

## CLINICAL STUDY

## Surgical treatment of primary hyperparathyroidism

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**Abstract:** *Objective:* The aim of the study was to evaluate the history, diagnostic procedures, extent and success of the surgical treatment, and possible complications in patients with primary hyperparathyroidism. The authors further discuss the findings in the context of literature data.

*Methods:* Retrospectively, 48 patients (7 males and 41 females) were analyzed with primary hyperparathyroidism treated between 1999–2006 at the Clinic of Otorhinolaryngology and Head and Neck Surgery JFM CU and FH in Martin at average age of  $56 \pm 9$  years.

*Results:* In 90 %, pHPT was caused by solitary adenoma and in 10% by hyperplasia. Eleven per cent of patients were asymptomatic. Ultrasonography was performed in all and sestamibi scintigraphy in 17 patients. In 3 cases adenoma was localized ectopically. All patients were treated with traditional bilateral cervical approach. Complications excluding transient hypocalcemia (one-side paralysis, subcutaneous haematoma and inflammation) were present in <1 % of patients.

*Conclusion:* Surgical removal of hormonally active tissue is safe and causal treatment of primary hyperparathyroidism with high success rate (Tab. 4, Ref. 21). Full Text (Free, PDF) [www.bmj.sk](http://www.bmj.sk).

Key words: parathyroid gland (PG), primary hyperparathyroidism, adenoma of PG, hyperplasia of PG.

Primary hyperparathyroidism (pHPT) is a hypercalcemic state due to excessive secretion of parathyroid hormone (1, 2). It is a common endocrine disease in countries where screening is commonly used, and hypercalcemia is readily detected (1). The incidence of pHPT is reported to be 1:1000 persons and 1:500 women older than 45 years (3). In Slovakia it is only 42:100000 (4).

There are many causes of pHPT, and optimal therapy must be individualized for each patient according to this etiology: 1) solitary adenoma (85 %); multigland hyperplasia (10 %); 3) double adenoma (3 %) and 4) carcinoma (2 %) (3, 5).

The aim of the study was to analyse the group of the patients that have been hospitalized at the Clinic of Otorhinolaryngology and Head and Neck Surgery, Jessenius Faculty of Medicine, Comenius University (JFM CU) in Martin and Faculty Hospital (FH) in Martin within 1999–2006 with the diagnosis of primary hyperparathyroidism. The authors evaluate the patient's history, diagnostic procedures, extent and success the of surgical treatment, and possible complications and their solution.

## Methods

Retrospectively, we analyzed 48 patients (7 males, 41 females) with primary hyperparathyroidism treated between 1999–2006

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at our Clinic. The group of patients was selected on the basis of cooperation with National Institute of Endocrinology in Lubochna, Clinic of Internal Medicine I. of JFM and FH in Martin and ambulatory endocrinologists. The data on patients' histories, diagnostic procedures, treatment and complications were acquired from medical records. Age interval was 17–81, average age  $56 \pm 9$  years. Two patients in second and third trimesters of pregnancy with solitary adenoma were included. Data on age and calcemia are shown as mean  $\pm$  standard deviation.

## Results

### *Affection of different systems*

In our study group, hyperparathyroidism was manifested by symptoms from different systems (Tab. 1) with uropoetic system most frequently affected. Twenty patients suffered from urolithiasis, nephrosclerosis or recurrent infections. About 30 % of patients suffered from hypertension, about 20 % from osteodystrophy and in less than 10 % symptoms arised from gastrointestinal

**Tab. 1. The overview of the systems affected in patients with primary hyperparathyroidism.**

Symptomatology	n	%
Uropoetic system	20	35.7
Skeletal system – osteodystrophy	10	17.9
Cardiovascular system – hypertension	15	26.8
Gastrointestinal system	5	8.9
Asymptomatic patients	6	10.7

**Tab. 2. Type and distribution of morphological changes of parathyroid glands.**

Type of histological change	n	%
Solitary adenoma	43	89.6
Hyperplasia	5	10.4
Location of solitary adenoma	n	%
gl. parathyroidea inf. sin.	12	28
gl. parathyroidea inf. dex.	10	23
gl. parathyroidea sup. sin.	9	21
gl. parathyroidea sup. dex.	9	21
ectopic	3	7

**Tab. 3. Type of surgical intervention.**

Surgery	n	%
Extirpation of adenoma	43	89.6
Subtotal parathyroidectomy for hyperplasia	5	10.4
Subtotal thyroidectomy with parathyroidectomy	8	16.7
Total thyroidectomy with parathyroidectomy	1	2.1

**Tab. 4. Complications observed in postoperative period.**

Complication	n	%
Clinical signs of hypocalcemia	12	25
One-side vocal cord paralysis	1	2
Subcutaneous haematoma	3	3.5
Inflammation	2	4.2
No complications	30	65.3

system. In 6 patients the diagnosis was completed during the asymptomatic stage. In some patients symptoms were combined.

#### Preoperative examination

The extent of examination was appointed by endocrinologist. Ultrasonic examination was performed in all patients with sensitivity of 90 %. In 17 patients Technecium (Tc)99m-scintigraphy was performed with falsely positive result in one case. CT examination of the neck and upper mediastinum was indicated in 8 patients. In one patient, angiography was performed prior to re-medial parathyroid surgery due to recurrent hyperparathyroidism.

#### Preoperative treatment

Preoperative treatment was based on close cooperation of the surgeon with the anaesthesiologist and endocrinologist. In two pregnant patients gynecologist-obstetrician was consulted. The average preoperative calcemia was  $2.87 \pm 0.3$  mmol/l. The maximum detected value was 3.67 mmol/l. Patients were surgically treated as long as calcemia was  $< 2.9$  mmol/l. The key element in the preparation of patients was represented by adequate hydration with application of diuretics and special attention paid to patients with reduced renal functions. Calcitonin was applied if needed. In 3 patients, hypercalcemia was the indication for dialysis.

#### Distribution of morphological changes of parathyroid glands

Most frequently, adenoma was localized in lower left parathyroid gland (Tab. 2). In three patients adenoma was placed ectopically – once under a. subclavia in upper mediastinum and twice in the right lower paratracheal and paraesophageal space.

#### Surgical treatment

All patients were surgically treated with the use of classical approach (Tab. 3). Forty-three patients were treated for solitary adenoma of parathyroid glands and 5 patients for hyperplasia that was proved by definite histological examination. In two cases, diagnosis of adenoma was done accidentally during thyroidectomy. In five patients with hyperplasia subtotal parathyroidectomy was done by extirpation of three parathyroid bodies and lateral 50 % of parenchyma of 4th parathyroid body. The retained tissue was marked by a single unresorbable stitch. Due to nodal changes of thyroid gland parenchyma in eight patients partial and in one patient total thyroidectomy had to be performed.

#### Postoperative course and complications

Calcemia was measured 8 and 24 hours after surgery. A significant decrease in calcemia was present already after the first measurement. Twelve patients had clinical signs of hypocalcemia and were treated with calcium preparations. In 47 patients (98 %) calcemia reached physiological values within 24 hours; in one patient (2 %) hypercalcemia sustained after surgical removal of parathyroid glands. There was one complication that involved one-side vocal cord paralysis on the left. The function of larynx completely recovered within 7 days after antiedematous and corticosteroid treatment. In some patients, postoperative course was complicated by subcutaneous haematoma and inflammation (Tab. 4).

#### Discussion

The average age of patients in our study ( $56 \pm 9$  years) corresponds with the reported average age at the time of diagnosis that is 55 years. The incidence of the condition increases with age and is more common in postmenopausal women (6).

Depending on the biochemical monitoring, the clinical profile of primary hyperparathyroidism (pHPT) was shifted from a symptomatic disorder, with hypercalcemic symptoms, kidney stones, bone disease, or a specific neuromuscular dysfunction, toward a more asymptomatic state (1). As in Slovakia serum calcium levels are not routinely monitored, in majority of patients the diagnosis is made after the development of clinical symptoms resulting from hypercalcemia. In our study, only 11 % of patients were submitted for surgery in asymptomatic stage. The highest value of calcemia was 3.67 mmol/l and before surgery, in all patients it was brought down to  $2.87 \pm 0.3$  mmol/l. In literature, an extreme hypercalcemia of 6.92 mmol/l associated with parathyroid adenoma was reported in young men. Hypercalcemia and symptoms were relieved by parathyroidectomy (7).

Ultrasonography can be a sensitive and accurate method for preoperative localization of enlarged parathyroid glands in pri-

mary hyperparathyroidism, comparable to overall utility to sestamibi scintigraphy. In all our patients, ultrasonography was performed with the sensitivity of 90 %. In 17 patients Tc99m-scintigraphy was done with 1 falsely positive result. The strategy of initial testing with one or the other method followed by the alternate imaging test when the first test is negative, would provide correct parathyroid imaging in most patients without prior parathyroid surgery (8). Tc99m-scanning is the most accurate technique also for localizing abnormal parathyroid glands. An ectopically placed parathyroid adenoma in the anterior mediastinum may be an important cause of failure in primary neck exploration. In our group, three patients (7 %) had ectopically localized adenomas, the fact of which is comparable to other authors who reported 3 cases amongst 70 surgically treated patients with pHPT (4.3 %) over 20-year period (9). The complementary use of parathyroid scintigraphy and ultrasonography is very valuable in the evaluation of concomitant thyroid disease and it is recommended in areas with high prevalence of thyropathies (10). The prevalence of concomitant hyperparathyroidism in study of Abboud et co-workers (11) was 13.5 %, in our study it was up to 19 %.

The standard surgical approach resides in bilateral neck exploration with parathyroidectomy that is the most effective treatment option for pHPT. It is a safe procedure with success rate between 95–98 % (3, 12, 13). All patients at our Clinic were surgically treated with the use of classical approach. In 90 % of patients, surgery was performed for solitary adenoma and in 10 % for hyperplasia. As the identification of all parathyroid (PT) glands is routinely done at our Clinic at each thyroid gland surgery, in two cases adenoma was found accidentally. Interestingly, in one patient adenoma was under a. subclavia and was identified and removed upon reoperation after localization by Tc99m-scintigraphy. After adenoma extirpation all remaining PT glands were identified and marked with an unresorbable stitch. In order to exclude the coincidence of adenoma and hyperplasia, biopsy of the lateral part of PT body was done. Up to year 2003 we were administering methylblue dye in 5 % glucose intravenously. Due to dark staining of PT bodies their identification has become easier.

Considerable controversy remains concerning the most appropriate treatment for patients with mild or asymptomatic pHPT. Some clinicians believe that patients over 60 years of age with uncomplicated pHPT can be treated nonoperatively (1). Others believe that all patients with pHPT should be treated by parathyroidectomy (14, 15). Some patients decline surgery and decide to be medically followed up. We do not have the knowledge of the number of such patients as we only treat the ones who agreed with the surgery. From the financial point of view, surgery is more effective than medical follow-up at a reasonable cost and can be preferred except in patients choosing medical follow-up (16).

Over the past decade, minimally invasive unilateral approaches have been developed. A unilateral approach may be used in patients with solitary adenomas that are preoperatively localized with use of imaging techniques. Bilateral neck exploration has been the traditional approach. However, due to the

fact that about 85 % of patients with pHPT have solitary adenomas, some surgeons recommend a unilateral or focused exploration (17) because minimally invasive surgery is cost-effective compared to the traditional approach (16).

Currently, it appears that excellent results can be obtained by either bilateral approach or selective use of focal or unilateral approach for patients with pHPT. The latter approaches require preoperative localization tests (18), they are less invasive, associated with fewer complications, and can be tolerated by most patients with pHPT (3).

Primary hyperparathyroidism during pregnancy is a pathological entity with unknown incidence. Fetal complications may include intrauterine growth retardation, low birth weight, preterm delivery, postpartum neonatal tetany, and permanent hypoparathyroidism (6). Both our pregnant patients were surgically treated, as it is generally accepted that surgery in the second and third trimesters constitutes a safe alternative to conservative treatment and is less risky than previously reported (19, 20). In the search of the literature published through/including January 2005 we identified and analyzed 16 cases of pHPT treated surgically after the 27th week of gestation. The postoperative incidence of clinically significant postsurgical complications was as low as 5.9 % in fetuses and 0 % in mothers (20). The review also suggests that postponing surgery may be hazardous as hyperparathyroidism should be considered a risk factor for preeclampsia.

Immediate postoperative management focuses on establishing the success of surgery and on monitoring the patient for complications such as persistent or recurrent hyperparathyroidism, postoperative hypoparathyroidism, recurrent laryngeal nerve paralysis (3), bleeding or laryngospasm (5). The serum calcium concentration typically reaches physiological values within 24 to 36 hours after surgery. As an adverse effect of parathyroidectomy, patients with large adenomas may develop “hungry bone syndrome”, which is associated with hypocalcemia, hypophosphatemia, and low urinary calcium excretion. Hypocalcemia after neck exploration for hyperparathyroidism is an important postoperative management issue. With increasing the acceptance of less invasive surgical approaches, hypocalcemia is less frequent (21). In study of Conn et al. (21) transient postoperative hypocalcemia occurred in 32 % after bilateral neck exploration and in 18 % after minimal invasive parathyroidectomy. In average, 21 % of patients after parathyroid surgery suffered from hypocalcemia. In concordance with literature data, in our study 12 patients (25 %) had clinical signs of hypocalcemia requiring pharmacological correction. When the whole of the hyperfunctioning tissue is not recognized and removed, persistent or recurrent pHPT will develop. Hypercalcemia after parathyroidectomy sustained in one patient in our group and required reexploration that always has a lower success rate and increases the risks of complications.

In conclusion, the management of primary hyperparathyroidism requires a multidisciplinary approach of endocrinologist, urologist/nephrologist, clinical biochemist, radiologist, anaesthesiologist, surgeon and pathologist. A causal solution of the primary hyperparathyroidism is the surgical removal of hormonally

active tissue aimed at normalizing the calcemia and minimizing the risk of postoperative complications. We advocate for the screening of serum calcium in order to detect and treat majority of patients already in their asymptomatic stage.

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Received November 6, 2007.

Accepted February 4, 2008.