Pre-operative Symptoms and Post-operative Improvement in Patients Diagnosed With Hyperparathyroidism. Analysis of 120 Consecutive Cases

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Objective: To compare the pre-operative and post-operative clinical symptoms in patients diagnosed as having hyperparathyroidism and given surgical treatment, in order to prove the existence of statistically significant improvement.
Material and method: We report here a retrospective study performed on 120 consecutive patients operated on following diagnosis of hyperparathyroidism between 1990 and 2003.
Results: Nephrolithiasis, generalized bone pain, and HBP were the most common clinical manifestations. Primary hyperparathyroidisms represented 76.7%, while secondary ones were 20.8%, and 2.5% were tertiary. We carried out 85 adenoma removals, 30 sub-total, and 5 total parathyroidectomies. We only encountered one case of recurrent palsy and about 25% of hypocalcemias (2 of them permanent). Osteoarticular pathology and nephrolithiasis suffered by our patients clearly improved after surgery ($P<.01$) after 2 years of follow-up. There was no significant improvement in HBP, digestive and psychiatric pathology, or pruritus.
Conclusions: The improvement in quality of life for most of the patients operated on for this condition amply justifies parathyroidectomy by an experienced otolaryngology team.

Key words: Hyperparathyroidism. Parathyroidectomy. Recurrent palsy. Hypocalcemia.

Clínica preoperatoria y mejoría postoperatoria en pacientes con diagnóstico de hiperparatiroidismo. Análisis de 120 casos consecutivos
Objetivo: Comparar los síntomas clínicos preoperatorios y postoperatorios en pacientes diagnosticados de hiperparatiroidismo y sometidos a tratamiento quirúrgico, para comprobar si se produce mejoría estadísticamente significativa.
Material y método: Estudio retrospectivo realizado sobre 120 pacientes consecutivos intervenidos con diagnóstico de hiperparatiroidismo entre 1990 y 2003.
Resultados: La litiasis renal, los dolores óseos generalizados y la hipertensión fueron las manifestaciones clínicas más frecuentes. El 76,7% eran hiperparatiroidismos primarios; el 20,8%, secundarios y el 2,5%, terciarios. Se practicaron 85 resecciones de adenoma, 30 paratiroidectomías subtotales y 5 paratiroidectomías totales. Sólo hemos constatado 1 caso de parálisis recurrencial y un 25% de hipocalcemias (2 definitivas). Mejoraron significativamente tras la cirugía ($p < 0,01$) la afección osteoarticular y la litiasis renal que presentaban los pacientes tras 2 años de seguimiento. No mejoraron de forma significativa la hipertensión, las enfermedades digestivas y psiquiátricas y el prurito.
Conclusiones: La mejoría en la calidad de vida de la mayoría de los pacientes operados por esta enfermedad justifica sobradamente la paratiroidectomía por un equipo otorrinolaringológico experimentado.

Palabras clave: Hiperparatiroidismo. Paratiroidectomía. Parálisis recurrencial. Hipocalcemia.

INTRODUCTION

Hyperparathyroidism is an illness with an incidence that has increased in recent years, particularly due to the increase in the number of analytical determinations with high levels of calcemias undergoing further study and differential diagnosis.[1] Its clinical manifestations, such as renal lithiasis, widespread bone pain, and arterial hypertension (HBP) may seriously affect patients' quality of life.[2,3]

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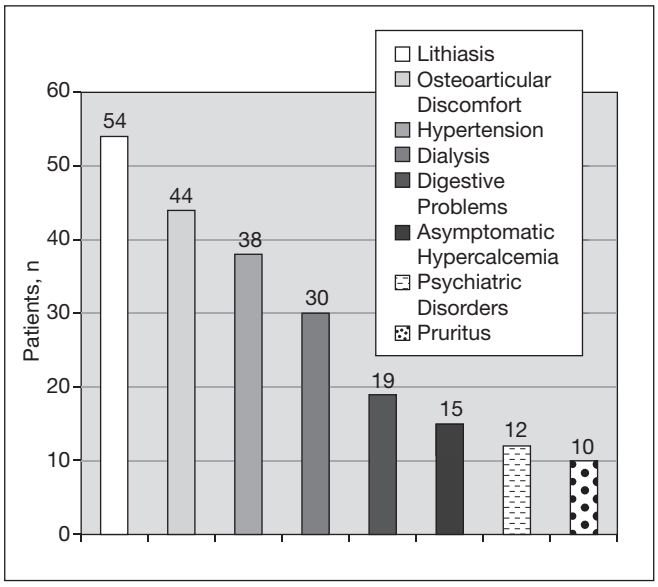

Figure 1. Initial clinical manifestations in the 120 patients referred for surgical treatment with a diagnosis of hyperparathyroidism.

On many occasions, surgery in the form of adenoma exeresis and sub-total or total parathyroidectomy represents the best treatment that can be offered to patients, with a high benefit/risk ratio in favour of the first. The main complications to be avoided are the persistence of hypercalcemia, recurrent palsy and post-surgical hypocalcemia, which is the most frequent and generally transient.[3]

In primary hyperparathyroidism, the classic bilateral examination is giving way to its unilateral version, based especially on the contribution of "turbo" determination of intact parathyrin (PTHi) and on the intra-operative gamma-probe detection of the adenoma or adenomas causing it. This allows a reduction in the morbidity and hospital stays in many cases that may even be subjected to minimally invasive surgery by a team of experienced otorhinolaryngologists.[4-7]

The subsequent clinical follow-up of patients must be multidisciplinary (otorhinolaryngology, nephrology, endocrinology) as this is fundamental to understand the improvement obtained in the medium and long term. In the review presented here, of 120 patients operated on in our department, we intend to analyze our real results and verify to what extent the pre-operative symptoms improve after parathyroidectomy with a final follow-up after 24 months.

MATERIAL AND METHOD

Retrospective study conducted between June 1990 and July 2003, during which time we studied 120 consecutive patients referred with a diagnosis of hyperparathyroidism and finally subjected to surgical treatment. By gender, 91 were female (75.83%) and 29 were male (24.17%), with ages between 14 and 79 years of age (mean, 52).

The endocrinology department referred 75 patients, 39 came from nephrology and the other 6 were seen directly by otorhinolaryngology. With respect to the type of hyperparathyroidism, 92 were primary (76.7%), 25 secondary (20.8%), and 3 tertiary (2.5%).

The following clinical manifestations have been studied: osteoarticular pain, gastrointestinal discomfort, HBP, nephrolithiasis, psychiatric disorders, pruritus, and asymptomatic hypercalcemia. We also reflected the number of patients included in a haemodialysis programme at the moment of diagnosis.

The types of surgery, 120 operations in total, were divided into: *a)* resection of adenoma; *b)* sub-total parathyroidectomy; and *c)* total parathyroidectomy. The post-operative complications seen were hypocalcemia (transient or definitive), recurrent palsy, post-operative bleeding, serohaematoma, wound infection, and persistence of hypercalcemia. To confirm the improvements obtained, we analyzed the follow-up and case history information collected after 1, 6, 12, and 24 months following surgery.

The SIGMA and SPSS statistical programmes were used and the results have been expressed in graphs and tables from MS Excel 2000. For the comparison of proportions between quantitative variables, we used the χ^2 and Fisher's tests.

RESULTS

The pre-operative PTHi values ranged between 62 and 2500 pg/mL, with a mean of 389 (53) pg/mL. Pre-operative calcemias were between 9.5 and 13.8 mg/dL (mean, 11.5 [0.8] mg/dL). We considered serum calcium values between 8.4 and 10.2 mg/dL to be normal, whereas for PTHi the normal values were between 10 and 55 pg/mL.

Radiologically confirmed renal lithiasis was the most frequent clinical symptom: 54 (45%) of the 120 patients in our study. These were followed in order of frequency by osteoarticular pain (36.7%) and HBP (31.7%). Only in 15 cases (12.5%) did we confirm asymptomatic hypercalcemia (Figure 1). Thirty patients were included in a dialysis programme prior to surgery, mostly with secondary and tertiary forms of the disease; 21 patients presented other thyroid involvement apart from their hyperparathyroidism, generally thyroid nodules or multinodular goitres. The highest PTHi values were found in secondary hyperparathyroidism due to glandular hyperplasia, in which figures >1000 pg/mL were relatively frequent, whereas in primary single adenomas, PTHi rarely exceeded 300 pg/mL.

A total of 85 adenoma resections were performed, along with 30 sub-total and 5 total parathyroidectomies (Figure 2). No numerical anomalies were observed in any of the 120 procedures on the parathyroid glands, that is to say no absence of any parathyroid nor any supernumerary ones; 5 glands were located in atypical situations (3 inside the thyroid, 2 in the thymic isthmus). Since 2000, we have been able to use turbo determination of PTHi intra-operatively and we have generally used this technique together with a request, generally pre-operative, for an ultrasound scan and

a gammagram of the thyroids as guidance for surgery. This has allowed us to apply unilateral examination in almost half the patients with primary hyperparathyroidisms instead of the classical bilateral examination, providing that the fall in PTHi obtained after exeresis of the adenoma was >60% with respect to the pre-operative value. We do not normally carry out intra-operative biopsies.

The pathology result reported a predominance of adenomas (72.5%) and hyperplasias (27.5%). None of the specimens sent was reported to be a carcinoma of the parathyroid. Most of the adenomas were located in the lower parathyroids (87.35%), a statistically significant result (P<.05).

The most common post-surgical complication was transient hypocalcemia, ie, it was considered normalized following medical treatment for a period of less than 34 months. Of the 30 patients who presented hypocalcemias, only 2 became definitive despite treatment and corresponded to total parathyroidectomies. In our series we only recorded 1 case of recurrent palsy that was definitive and 2 cases of persistent hypercalcemia after parathyroidectomy, of which 1 was subject to repeat surgery and was finally treated for a double adenoma not discovered in the first procedure.

After a mean stay of 7 days, the patients were checked up at external ENT clinics or at endocrinology and/or nephrology clinics.

Table reflects the improvement obtained and reported by each patient according to their symptoms. Renal lithiasis was the condition that most improved after parathyroidectomy, since more than 90% of patients reported this after 2 years of follow-up. Widespread bone pain reduced and even disappeared in more than three quarters of cases, and we also found radiological improvements in the check-ups effected for osteopenia. In both conditions, when we performed the χ^2 test for comparison of proportions between quantitative variables, the result was statistically significant (P<.01 and P<.05, respectively).

The rest of the clinical manifestations also experienced an improvement after surgery, although to a lesser extent than in the previous 2 with P>.05. Subjectively, pruritus was the symptom that improved least after 2 years of monitoring.

Finally, we wish to mention the advantages of turbo determination of PTHi intra-operatively for our otorhinolaryngological department, as it has in many cases allowed us to find out the reduction achieved in only a few minutes, so that we were able to be practically absolutely sure of not leaving any hyperfunctioning parathyroid tissue before deeming the procedure concluded.

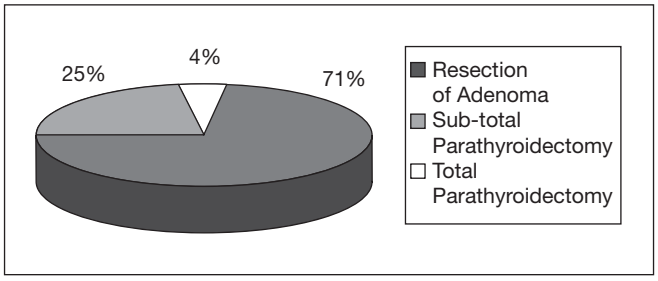

Figure 2. Type of surgery performed as total percentage.

Patients Who Improved, by Symptom, After Surgery and Clinical Follow-up Over 2 Years

	Pre-operative Clinical Signs, No.	*Improvement Reported, No (%)*	*P*
Renal lithiasis	54	49 (90.74)	<.01
Osteoarticular pain	44	34 (77.27)	<.05
Arterial hypertension	38	20 (52.63)	.12
Digestive problems	19	9 (47.36)	.21
Psychiatric disorders	12	5 (41.67)	.27
Pruritus	10	2 (20)	>.3

DISCUSSION

Hyperparathyroidism is a condition that predominately affects females and generally after the fourth decade of life.[1] Primary and secondary hyperparathyroidism are manifested by a disorder, to a greater or lesser degree, in the metabolism of calcium, phosphorus or bone tissue, produced by an increase in the parathyroid function. The first is due to primary hypersecretion of PTH, whereas in the secondary forms of the illness the glands increase their secretion as a compensatory response to an extraglandular process; kidney failure is the most important aetiology. Tertiary hyperparathyroidisms are much less frequent autonomous forms that occur particularly in patients with functional failure after a kidney transplant.

The most frequent clinical manifestations, in most of the series consulted, are osteomusculoarticular manifestations (widespread bone pain, myalgias, and joint pain) and repeated renal lithiasis.[1-3] Patients are frequently asymptomatic or have very mild symptoms at the moment of the diagnosis.

Prior to surgery, we usually request or make use of complementary imaging tests such as ultrasound scans or gammagraphy with technetium-99 sestamibi and, occasionally, computed tomography or magnetic resonance, but we are convinced that the expertise of the surgical team is primordial and irreplaceable.[4,5] Nonetheless, we feel there is no convincing reason for not requesting an imaging test pre-operatively, as it may direct surgery in many cases or rule out concomitant thyroid disease.[6]

Intra-operatively, in secondary and tertiary hyperparathyroidisms, we always proceed with bilateral exposure in search of the 4 parathyroids. In primary cases unilateral examination is possible on many occasions, particularly thanks to new intra-operative techniques such as PTHi determination. Dackiw et al[7] carried out a study combining both methods in 32 patients, with positive results in all cases. Mandell et al[8] have shown the usefulness of turbo PTH determination to predict surgical success after extirpation of anomalous glands. Other papers have

confirmed these statements[9,10] and coincide in pointing out other advantages, such as the reduction in surgical time and the possibility, in selected cases of primary hyperparathyroidism, of opting for a minimally invasive procedure with video assistance, even with local anaesthesia, with good aesthetic results and a demonstrated reduction in post-operative pain.[11,12]

In most series, renal lithiasis and osteoarticular conditions are the symptoms that most improve after parathyroidectomy. These symptoms are found in both primary and secondary or tertiary hyperparathyroidisms and surgery produces an improvement in affected patients' quality of life and was the treatment of choice.[13-15] The possibility of recurrence or relapse, with persistence of clinical hypercalcemia despite treatment, varied between 5% and 11% depending on the author.[2,16,17]

Unlike other published series,[1] we can confirm, in the light of the pathology study, a predominance of adenomas in inferior rather than superior parathyroids. So far, we have not encountered any convincing explanation for this in the literature. The number of hyperplasias found is also somewhat higher than that published in other papers. With respect to the percentage of recurrent palsies out of the total number of nerves exposed, this was within expected levels, as up to 1% of cases with this complication are considered normal or expected in a first procedure.[13,16]

CONCLUSIONS

Hyperparathyroidism is an illness increasingly diagnosed and, if not treated, affects the quality of life of affected patients.

Parathyroidectomy is a clean surgery, with scant morbidity and demonstrated benefit, requiring expertise on the part of the otorhinolaryngological team.

The most common clinical manifestations in most series including ours are osteoarticular pain and nephrolithiasis.

The symptoms that experienced the best improvement after surgery were renal lithiasis and widespread bone pain.

Clinical follow-up of trial patients is necessary because of the possibility of a relapse in the hyperparathyroidism, even where the parathyroidectomy has been successful.

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