, Crohn's disease, short bowel syndrome, ulcerative colitis, bariatric surgery	Severe secondary hyperparathyroidism
Muscular diseases: myasthenia gravis and muscular dystrophies	Bile duct pathology	Refractory to oral medical treatment
Cancer: tumours in the mouth, pharynx or larynx	Pancreatic pathology, such as chronic pancreatitis	Patients who develop hypercalcaemia with oral calcitriol treatment
Oesophageal pathology: oesophageal stricture, achalasia, oesophagitis, oesophageal diverticula, oesophageal cancer	Drugs: anticonvulsants, some HIV drugs, and certain cholesterol-lowering drugs (such as bile acid sequestrants)	To avoid surgical parathyroidectomy in some cases

Based on the premise that calcitriol has immunomodulatory and anti-inflammatory properties, another use to which intravenous calcitriol is being found to be applicable is in sepsis. There are studies in obese mice, in which intravenous calcitriol has promising results alleviating inflammation and intestinal injury [22, 28].

However, there are practically no publications describing the use of intravenous calcitriol for the management of primary hypoparathyroidism with severe symptomatic hypocalcemia. There is one article in which intravenous calcitriol was used for the treatment of a patient with previous primary hypoparathyroidism, who underwent bariatric surgery that was complicated and required admission to the ICU, with the impossibility of using the digestive tract to replenish calcemia given the established abdominal sepsis [29]. In this article, intravenous calcitriol 1 µg every other day was used, but was discontinued due to shortage of stock and high cost. Weeks later, it was reintroduced at the described dose, achieving a preservation in calcemia until the oral route could be used.

In our experience, we recommend the use of intravenous calcitriol at initial doses of between 1 µg to 2 µg per day, administered three times a week, approximately every other day. This dose should be progressively increased by 0.5 µg to 1 µg per day depending on the response of calcium levels. Table 3 shows the difference in the dosage of calcitriol and calcium treatments during hospitalization and at home.

Table 3. Difference in doses and routes of administration of calcium and calcitriol during admission and at home to achieve adequate serum calcium levels

Treatments	Hospital treatment	Home treatment
Calcitriol	7.5 µg IV (2.5 µg 3 days per week every other day)	3.5 µg oral (0.5 µg per day)
Calcium	Calcium carbonate 1 gram per nasogastric tube every 8 hours	Calcium carbonate 1 gram oral 1 gram every 12 hours

This case highlights the importance of proper management of severe acute hypocalcemia in primary hypoparathyroidism. In addition, its management is reviewed when the oral route is not available and vitamin D in its active form must be administered intravenously.

Abbreviations

ICU: Intensive Care Unit

PTH: parathyroid hormone

Declarations

Author contributions

IJH, LGF, and MPN: Conceptualization, Investigation, Writing—original draft, Writing—review & editing, Validation. All authors read and approved the submitted version.

Conflicts of interest

All authors declare that they have no conflicts of interest.

Ethical approval

The study "Intravenous calcitriol: a critical intervention for severe postoperative hypoparathyroidism when oral administration is not feasible", carried out by Dr. Ignacio Jiménez Hernando from the Department of Endocrinology and Nutrition Service of the Hospital General Universitario Gregorio Marañón has been reviewed by the Ethics Committee of the Hospital General Universitario Gregorio Marañón (CEIm HGUGM), and CEIm HGUGM found no ethical impediment to the study's publication and dissemination, as stated in Minute 05/2025, of March 3.

Consent to participate

Informed consent to participate in the study was obtained from the participants.

Consent to publication

Informed consent to publication was obtained from the relevant participants.

Availability of data and materials

The datasets that support the findings of this study are available from the corresponding author upon reasonable request.

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