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Original Research

The Relationship of Magnesium Level with the Recovery of Parathyroid Function in Post-thyroidectomy Hypoparathyroidism

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Abstract

Objectives: Hypocalcemia is the most common complication and acute parathyroid gland insufficiency is the main cause of it after thyroidectomy. In this study, we aimed to evaluate the relationship between the recovery time of parathyroid gland function and patient characteristics, preoperative and postoperative electrolyte changes, and intraoperative parathyroid findings in patients with postoperative hypoparathyroidism.

Methods: Patients who underwent total thyroidectomy (TT) with or without central neck dissection ± lateral neck dissection with a parathyroid hormone (PTH) value of <15 pg/mL within the postoperative 4th hour were included in this study. Postoperative calcium level of <8mg/dL was defined as biochemical hypocalcemia and a PTH value of <15 pg/mL was defined as hypoparathyroidism. The patients were divided into three groups according to the time of PTH recovery (>15 pg/mL); within the first 24 hours, between one day and 30 days, after 30 days, respectively.

Results: One hundred eleven patients (mean age, 49.3±14.4 years) consisted of Groups 1, 2 and 3, including 19 (16F, 3M), 67 (54F, 13M) and 25 (19F, 6M), respectively. Vitamin D deficiency rates for Groups 1, 2, 3 were 41.7%, 53.1% and 88.2%, respectively (p=0.018). Postoperative day 0 PTH values were 11.69±2.79pg/mL, 6.92±3.45 pg/mL, 4.99±2.36 pg/mL, (p<0.001). Biochemical hypocalcemia rates of Groups 1, 2, 3 on postoperative day 1 were 15.8%, 53.7%, 64%, (p=0.004) respectively, and calcium values were 8.68±0.67 mg/dL, 8.15±0.66 mg/dL, 7.75±1 mg/dL, (p=0.014), respectively. Magnesium values on postoperative day 1 and 7 for Groups 1, 2, 3 were 1.85±0.1 mg/dL, 1.77±0.17 mg/dL, 1.64±0.17 mg/dL, (p=0.005), and 1.86±0.16mg/dL, 1.82±0.21mg/dL, 1.59±0.15mg/dL (p=0.001), respectively. PTH values on postoperative day 1 and 7 in Groups 1, 2, 3 were 20.5±6.4 pg/mL, 7.06±4.35 pg/mL, 4.66±3.26 pg/mL (p<0.001), and 31.04±10.54pg/mL, 18.72±13.84pg/mL, 4.55±4.9pg/mL (p<0.0001), respectively. Parathyroid function improved in 106 patients, and permanent hypoparathyroidism developed in five patients (4.5%).

Conclusion: Hypoparathyroidism can recover rapidly in the first 24 hours in patients with a PTH value of around 10 pg/mL at postoperative 4th hour. As the number of preserved parathyroids increased, recovery time decreased. In patients with postoperative hypoparathyroidism, postoperative low magnesium levels may be associated with delayed recovery of parathyroid function.

Keywords: Parathyroid hormone recovery time; magnesium; vitamin D.

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Thyroid surgery is the most common endocrine surgical intervention, and hypocalcemia is the most common complication of bilateral thyroidectomy.^[1] However, the actual incidence of hypocalcemia is controversial due to the heterogeneity of the studies. In a large meta-analysis, including 115 studies, the incidences of transient and permanent hypoparathyroidism were reported to be ranging from 19 to 38% and 0 to 3%, respectively.^[2]

Although the etiology of postoperative hypocalcemia is multifactorial, the most common cause is hypoparathyroidism due to direct injury or devascularization of parathyroid glands during thyroidectomy.^[2,3]

Especially in recent years, total thyroidectomy (TT) has been the first-line surgical treatment of patients with bilateral benign disease and thyroid cancer. It is noteworthy that hypoparathyroidism affects more patients with an increase in total thyroidectomy.^[4]

Most of the postoperative hypoparathyroidisms are temporary, and the number of studies evaluating the recovery time of parathyroid functions and related factors is limited.^[5-8]

In this study, we aimed to evaluate the relationship between the recovery time of parathyroid gland function and patient characteristics, preoperative and postoperative electrolyte changes, and intraoperative parathyroid findings in patients with postoperative hypoparathyroidism.

Methods

The data of patients who underwent thyroidectomy between 2012 and 2017 were retrospectively evaluated after obtaining approval from the local ethical committee. One hundred eleven patients (26.3%) out of 422 patients over the age of 18, who underwent total thyroidectomy with or without central ± lateral neck dissection by a single endocrine surgeon, with PTH value of <15 pg/mL in the first postoperative four hours (4-hour PTH) were included in this study. Patients with lobectomy (83 patients), completion thyroidectomy, simultaneous thyroid disease and hyperparathyroidism, re-do surgery for recurrence, and also patients without hospital file data and postoperative follow-up were excluded from this study.

Thyroidectomy Technique: The operations have been performed under general anesthesia with the routine use of intraoperative nerve monitoring (IONM) for the preservation of the recurrent laryngeal nerve (RLN), and external branch of the superior laryngeal nerve (EBSLN) and the technical details were given in other studies.^[9-11]

During the lateral and posterior dissection of the thyroid lobe, the tertiary branches of the inferior thyroid artery were divided on the thyroid capsule using the capsular

dissection technique with the help of magnifying loupes, and parathyroids were tried to be visualized in the surgical region, usually in its normal localization areas.^[12] If a parathyroid gland was not able to be seen in the surgical region, no additional attempt was made to find the gland in its orthotopic or non-orthotopic position.

If the parathyroid gland was not able to be preserved in situ with its vessels or was unintentionally removed, it was chopped into pieces of 1 mm³ and implanted into 2-3 pockets made in the sternocleidomastoid muscle on the same side and marked with prolene suture. Central neck dissection was performed in patients with papillary thyroid cancer if clinically indicated and preoperatively diagnosis of medullary thyroid cancer. Selective lateral neck dissection was also performed in patients with lateral metastases.

Preoperative thyroid function tests, calcium (Ca), phosphorus (P), magnesium (Mg), alkaline phosphatase (ALP), parathyroid hormone (PTH), 25 (OH) vitamin D3 level, postoperative 4th hour PTH level, postoperative 1st day Ca, P, Mg, PTH levels and postoperative 7th day Ca, P, Mg, PTH levels and parathyroid functions in control examinations of the patients and the time of normal parathyroid function after the cessation of the treatment were evaluated.

Postoperative hypoparathyroidism was defined as a PTH value of <15 pg/mL at the postoperative 4th hour.^[4] The patients were divided into three groups according to the time when the PTH value increased to >15 pg/mL. Group 1 included the patients with PTH values recovering in the first 24 hours; Group 2 included the patients with PTH values recovered between 1-30 days; and Group 3 included patients whose PTH values improved or did not improve after 30 days.

A PTH value below the normal range and/or still a requirement for calcium treatment at the 6th month was defined as "permanent hypoparathyroidism".^[14]

Hypocalcemia Treatment: In our clinic, patients with a PTH value of <10 pg/mL or experiencing symptomatic hypocalcemia were treated with calcitriol (0.25-1mcg × 2-3/day) and elemental calcium (1-2 g × 3/day), considering the severity of symptoms and calcium level. Patients with PTH values of 10-15 pg/mL received elemental calcium (1-2 g × 3/day). Patients with a calcium level of <7 mg/dL and/or severe hypocalcemia symptoms were given oral calcium and calcitriol treatment, as well as intravenous calcium (10 mL ampoule of 10% calcium gluconate) treatment. Intravenous calcium therapy was continued until albumin-adjusted total serum calcium level increased above 7.5 mg/dL and/or severe hypocalcemia symptoms regressed. Asymptomatic patients with calcium values above 7 mg/dl or patients with mild symptoms with a calcium value of 7.5 mg/dl were discharged.

Postoperative Follow-up: Patients with hypoparathyroidism were evaluated clinically and with laboratory values weekly in the first month, every 15 days between 1st and 3rd months, and once a month between 3rd and 6th months. If the PTH value was >15 pg/dl and asymptomatic patients experienced no symptoms with the discontinuance of the treatment, then the follow-up was terminated. In the postoperative hospital and post-discharge outpatient clinic controls, the patients were evaluated in detail for symptoms of mild and severe hypocalcemia, such as perioral numbness and numbness at extremities, tingling, muscle spasm, carpopedal spasm, Chvostek's sign, Trousseau's sign, tetany, seizure, bronchospasm, laryngospasm, confusion, disorientation, arrhythmia and heart failure.

Statistical Analysis

The data were evaluated using the IBM SPSS Statistics V22 program (IBM, Armonk, NY, USA). Data are presented as mean \pm standard deviation (SD) values. Pearson Chi-Square and Fisher exact tests were used for comparing categorically independent groups. In the comparison of continuous values in more than two groups, the Kruskal Wallis test and paired comparisons; The Mann-Whitney U test with Bonferroni correction was performed.

$P < 0.05$ values were considered statistically significant.

Results

One hundred eleven patients with a mean age of 49.3 ± 14.4 (ranging, 17-82) years consisted of Group 1, 2 and 3, includ-

ing 19, 67 and 25, respectively. No difference was found concerning age, gender distribution, preoperative hyperthyroidism, and post-operative malignant disease of the patients in the groups (Table 1). No significant difference was found concerning preoperative calcium, P, Mg, ALP, PTH, TSH levels of the patients in the groups (Table 2). 25-OH vitamin D3 level was measured in 61 patients preoperatively, and although it was lower in Group 3 compared to Groups 1 and 2, the difference was not significant (20.6 ± 14 ng/mL and 19.5 ± 17.1 ng/mL, 10.9 ± 7.2 ng/mL respectively) ($p = 0.078$) (Table 2). In addition, vitamin D deficiency rates were 41.7%, 53.1% and 88.2% in Groups 1, 2, 3, respectively, and the level was higher in Group 3 and the differences between groups were significant ($p = 0.018$) (Table 1).

Operative Results

The rates of central neck dissection with total thyroidectomy were 21.1%, 28.4%, and 44% in Groups 1,2,3, respectively; although the rate showed an increase, the difference between the groups was not significant. In 102 patients, the number of intraoperatively visualized parathyroid glands were evaluated, and the difference was almost significant ($p = 0.053$) (Table 1). In Groups 1, 2 and 3, the rates of visualization of >3 parathyroid glands were 94.5%, 74.2%, 59.1%, respectively, and as the recovery time of parathyroid function increased, the rate of visualization of above three parathyroid glands decreased. There was no difference between the groups concerning parathyroid autotransplantation and the presence of parathyroid in the specimen (Table 1).

Table 1. General characteristics of the groups

	Group 1 (n=19)	Group 2 (n=67)	Group 3 (n=25)	p
Age (Mean \pm SD)	49.1 \pm 17.8	49.4 \pm 12.9	49.3 \pm 16	0.921
Gender (F/M), n (%)	16 (84.2)/3 (15.8)	54 (80.6)/13 (19.4)	19 (76)/6 (24)	0.788
Hyperthyroidism, n (%)	2 (10.5)	11 (16.4)	5 (20)	0.698
TT+ Central dissection, n (%)	4 (21.1)	19 (28.4)	11 (44)	0.214
Number of visualized PTs				0.053
	No visualized n: 2	0	2	0
	1 (6)	0	2	4
	2 (18)	1	12	5
	3 (30)	7	15	8
	4 (46)	10	31	5
Parathyroid autotransplantation, n (%)	3 (15.8)	13 (19.4)	7 (28)	0.592
Parathyroid presence in the specimen, n (%)	7 (36.8)	17 (26.6)	11 (47.8)	0.393
Postop Diagnosis [benign/malignant], n (%)	10 (52.6)/9 (47.4)	33 (49.3)/34 (70.7)	8 (32)/17 (68)	0.273
D vit deficiency, n (%)	5/12 (41.7)	17/32 (53.1)	15/17 (88.2)	0.018
PTH (0 day) pg/mL (Mean \pm SD) (min-max)	11.7 \pm 2.78 (6.6-14)	6.9 \pm 3.45 (1-14.9)	5 \pm 2.36 (1.2-10.69)	<0.0001
PTH recovery time (day) (Mean \pm SD) (min-max)	1 (1-1)	12 \pm 7.5 (2-30)	58.6 \pm 25 (20-130)	<0.0001
Persistent hypoparathyroidism, n (%)	0	0	5 (20)	<0.0001

Table 2. Preoperative biochemical values

	Group 1 (n=19)	Group 2 (n=67)	Group 3 (n=25)	p
TSH (uU/mL) (mean±SD) (min-max)	1.71±1.35 (0.2-6.69)	2.05±2.13 (0.1-9.26)	2.67±3.06 (0.35-13.38)	0.589
Ca (mg/dL) (mean±SD) (min-max)	9.5±0.41 (8.9-10.2)	9.3±0.44 (8.7-10)	9.4±0.48 (8-10.2)	0.5
P (mg/dL) (mean±SD) (min-max)	3.6±0.61 (2.6-5.3)	3.9±2.01 (2.2-5.2)	3.6±0.68 (2.6-5.5)	0.967
Mg (mg/dL) (mean±SD) (min-max)	1.95±0.14 (1.7-2.2)	2.28±2.11 (1.43-2.3)	1.9±1.76 (1.6-2.2)	0.66
ALP U/L (mean±SD) (min-max)	83.4±32.6 (40-169)	77±30.5 (32-173)	68.3±18 (42-105)	0.141
PTH (pg/mL) (mean±SD) (min-max)	48.9±16.3 (25.6-83.1)	47.1±23.6 (21.4-102.2)	62.9±33.5 (26-127)	0.142
D vit (ng/mL) (mean±SD) (min-max)	20.6±14 (3-46)	19.5±17.1 (3-95)	10.9±7.2 (3-95)	0.078

Permanent hypoparathyroidism rate was 1.2% in 422 patients and 4.5% in 111 patients with post-thyroidectomy hypoparathyroidism (Table 1). In patients with transient hypoparathyroidism, PTH recovery time was 18.81±23.17 days. PTH recovery time was found significantly different between the groups (Table 1).

Postoperative Calcium Values

In Groups 1, 2, 3, postoperative 1st day Ca values were 8.7±0.67 mg/dL, 8.3±0.66 mg/dL and 7.7±1 mg/dL, respectively, and the difference between the groups was significant (p=0.014) (Table 3). On the postoperative 1st day, the biochemical hypocalcemia rates of Groups 1, 2, 3 were 15.8%, 53.7%, 64%, respectively, and there was a significant difference between the groups (p=0.004) (Table 1). No difference was found between the groups concerning postoperative 7th day Ca values (Table 4).

Postoperative Parathyroid Hormone Values

PTH values on postoperative day 0 in Groups 1, 2, 3 were 11.69±2.79 pg/mL, 6.92±3.45 pg/mL, 4.99±2.36 pg/mL, respectively, and the difference was significant (p<0.001)

(Table 1). It was significantly lower in the second group (p<0.001) and the third group (p<0.001) compared to the first group. The difference between the Groups 2 and 3 was not significant. PTH values on postoperative day 1 in Groups 1, 2, 3 were 20.5±6.4 pg/mL, 7.06±4.35 pg/mL, 4.66±3.26 pg/mL, respectively, and the difference was significant (p<0.001) (Table 3). In pairwise comparison, it was significantly lower in Group 2 and 3 than in Group 1 (p=0.0001, p=0.0001). Postoperative 7th day PTH values were 31.04±10.54 pg/mL, 18.72±13.84 pg/mL, 4.55±4.9 pg/mL in Groups 1, 2, 3, respectively, and the difference was significant (p<0.0001) (Table 4).

Postoperative Phosphorus Values

There was no difference between postoperative day 1 P levels (Table 3). P-values of postoperative day 7 were 3.71±0.75 pg/mL, 3.88±0.76 pg/mL, 4.76±0.69 pg/mL in Groups 1, 2, 3, respectively and the difference was significant (p=0.002).

Postoperative Magnesium Values

Magnesium values on postoperative day 1 in Groups 1, 2, 3

Table 3. Biochemical values on postoperative 1st day

	Group 1 (n=19)	Group 2 (n=67)	Group 3 (n=25)	p
Ca (mg/dL) (mean±SD) (min-max)	8.7±0.67 (7.29-9.83)	8.3±0.66 (6.55-9.54)	7.7±1 (4.9-9.83)	0.014
P (mg/dL) (mean±SD) (min-max)	3.8±0.76 (2.4-5.5)	4±0.82 (2.5-5.5)	4±0.78 (2.3-5)	0.422
Mg (mg/dL) (mean±SD) (min-max)	1.85±1 (1.67-2.04)	1.76±0.17 (1.44-2.15)	1.64±0.17 (1.41-1.95)	0.005
PTH (pg/mL) (mean±SD) (min-max)	20.5±6.4 (15.2-35.67)	7.06±4.35 (1-14.32)	4.66±3.26 (1.2-10.92)	<0.0001

Table 4. Biochemical values on postoperative 7th day

	Group 1 (n=19)	Group 2 (n=67)	Group 3 (n=25)	p
Ca (mg/dL) (mean±SD) (min-max)	9.3±0.6 (8.1-10.17)	8.66±0.9 (6.42-10.39)	8.65±1.1 (7.24-10.5)	0.064
P (mg/dL) (mean±SD) (min-max)	3.71±0.75 (2.84-4.9)	3.88±0.76 (2.6-5.72)	4.76±0.69 (3.7-5.9)	0.002
Mg (mg/dL) (mean±SD) (min-max)	1.86±0.16 (1.49-2.19)	1.82±0.21 (1.22-2.17)	1.59±0.15 (1.39-1.87)	0.001
PTH (pg/mL) (mean±SD) (min-max)	31.04±10.54 (17.36-56.17)	18.72±13.84 (1.95-55.2)	4.55±4.98 (1-12.2)	<0.0001
D vit (ng/mL) (mean±SD) (min-max)	35.8±37.8 (6.6-102)	19.26±11.7 (3.17-59.18)	25.69±8.17 (13.3-40.73)	0.157

were 1.85±0.1 mg/dL, 1.77±0.17 mg/dL, 1.64±0.17 mg/dL, respectively, and the difference was statistically significant ($p=0.005$) (Table 3). Magnesium values on postoperative day 7 in Groups 1, 2, 3 were 1.86±0.16 mg/dL, 1.82±0.21 mg/dL, 1.59±0.15 mg/dL, respectively, and the difference was statistically significant ($p=0.001$) (Table 3).

Discussion

Postoperative hypoparathyroidism developing after thyroidectomy is the most common etiological cause of hypoparathyroidism.^[14] Impaired PTH secretion leads to hypocalcemia developing as a result of inhibition of bone resorption and reduced intestinal absorption of calcium due to reduced synthesis of 1,25-dihydroxy vitamin D in the kidney.^[15]

Although devascularization or inadvertent resection of the parathyroid glands in thyroidectomy is considered the main cause of postoperative hypoparathyroidism, some clinical and biochemical factors may also be associated with postoperative hypocalcemia. In this study, we found a relationship between vitamin D deficiency and postoperative Mg and P levels and recovery time of hypoparathyroidism.^[2]

In our study, although the vitamin D level was not statistically different between the groups, it was at the level of half of the other two groups (10.9±7.2 ng/mL) in the patient group who recovered after a month, and vitamin D deficiency was significantly higher in the long-healing group (88.2%) than the other two groups (41.7%, 53.1%) ($p=0.018$). Until today, it has been revealed in some studies that low vitamin D level is associated with postoperative hypocalcemia.^[16, 17]

Al-Khatip et al. identified severe preoperative vitamin D deficiency (<25 nmol/L) as an independent factor in predicting postoperative biochemical hypocalcemia.^[18]

Donan et al. reported vitamin D deficiency as a predictor

of postoperative hypocalcemia in patients with intraoperatively identified three or more parathyroid glands.^[19] However, in other studies, no relationship was found between vitamin D deficiency and postoperative hypocalcemia.^[20-22] In humans, only the negative feedback inhibition of elevated vitamin D levels on PTH has been demonstrated but not any other effects on parathyroid cells.^[23]

This is the only study revealing the relationship between vitamin D deficiency and the recovery of parathyroid function, but further studies are needed related to this effect.

Magnesium has a complicated role in controlling secretion and action of PTH secretion. Normal Mg level is required for normal PTH secretion. Magnesium stimulates calcium-sensitive receptors (CaSR) on parathyroid cells; in case of hypermagnesemia, PTH synthesis and secretion is decreased. Mild hypomagnesemia stimulates the secretion of PTH. However, with a paradoxical effect, severe hypomagnesemia reduces PTH secretion. This paradoxical block is believed to reduce PTH secretion due to the effect of decreased intracellular magnesium on the CaSR-associated G protein subunit. In addition, hypomagnesemia leads to target tissue resistance to the effects of PTH due to a decrease in PTH receptor sensitivity, especially in the renal tubules and bones.^[14] In addition, Mg competes with Ca at the transporter level in the renal tubules and regulates Ca excretion. PTH stimulates Mg reabsorption from the kidney and small intestines, and provides Mg release from bones.^[24]

In our study, magnesium values on postoperative day 1 in Groups 1, 2, 3 were 1.85±0.1 mg/dL, 1.77±0.17 mg/dL, 1.64±0.17 mg/dL, respectively ($p=0.005$) (Table 3), and 1.86±0.16 mg/dL, 1.82±0.21 mg/dL, 1.59±0.15 mg/dL on day 7, respectively ($p=0.001$), and the differences were statistically significant. In addition, Mg value was lower in all three groups compared to preoperative values, and this decrease was more significant in Group 3. We think that

this decrease in Mg is related to the effect of both PTH decrease and hypocalcemia. The low levels of Mg on both postoperative day 1 and day 7 in Group 3 suggest that the parathyroid function recovery time was longer in the group with low Mg levels. Although the relationship between PTH recovery time and Mg has not been evaluated, some studies have demonstrated the relationship between hypoparathyroidism and hypomagnesemia. They found that post-thyroidectomy hypomagnesemia was significantly associated with both early hypocalcemia and permanent hypoparathyroidism.^[25-27]

We think that the high phosphorus level on postoperative day 7, especially in Group 3 is associated with phosphorus retention due to low PTH levels. Calcium has an inverse relationship to phosphorus and PTH controls the small intestine and renal absorption of phosphorus. PTH directly affects the proximal tubules in the kidney, leading to a decrease in phosphorus reabsorption and increase in phosphaturia.

Most of the hypoparathyroidisms developing after thyroidectomy are temporary. Studies related to the recovery time of parathyroid function have generally limited number of cases. The recovery time of a parathyroid function is important regarding the patient's follow-up intervals and the duration of postoperative hypocalcemia treatment.

Since the half-life of PTH is less than five minutes, it has been shown in previous studies that serum PTH measurement in the early postoperative period is a sensitive and specific method for determining the risk of hypocalcemia. Barczyński et al. reported that the measuring PTH serum level at four hours postoperatively is the most appropriate time to predict hypocalcemia postoperative 24 hours after total thyroidectomy.^[28] While forming the groups for postoperative hypoparathyroidism, we preferred the 4-hour PTH measurement.

According to our results, parathyroid function improved within the first six months in 95.5% of patients with hypoparathyroidism after thyroidectomy, and 4.5% resulted in permanent hypoparathyroidism. Parathyroid function recovered in 17.1% of hypoparathyroidisms within the first 24 hours, 60.4% within 1-30 days, and 18% within 1-6 months. The rates of intraoperative visualization of three and four parathyroid glands was 94.5%, 74.2%, 59.1% in the Group 1,2,3, respectively, and as the rate of visualized parathyroids decreased, the recovery time of parathyroid function was prolonged ($p=0.053$). Postoperative 4-hour PTH level was significantly higher in Group 1 compared to the other 2 groups (11.7 ± 2.78 pg/mL, 6.9 ± 3.45 pg/mL, 5 ± 2.36 pg/mL, respectively; $p<0.0001$). PTH values in Groups 1,2,3 on postoperative day 1 (20.5 ± 6.4 pg/mL, 7.06 ± 4.35 pg/mL,

4.66 ± 3.26 pg/mL, respectively; $p<0.001$) and on postoperative day 7 (respectively; 31.04 ± 10.54 pg/mL, 18.72 ± 13.84 pg/mL, 4.55 ± 4.9 pg/mL, respectively; $p<0.0001$) were significantly different. According to our results, we think that hypoparathyroidism can recover in the early period, especially in patients with PTH values around 10 pg/mL on day 0. In addition, PTH values, which tend to increase in the 1st week compared to day 1, suggest that PTH function may recover within the 1st month, and hypoparathyroidism may last longer than a month in patients with PTH values similar to day 1.

Youngwirth et al. defined PTH insufficiency as the PTH value of <10 pg/mL (normal range: 10-72 pg/mL) at the postoperative 4th hour and on the postoperative 1st day, in 33 (12%) of 271 patients who underwent total thyroidectomy. They found that PTH level improved in 24 (73% of 33 patients in a week, and parathyroid function returned to normal in 27 (82%) patients.^[7]

Al-Dhahri et al. defined hypoparathyroidism as PTH level of <15.5 pg/mL (or <1.7 pmol/L) measured within the first hour after surgery. The researchers found that 62.3% of hypoparathyroidisms improved in 1 month, 18.9% in 1-6 months, 13.2% did not recover in 6 months, and 5.6% disappeared during follow-up. The researchers reported that the baseline PTH value and the rate of decrease in postoperative PTH may be related to the severity of hypoparathyroidism. They found that patients with preoperative PTH values of <5 pmol/L should wait 3.2 times longer for the median recovery time of hypoparathyroidism, than those with >5 pmol/L. In addition, they found that a median value of 5.7 times longer recovery time should be waited for the recovery of hypoparathyroidism in cases of $>88\%$ decrease in postoperative PTH according to preoperative value, compared to $<88\%$ PTH decrease. In addition, they found that the recovery time of hypothyroidism was 2.7 times higher in diabetic patients than in non-diabetic patients.^[6]

Sormaz et al. showed in their study that although PTH decline significantly correlated with symptomatic hypocalcemia, a considerable number of patients might experience hypocalcemic symptoms in spite of normal postoperative PTH levels. They suggested that analysis of serum Ca concentrations at 24 hours postoperatively might help to achieve a more precise prediction of patients who bear a high risk for developing hypocalcemic symptoms.^[29]

Sitges-Serra et al. reported in a multicentric prospective study that in 91 (63%) of 145 patients with parathyroid failure (PTH <15 pg/mL at postoperative 4th hour and Ca <8 mg/dL at 24th hour), hypocalcemia improved in 1 month, and they observed protracted hypoparathyroidism in 54

(37%) patients. They stated that 32 (22%) of these patients recovered in a year, 22 (15%) developed permanent hypoparathyroidism within 1-year follow-up. They found that protracted hypoparathyroidism was associated with a lower number of preserved parathyroids in situ. This is consistent with our finding that as the recovery time increased, the rate of 3-4 parathyroid glands seen and preserved intraoperatively decreased. They found a positive correlation between serum Ca level in the postoperative 1st month and the rate of recovery from hypoparathyroidism in patients with protracted hypoparathyroidism. In addition, they found higher PTH concentrations in patients who recovered at 1 month. They reported that high normal Ca level and low but detectable PTH level in the postoperative 1st month was associated with a better outcome in patients with protracted hypoparathyroidism. The combination of these two variables could predict the improvement of parathyroid function with a rate of 90%.^[4]

Ritter et al. detected postoperative hypoparathyroidism with a rate of 18% according to the PTH value (<10 pg/mL) measured in the first 24 hours in 1054 patients who underwent total thyroidectomy. 70% of these hypoparathyroidisms improved in two months, 15% in 2-6 months and 5% in 6-12 months. However, half of 20 patients (11%) who were accepted as permanent hypoparathyroidism in a year were defined as permanent hypoparathyroidism by the researchers, since supplementary treatment was required although PTH level was >10pg/mL.^[5]

Villarroya-Marquina et al. found protracted hypoparathyroidism in 142 of 854 patients who underwent total thyroidectomy. Thirty-six of them (25%) developed permanent hypoparathyroidism, and 106 of them (75%) had hypoparathyroidism improved during follow-up. Of the 106 patients who recovered, 73 (69%) recovered in 1-6 months, 21 (20%) after 6-12 months, and 12 (11%) after a year. The number of parathyroids preserved in situ intraoperatively and serum calcium level >2.25 nmol/L in a month postoperatively were determined as factors associated with recovery of parathyroid function. They reported that there is a possibility of recovery of parathyroid function after a year, especially in patients with four preserved parathyroids and a serum calcium value of >2.25 nmol/L in the 1st month.^[8]

Kim et al. reported that the PTH value in five of 22 patients with permanent hypoparathyroidism after thyroidectomy returned to normal in 27.6 months after the first year and supportive treatment was discontinued.^[30]

Today, the diagnosis of permanent hypoparathyroidism is still controversial. Some guidelines take six months limit for permanent hypoparathyroidism, while others accept 1-year limit.^[14,31]

For the recovery time of parathyroid function, PTH is generally evaluated within the first four hours, and in some studies, within the first 24 hours. There is no study similar to our study comparing the PTH on day 0 and day 1. In our study, postoperative PTH returned to normal in 19 (17.1%) patients with hypoparathyroidism according to the PTH value at the 4th hour. In addition, biochemical hypocalcemia on postoperative day 1 was present in only 15.8% of the patients in this group. In the literature, hypoparathyroidism is defined as transient hypoparathyroidism when PTH improves within a month, as protracted hypoparathyroidism when it recovers within a month to a year, and as permanent hypoparathyroidism if it does not recover in a year.^[6,8]

We suggest that hypoparathyroidism that recovers on this 1st day can be defined separately as early improving hypoparathyroidism. True hypoparathyroidism incidence can be predicted more accurately with PTH value on day 0. Generally, thyroidectomy patients are discharged on postoperative day 1. Instead of measuring PTH early on day 0, the PTH value measured on the first day may be more appropriate in the selection of patients to be treated with selective Ca replacement therapy while discharging them. With PTH measured on the 1st day, we can eliminate unnecessary Ca and/or calcitriol treatment while discharging patients with hypoparathyroidism, who constitute about 20% of hypoparathyroidism and recover early.

The main limitations of our study are that it is retrospective, and there is no preoperative vitamin D measurement available in all patients, and electrolyte values were not compared after the first week.

Conclusion

Hypoparathyroidisms after thyroidectomy are usually transient. Approximately 80% of them improve within 1 month. Hypoparathyroidism may improve rapidly in the first 24 hours in patients with a PTH value around 10 pg/mL at the postoperative 4th hour. PTH values, which tend to increase in the 1st week compared to day 1, suggest that PTH function may recover within the 1st month, and hypoparathyroidism may last longer than a month in patients with PTH values similar to day 1.

D vit deficiency rate is higher in patients with hypoparathyroidism, leading to a recovery in a longer period. As the rate of patients with three or four parathyroid glands visualized and preserved increases, recovery time decreases. Patients with hypoparathyroidism recovering late have lower Mg levels on day 1 and day 7, and postoperative low Mg levels may be associated with delayed recovery of parathyroid function.

Disclosures

Ethics Committee Approval: The study was approved by the Local Ethics Committee (date: 08.09.2020, number: 2982).

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Conflict of Interest: None declared.

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