

EDITORIAL

Post-surgical hypoparathyroidism: a condition of growing interest among endocrinologists[☆]



Hipoparatiroidismo postquirúrgico: un trastorno de interés creciente entre los endocrinólogos

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Hypoparathyroidism is an endocrine disorder characterized by low serum calcium levels in the presence of undetectable or inadequately low parathyroid hormone (PTH) levels.^{1,2} Postsurgical hypoparathyroidism, which is the most common form of presentation of the disease, occurs as a complication of neck surgery (thyroid, parathyroid or laryngeal surgery), and may manifest in an acute and severe form requiring the rapid administration of intravenous calcium to relieve the symptoms.³ The underlying cause of the disorder is intentional ablation or accidental damage to the parathyroid glands during surgery. Other forms of hypoparathyroidism include autoimmune damage to the parathyroid glands (autoimmune hypoparathyroidism) and genetic defects in PTH synthesis, secretion, or function, or in the development of the parathyroid glands. These less common forms of the disorder may occur alone or in association with other autoimmune syndromes or genetic abnormalities in other organs.⁴

Population-based epidemiological studies have shown hypoparathyroidism to be an infrequent condition. The Rochester Epidemiology Project documented a prevalence of 37 cases per 100,000 inhabitants in the period 2006–2008.⁵ Most cases (78%) were caused by neck surgery, and only a small proportion were familial (7%) or idiopathic (6%). In a study based on the large databases of insured North American patients, Powers et al.⁶ found a prevalence of 58,793 adults diagnosed with hypoparathyroidism in the period 2007–2008, out of a total of 77 million patients. Seventy-five percent of the patients were females, and the prevalence increased with age. A European study, the Danish Patient Registry, found a prevalence of 22 patients with postsurgical hypoparathyroidism per 100,000 cases and 2.3 patients with nonsurgical hypoparathyroidism per 100,000 cases.⁷

The prevalence of transient and permanent postoperative hypoparathyroidism has not been precisely established, and the figures found in the literature vary greatly. Some authors estimate the proportion of patients with postsurgical hypoparathyroidism or hypocalcemia to range between 10–60%.^{2,8–11} Most cases of hypoparathyroidism resolve within the first 6 months after surgery, but the estimates found in the literature regarding the persistence of the deficiency also vary greatly from 0.12 to 6.6%.^{8–10} In the study published by Powers et al.,⁶ the prevalence of hypoparathyroidism was found to be 7.6% in a cohort of 117,342 surgeries

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of the anterior neck region. Of these cases, 75% were of a transient nature (duration ≤ 6 months) while 25% proved permanent (duration > 6 months).

Interest in hypoparathyroidism among endocrinologists has increased in recent years, as shown by the many published clinical guides and consensus documents.^{1,2,12} Unlike these guides and consensus documents, which address all types of hypoparathyroidism, and as reflected in a recent statement by the American Thyroid Association,¹³ the consensus document published in this issue of the journal *Endocrinología, Diabetes y Nutrición*¹⁴ only focuses on the form of hypoparathyroidism that most concerns endocrinologists, ear, nose and throat specialists, and surgeons, i.e., postsurgical hypoparathyroidism, and more specifically, hypoparathyroidism manifesting after thyroid surgery. The executive summary offers an eminently practical view and provides clinicians with easy-to-access recommendations regarding both management in the immediate postoperative period and chronic treatment of the disorder. In addition, the authors provide recommendations on the prevention of hypocalcemia, covering both the pre- and intraoperative stages.

These recommendations underline some of the known risk factors for the development of postsurgical hypoparathyroidism. The experience of the surgical team has been positively correlated to the recovery of parathyroid function⁸; it is therefore always advisable for neck surgery to be performed by surgical experts. Wider and more complex surgical procedures,^{8,11} as well as lymphadenectomy,¹⁵ have also been related to increased rates of hypoparathyroidism. Surgery for Graves' disease, recurrent goiter, or second surgery due to bleeding have also been related to permanent hypoparathyroidism.⁹

One of the salient aspects of this consensus is the importance of stratification into clinical hypocalcemia risk groups based on the reduction of PTH concentration in the immediate postoperative period. The authors, drawing upon the experience gained at Hospital La Paz,¹⁶ categorize patients into three risk groups based on the percentage postoperative reduction of PTH with respect to preoperative PTH and the absolute postoperative PTH concentration. Although these criteria are not accepted in generalized terms and may not be reproducible in other centers and with other PTH measurement procedures different from those employed by the authors, this recommendation emphasizes the usefulness of PTH measurement as a factor conditioning recovery or the permanent failure of parathyroid function, as shown by different studies.¹⁰ According to a recent study, the risk of permanent hypoparathyroidism is also related to the number of parathyroid glands remaining in situ after surgery.¹⁵ In this regard, the consensus recommends the careful identification and preservation of the vascular pedicles, as well as the assessment of gland status at the end of surgery.

In its final recommendations, the consensus document considers that the aims of the chronic management of hypoparathyroidism include keeping the patient free of signs and symptoms of hypocalcemia, with calcium levels at the lower end of the reference range, normal serum phosphorus levels, and a calcium-phosphorus product ($\text{Ca} \times \text{P}$) of $< 55 \text{ mg}^2/\text{dl}^2$. Other objectives include keeping calciuria within the gender-specific reference range of the patient, with normal serum magnesium levels, and adequate vitamin D

status. The need to care for patient well-being and quality of life is also emphasized, these being aspects of which clinicians are becoming increasingly aware.

The authors recommend treatment with oral calcium salts and active vitamin D analogs. In Spain, the vitamin D analog used to treat hypoparathyroidism is calcitriol (1,25-dihydroxyvitamin D), at variable doses. Thiazides and a low-salt diet may be prescribed in hypercalciuria. Hyperphosphatemia can be managed through a reduction in dietary phosphate or an increase in calcium supplements and a reduction in calcitriol. Although recombinant human PTH (rhPTH [1–84]) is not recommended in the routine treatment of hypoparathyroidism, as stated in the consensus document, several American and European drug agencies have approved its use in selected patients with chronic hypoparathyroidism who cannot be adequately controlled with standard treatment.

This consensus document and the other recently published guides coincide on most of the key points referring to the prevention and treatment of hypoparathyroidism. However, there are aspects of this hormone deficiency which are still not well known and which require active clinical research. Although published data from some groups are available, the prevalence of transient and permanent hypoparathyroidism in Spain is not precisely known. In addition, the definition of the time course of hypoparathyroidism, as well as the concept of chronic hypoparathyroidism, varies among authors. The late recovery of parathyroid function is a documented fact, but the underlying causes and mechanisms are difficult to analyze. On the other hand, clinicians are increasingly aware of the impact of chronic hypoparathyroidism upon quality of life, renal function and the nervous, cardiovascular, and musculoskeletal systems. While not very numerous, patients who are poorly controlled biochemically or symptomatically with standard treatment pose a considerable challenge. The results obtained to date regarding the efficacy and safety of rhPTH (1–84) are encouraging in these patients, even over the long term,¹⁷ though the high cost involved poses a limit to the clinical use of such treatment.

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Conflicts of interest

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