Evaluation of the Consequences of Targeted or Focused Mini-Incision Parathyroidectomy in Patients With Primary Hyperparathyroidism

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Abstract- Surgical approaches to primary hyperparathyroidism (PHPT) have been associated with a change from invasive to non-invasive methods in the last 20 years. In this cross-sectional descriptive study, 55 patients with primary adenoma-induced HPT underwent surgery. The parathyroid gland in patients with primary hyperparathyroidism caused by parathyroid adenoma was removed by open surgery with an incision of about 2 cm in the neck in a targeted manner in a site localized by ultrasound or Sestamibi scan. The patients' personal information, including age, sex, length of hospital stay, serum calcium and parathyroid hormone (PTH) levels, success rate, and problems and unwanted adverse consequences of surgery (e.g. infection and bleeding) were recorded for each patient and collected information was analyzed in SPSS software. Most patients were women (80%) and individuals in the age range of 41-60 years (47.3%). The hospital stay length ranged from 2 to 5 days with an average of 3.25±0.9 days. Success was considered as a decrease in PTH and calcium levels during the first 24 h after the intervention, and success rates of 100, 98.2, and 69.1%, respectively, were evaluated for a reduction of at least 50% in PTH levels and less than 40 ng/ml of PTH levels. No major complications were reported in the studied patients. Wilcoxon test revealed significant decreases in patients' postoperative serum calcium and PTH levels (*P*=0.000). Mini-incision Parathyroidectomy with limited incision was associated with significant reductions in serum calcium and PTD without complications.

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Introduction

The parathyroid glands (PTGs) are located near the thyroid gland and are responsible for regulating blood calcium levels by the secretion of a parathyroid hormone (PTH). Blood calcium is normally maintained in the range of 8.5-10.2 mg/dl. There are often four PTGs posterior to the thyroid. Primary hyperparathyroidism (HPT) results from the spontaneous and uncontrolled secretion of PTH from one or more PTGs. As the main feature of this disease, hypercalcemia cannot inhibit the secretion of PTH from PTGs, unlike normal conditions. The abnormal source of PTH secretion can be an adenoma that emerged in one PTG or (with less prevalence) hyperplasia of all four PTGs. Parathyroid carcinoma can rarely cause hyperparathyroidism (1). PTH is a parathyroid hormone test to help diagnose the reasons for high or low calcium levels and parathyroid and non-parathyroid disease. It may also be used to control the effectiveness of treatment in a parathyroid patient. Examining PTH levels is recommended to monitor people with chronic hypocalcemia or those who have been under treatment or have a parathyroid tumor surgery (2).

Primary hyperparathyroidism (PHPT) is a relatively common disease with a prevalence of about 25%, caused by a parathyroid adenoma (PTA) in most cases (3,4). Clinical manifestations of this disease include renal calculi, bone diseases, gastric ulcers, and hypertension, as well as other non-specific symptoms such as asthenia and

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lethargy, nausea and anorexia, decreased muscle tone, cerebral symptoms, etc. This disease often occurs in the 5th and 6th decades of life (5,6). Nearly 85% of PHPT cases are associated with PTA (7).

As the leading cause of PHPT, PTA requires surgical treatment. Bilateral neck exploration (BNE) surgery, which is a routine method of parathyroidectomy (PTD), is gradually being replaced by minimally invasive parathyroidectomy (MIP), which is gaining acceptance among head and neck endocrine surgeons. Rapid evaluation of intraoperative parathyroid hormone (IOPTH) and the use of methods such as Sestamibi scan and ultrasound have resulted in targeted PTD through unilateral cervical exploration, referred to as targeted methods with limited incision or MIP. The PTG in PTA-induced PHPT patients is removed by open surgery with an incision of about 2 cm on the neck in a targeted manner at a site localized by ultrasound or Sestamibi scan, where the adenoma is localized preoperatively by making an incision of less than 2.5-3 cm (8). The advantages of MIP include a lower duration of surgery, less scarring, lower pain, and lower hypocalcemia rates, along with the economic benefits of MIP compared to the BNE method due to lower surgical costs and reduced length of hospital stay in the former (9).

PTD has evolved significantly over the past 25 years. In the past, the BNE was considered the standard treatment approach for abnormal gland resection (10). In targeted PTD with limited incision, localization is performed preoperatively by ultrasound or Sestamibi scan to determine an incision site of about 2 cm. The targeted method with the limited incision is not recommended in patients with suspected parathyroid cancer, in cases with the coexistence of parathyroid and thyroid disease, or cases of secondary hyperparathyroidism (11). The main advantage of this method is the lack of adhesion in the neck area and not interfering with possible future surgeries in the neck area due to thyroid problems, etc. A minor surgical wound in the neck and the greater satisfaction of patients is higher in this method, along with less pain and less duration of hospital stay. PTD is one of the main methods of PHPT treatment, and accurate diagnosis of the operation site and parathyroid tissue is necessary to improve this disease (12,13).

Based on the abovementioned issues, the issue's importance, and the absence of sufficient studies in this field, this study was designed and implemented to determine MIP's effectiveness and side effects in PHPT patients.

Materials and Methods

This cross-sectional descriptive study consisted of 55 patients with adenoma-induced PHPT who underwent surgery at Razi Hospital in Rasht during 2015-2020. These patients were sampled by the conventional method. PTGs in patients with adenoma-induced PHPT was removed by open surgery with an incision of about 2 cm in the neck in a targeted manner in a site localized by ultrasound or Sestamibi scan (Figure 1). A skin incision was made in the inner edge of the sternocleidomastoid muscle to open the subcutaneous layer (Figure 2). To find PTGs, the sternocleidomastoid muscle and the lateral Strap muscle were dissected on the carotid sheet, and the skin was sutured after PTD (Figure 3). The success rate of the surgery was also evaluated in three modes.

1. Decreased serum calcium and PTH levels within 24 h after PTD, which indicates success in the dissection of adenoma-containing PTGs.
2. A reduction of ≥ 50% in PTH levels compared to that obtained from therapeutic intervention.
3. PTH levels ≤ 40 ng/ml.

The patients' personal information, including age, sex, length of hospital stay, serum calcium and parathyroid hormone (PTH) levels, success rate, and problems and unwanted adverse consequences of surgery (e.g. infection and bleeding), was recorded for each patient and collected information was analyzed in SPSS software.

Ethical considerations

This study was conducted according to Guilan University of Medical Sciences principles and was approved by this university's ethics committee (IR.GUMS.REC.1399.280). The study's protocol, the type of intervention, and the benefits were carefully explained to the participants before obtaining informed consent forms. They were also assured about the confidentiality of their information, the right to exit the study upon their request, and no forced or continued participation in the study.

Figure 1. Preoperative localization of parathyroid adenoma with ultrasound

Figure 2. A skin incision and Parathyroid adenoma

Figure 3. Final image

Results

Findings obtained from Kolmogorov-Smirnov and Shapiro-Wilk tests of quantitative data distribution indicated that the distribution of data was not a normal distribution function for all quantitative variables, except age, in this study ($P<0.05$) (Table 1). Sex frequency, age distribution, and days of hospital stay in PHPT patients undergoing MIP are shown in Table 2. Accordingly, 44 (80%) and 11 (20%) of the subjects were women and men, respectively. Most patients (n=26, 47.3%) were in the age group of 41-60 years. The mean age and duration of hospitalization in PHPT patients undergoing MIP are shown in Table 3, indicating that the subjects aged 18-81 years with an average of 53.96±15.31 years. Most patients (n=35, 63.6%) experienced 2 and 3 days of hospitalization. The duration of hospitalization ranged from 2 to 5 days, with an average of 3.25±0.9 days. The frequencies of surgical success and complications in PHPT patients undergoing MIP are shown in Table 4. Success rates of 100%, 54 (98.2%), and 38 (69.1%) were assessed considering the success as decreased PTH and calcium levels during the first 24 h after the intervention, surgical success as a minimum reduction of 50% in PTH levels, and surgical success as a minimum reduction of <40 ng.ml in PTH levels. No significant complications were reported in the studied patients (Table 4). Pre- and postoperative mean serum calcium levels in PHPT patients undergoing MIP were 1.84±11.29 and 1.05±8.57 mg/L, respectively (Table 5). The Wilcoxon paired comparison test revealed significantly decreased mean serum calcium levels in the patients, ranging from 0.4 to 8.7, with an average of 2.72±1.55 mg/dL. Table 5 shows pre- and postoperative mean serum PTH levels in PHPT patients undergoing MIP were 628.8±534.26 and 33.75±37.58 ng/L, respectively. Wilcoxon test showed a significant decrease in postoperative PTH levels, which ranged from 14 to 3404 with a mean value of 496.68±616.52 ng/L (P=0.000). (Table 6) represents the mean changes in calcium and PTH levels before and after therapeutic intervention.

Table 1. Kolmogorov-smirnov and shapiro-wilk tests for quantitative data distribution

Variable	Kolmogorov-Smirnov[a]			Shapiro-Wilk		
	Statistic	df	Sig.	Statistic	df	Sig.
Pre-intervention Ca levels	.143	53	.009	.846	53	.000
Post-intervention Ca levels	.140	53	.011	.891	53	.000
Pre-intervention PTH levels	.241	53	.000	.691	53	.000
Post-intervention PTH levels	.150	53	.005	.798	53	.000
Changes in Ca levels	.186	53	.000	.878	53	.000
Changes in PTH levels	.257	53	.000	.674	53	.000
Length of hospital stay	.251	53	.000	.870	53	.000
Patients' age	.064	53	.200*	.974	53	.288

Table 2. Sex frequency, age distribution, and days of hospital stay in PHPT patients undergoing MIP

Variable		Frequency	%	Valid percent	Cumulative percent
Sex frequency	F	44	80.0	80.0	80.0
	M	11	20.0	20.0	100.0
	Total	55	100.0	100.0	
Age distribution	= < 40	10	18.2	18.2	18.2
	41-60	26	47.3	47.3	65.5
	60<	19	34.5	34.5	100.0
	Total	55	100.0	100.0	
Days of hospital stay	2	12	21.8	21.8	21.8
	3	23	41.8	41.8	63.6
	4	15	27.3	27.3	90.9
	5	5	9.1	9.1	100.0

Table 3. Mean age and duration of hospitalization in PHPT patients undergoing MIP

Descriptive Statistics					
Variable	**N**	**Min.**	**Max.**	**Mean**	**SD**
Age	55	18.00	81.00	53.9636	15.30670
Valid N (listwise)	55				
Duration of hospitalization	55	2.00	5.00	3.2364	.90192
Valid N (listwise)	55				

Table 4. Frequencies of surgical success and complications in PHPT patients undergoing MIP

Variable		Frequency	%	Valid percent	Cumulative percent
Success	**Decreased PTH and Ca levels**	55	100.0	100.0	100.0
	A minimum reduction of 50% in PTH levels	54	98.2	98.2	98.2
	PTH levels < 40 ng.ml	38	69.1	69.1	69.1
Complications	+	0	0	0	0
	-	55	100.0	100.0	100.0

Table 5. Comparison of pre-and postoperative mean serum calcium and PTH levels in PHPT patients undergoing MIP

Variable		Mean	N	SD	*P* (Wilcoxon)
Calcium (mg/dl)	**Before intervention**	11.2873	55	1.83808	0.000
	After intervention	8.5682	55	1.05257	
PTH (ng/l)	**Before intervention**	534.2564	55	628.81701	0.000
	After intervention	37.5791	55	33.75489	

Table 6. Mean changes in calcium and PTH levels before and after therapeutic intervention

Variable	N	Min.	Max.	Mean	SD
Changes in Ca levels	55	.40	8.70	2.7191	1.55154
Changes in PTH levels	55	14.00	3404.00	496.6773	616.52510

Discussion

In the present study, decreased levels of PTH and calcium, a minimum decrease of 50% in PTH levels, and PTH levels of <40 ng/ml were reported in 100, 98.2, and 69.1% of subjects, respectively. Assuming a 5% calculation error and using the following formula, decreased levels of PTH and calcium, a minimum decrease of 50% in PTH levels, and PTH levels of <40 ng/ml are represented.

Altogether, our findings indicate a high success rate of targeted PTD with limited or minimally invasive incisions, which is in line with those reported in most previous studies. At follow-ups of 6 to 12 months, normal PTH and calcium levels were recorded in 63.6% of subjects, and 37.5% of patients experienced a relative decrease in calcium and PTH levels (14). In a study by Urkan *et al*., normal postoperative calcium and PTH levels were reported in all but one patient (15).

Ekici *et al.*, claimed that MIP was a safe and successful approach to treating primary hyperthyroidism in patients over 65 years of age (16). In a study by Ha *et al*., a significant gland size and volume reduction were observed following targeted PTD during 6-12 months of follow-up. Normal PTH and calcium levels were found in 63.6% of subjects, and 37.5% of patients experienced a relative decrease in calcium and PTH levels (14). A success rate of 95.5-100% with an average of 96.9% was reported following MIP in a meta-analysis study by Ishii *et al*., with a mean follow-up period between 1 and 145 months (33 months on average) (17). In the present study, a satisfactory surgical success rate was also assessed during the first 24 h. Edna *et al*., analyzed the results of MIP in children with adenoma-induced PHPT and observed reduced PTH levels and 100% efficacy (18), which corresponds to the current study's findings.

Thanyawat *et al*., showed that MIP, with a success rate of 89.4% (surgical cases without general anesthesia), was more effective than other methods. The prevalence of complications was 1.45% in the MIP group (19). In our study, there were no reports of complications. In a review study, Amanda *et al*., presented evidence that MIP was associated with surgery duration, recovery time, and higher patient satisfaction, and recurrence rates were not different between the studied groups (20). Kurganov *et al*., reported a 6.1% incidence of complications following the use of MIP in treating HPT (21). An incidence of 0% was estimated in the current study and Gramática *et al*., (22).

In a review study, Laird *et al*., also found that MIP reduced surgery time, recovery time, duration of surgery, pain, and complication rates (20). The success rate of MIP estimated in our study is in agreement with those of 98.3% (25-35).

In agreement with most similar studies, MIP was associated with significant reductions in serum calcium and PTH levels without complications in the present study. Therefore, decreased levels of PTH and calcium, a minimum decrease of 50% in PTH levels, and PTH levels of <40 ng/ml demonstrate the high success rate of this therapeutic approach along with high safety (a complication incidence rate of 0%).

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