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Real-life data of patients with hypoparathyroidism: a case-control study

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ABSTRACT

Objective: This study aims to investigate real-life data of patients with hypoparathyroidism.

Material and Method: This retrospective case-control study was carried out in a tertiary endocrine center between 1 January 2010 and 31 December 2019. Patients with a confirmed diagnosis of persistent hypoparathyroidism and healthy controls were included. Demographic characteristics of the patients, laboratory findings, etiologies of hypoparathyroidism, treatments they received, reasons for hospitalization, and complications were investigated.

Results: Sixty-five patients (mean age 42.80±13.4 years, 91% female) with hypoparathyroidism, and 54 healthy controls (mean age 33.58±11.9 years, 65% female) were included. Mean calcium level 7.95±0.92 mg/dl, and mean PTH level 9.99±6.30 pg/ml in hypoparathyroidism. Regarding the etiology of HypoPT, 51 (78%) patients had hypoPT due to surgery; 14 (22%) patients developed HypoPT due to non-surgical causes. In patients with hypoPT who underwent surgery, the mean calcium value was 8.03±0.93 mg/dl; the mean calcium value in patients with non-surgical HypoPT was 7.67±0.85 mg/dl. The mean PTH levels in non-surgical group, other group 10.16±6.21 pg/ml and 9.36±6.82 pg/ml, respectively. The most common surgery was due to multinodular goiter (72%). In 46 percent, the most common treatment was calcitriol 0.5 mcg/day and calcium 2000 mg/day. Nearly half of the patients had treatment non-compliance (46%). Eighteen percent of patients had kidney stones. Forty-three percent of the patients had been hospitalized in the last year. The most common reason for the hospitalization of patients with hypoparathyroidism was hypocalcemia, and the most common reason for this was treatment non-compliance.

Conclusion: In our study, the most common cause of hypoparathyroidism is surgery due to multinodular goiter. The most common reason for hospitalization is treatment non-compliance. Up to one-fifth of patients had kidney stones.

Keywords: Hypoparathyroidism, real-life data, hypocalcemia

INTRODUCTION

Hypoparathyroidism (HypoPT) is a rare disease characterized by low/normal parathyroid hormone (PTH) concentration despite low calcium and increased phosphorus levels (1). The most common cause of hypoPT is unintentional removal or damage to the parathyroid glands during head/neck surgery. Non-surgical hypoPT accounts for 25 percent of all patients. Although the etiology in these patients is autoimmune, infiltrative diseases, and genetic causes, most patients are idiopathic hypoPT (2-4).

Classical laboratory findings hypoPT are hypocalcemia, hyperphosphatemia, low PTH, and hypercalciuria. Symptoms of hypoPT result from neuromuscular irritability caused by hypocalcemia and include tingling, muscle cramps, and seizures. Hypocalcemia has life-threatening acute complications such as laryngospasm, seizures and cardiac arrhythmias. It has chronic complications such as cerebral calcification and kidney stones (5-7).

Conventional treatment includes orally active vitamin D and calcium. However, this treatment cannot fully fulfill the role of PTH and causes first short-term problems (such as hypocalcemia, hypercalcemia, and increased urinary calcium excretion) and then long-term complications (nephrocalcinosis, kidney stones, brain calcifications, cataracts, etc.). HypoPT is a rare endocrine disease for which replacement therapy of deficient parathyroid hormone is not the standard treatment option (8). Patients are at risk of many complications such

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as kidney failure, psychiatric diseases, and infections. In addition, patients often have neurocognitive complaints. Symptoms such as inability to focus and concentration problems are observed (9).

This study aims to investigate real-life data of patients with hypoparathyroidism.

MATERIAL AND METHOD

Approval for the study was granted by the Non-Interventional Studies Ethics Committee of Dicle University Medical Faculty (Date: 14.11.2019, Decision No: 245). All procedures were carried out in accordance with the ethical rules and the principles of the Declaration of Helsinki.

This retrospective case-control study was conducted between 1 January 2010 and 31 December 2019 by examining the records of the hypoparathyroidism database of Dicle University Faculty of Medicine, Department of Endocrinology, which is a tertiary endocrine center.

The physician confirmed the diagnosis of permanent hypoparathyroidism was confirmed that calcium and active vitamin D treatment continued to keep serum calcium in the normal range in the sixth post-operative month, and PTH level was below average at least once.

In our study, the demographic data of the patients (age, gender), laboratory parameters at the time of admission (Ca, albumin, P, Mg, ALT, Cr, PTH, 25-OH Vit D, calcium in 24-hour urine, hemogram) were examined by the information in the hospital records. The device used for PTH measurement is Siemens Advia Centaur XP; the method used is an immunoassay, reference values are 15-65 pg/ml.

Patients with post-operative hypoPT, autoimmune hypoPT, and idiopathic hypoPT were included in the study. The patients were selected from patients aged >18 <80 years, and patients with diseases other than hypoPT complications (such as hypertension, vascular diseases) were not included in the study. The control group included people aged 15-79 years, with normal PTH levels and 25-OH Vit D >20 ug/L without any other disease.

The patients complications of hypoPT (nephrolithiasis, cataract, basal ganglia calcification) were analyzed from hospital records.

Statistical analyzes of the results obtained in the study were performed using SPSS (Statistical Package for the Social Sciences) 22 statistical software packages. Descriptive statistics for continuous variables from the parameters in the study will be expressed as mean ± standard deviation, minimum and maximum values, and categorical variables will be expressed as numbers and percentages. Student's t-test data of patient group and control group; Chi-square test will be used to analyze categorical variables. The statistical significance limit will be accepted as $p<0.05$.

RESULTS

Sixty-five patients (mean age 42.80±13.4 years, 91% female) with hypoPT, and 54 healthy controls (mean age 33.58±11.9 years, 65% female) were included. Mean calcium level 7.95±0.92 mg/dl, and mean PTH level 9.99±6.30 pg/ml in hypoPT patients. Regarding the etiology of hypoPT, 51(78%) patients had hypoPT due to surgery; 14 (22%) patients developed hypoPT due to non-surgical causes. In patients with hypoPT who underwent surgery, the mean calcium level was 8.03±0.93 mg/dl; The mean calcium level in patients with non-surgical hypoPT was 7.67±0.85 mg/dl. While the mean PTH level was 10.16±6.21 pg/ml in patients with hypoPT who underwent surgery, in non-surgical patients with hypoPT, the mean was 9.36±6.82 pg/ml. The most common surgery was due to multinodular goiter (72%). Twelve percent of the patients had thyroid cancer surgery. In 46 percent, the most common treatment was calcitriol 0.5 mcg/day and calcium 2000 mg/day. Nearly half of the patients had treatment non-compliance (46%). A cataract is present in two patients. Three patients had basal ganglia calcification. Twelve patients had kidney stones. Forty-three percent of the patients had been hospitalized in the last year. The most common reason for hospitalization was symptomatic hypocalcemia. The most common reason for this was treatment non-compliance. The most frequent follow-up frequency of the patients was three months (**Table 1**). The data of patients with hypoPT and the control group are compared in **Table 2**.

Table 1. Characteristics of patients with hypoparathyroidism

n	65
Female	90.7%
Age(year)	42.80±13.37
Ca (mg/dl)	7.95±0.92
PTH (pg/ml)	9.99±6.30
Surgical/non-surgical (n)	51/14
Most common surgery	Multinodulary goitre (72%)
Malignancy	12.3%
Graves disease	4.6%
Nephrolithiasis	18.4%
Reason for hospital readmission	Treatment non-compliance (46%)

Table 2. Comparison of hypoparathyroidism group and control group

	Hypoparathyroidism	Control	p value
n	65	54	NS
Gender (F/M)	56/9	35/16	<0.05
Age (year)	42.80±13.37	33.58±11.9	<0.05
Ca (mg/dl)	7.95±0.92	9.39±0.35	<0.05
PTH (pg/ml)	9.99±6.30	46.76±11.01	<0.05
25 OH D-vit (ug/L)	23.35±9.14	>20	NS
P (mg/dl)	4.45±0.94	3.56±0.36	<0.05
Mg (mg/dl)	1.72±0.17	1.83±0.15	NS

DISCUSSION

HypoPT; is a chronic disease characterized by hypocalcemia, hyperphosphatemia. The parathyroid hormone is low or normal. Surgery is the most common cause of acquired hypoPT, accounting for 75% of all cases. Non-surgical causes of hypoPT include autoimmune, genetic diseases, infiltrative, metastatic, radiation, mineral deposition, magnesium deficiency or excess, or idiopathic causes (1-3).

In our study, the most common cause of hypoPT was surgical, with 78%. The type of surgery with the highest risk of hypoPT is head and neck surgery. Performing thyroid surgery in centers of excellence reduces the risk of surgery related hypoPT (10). Another reason that increases the risk of hypoPT is secondary/completion surgeries. Completion surgery has been found to increase the risk of hypoPT in patients who have undergone hemithyroidectomy. Failure to localize the parathyroid glands by the surgeon in initial surgery and complementary surgery is a risk for permanent hypoPT (11). In our study, the most common cause of hypoPT (72%) was total thyroidectomy due to multinodular goiter. Anterior neck surgery is the most common cause of acquired hypoPT and is responsible for almost three-quarters of cases (1)

In the literature, the age of occurrence of hypoPT is generally in the fourth decade (1). In our study, the mean age of patients with hypoPT was 42 years. The reason why hypoPT is seen at these ages seems to be related to the increased frequency of surgeries about multinodular goiter at this age (12).

HypoPT is a disease primarily seen in women, and this may be related to the increased frequency of surgery for thyroid nodules in women. In our study, 90,7% of the patients were female, and 9,3% were male. In the literature, at least 75% of the patients are women, just as in our study. Apart from the multinodular goiter etiology of hypoPT, the frequent occurrence of autoimmune diseases in women may explain this rate (13).

In our study, 0.5-1 mcg/day calcitriol and 1-3 g calcium/day were used to achieve target calcium and phosphorus levels in most of our patients with hypoPT. Our literature review suggests that the oral calcium dose for adults with stable chronic hypoPT in the guidelines is 1 to 2 g of elemental calcium daily, in divided doses. The starting dose of calcitriol is 0.25 mcg twice daily with weekly dose increments to achieve low normal serum calcium. Most adults need up to 2 mcg per day. Vitamin D requirements vary significantly from patient to patient, and the correct dose in any given patient can be determined in the patient's biochemical follow-up (14).

In our study in patients with hypoPT, the most common complications were found to be renal and neurological complications. In the study of Underbjerg L. et al. (15) in Denmark, the risk of all types of renal disease was found to be significantly higher in both surgical hypoPT patients and non-surgical hypoPT patients compared to the general population. Patients with post-surgical hypoPT have a 4-fold increased risk of hospitalization for kidney stone disease.

Basal ganglia calcification in patients with hypoPT is related to the deterioration of calcium/phosphorus balance and is mostly associated with phosphorus elevation. According to the study of Shoback DM et al. (6), the primary biochemical abnormalities of hypoPT are hypocalcemia and hyperphosphatemia. While hypocalcemia causes most neuromuscular symptoms and signs of hypoPT, hyperphosphatemia contributes significantly to ectopic mineralization in soft tissues (vascular system, brain, kidneys, and other organs). The basal ganglia calcification rate of the patients in our study was 4.6%; the Intrarenal calcification rate was determined as 18%. In the study of Mitchell et al. 31% of the patients had intrarenal calcification, and 52% of them had basal ganglia calcification (16). The form of calcification may be more extensive involvement in the brain in some patients, mainly in the basal ganglia.

In our study, the most common hospitalization reason was due to hypocalcemia. In the study conducted by Underbjerg L et al. (17) in Denmark, hospitalizations due to seizures and symptomatic hypocalcemia increased ten times, and hospitalizations due to kidney stones and kidney damage increased six times.

Our study has some limitations; retrospective study design, the number of patients is small, complications related to hypoPT have not been investigated in detail in all patients and include only data from a tertiary endocrine center.

In conclusion, in our study, the most common cause of hypoparathyroidism is surgery due to multinodular goiter. The most common reason for hospitalization is treatment non-compliance. Up to one-fifth of patients had kidney stones.

ETHICAL DECLARATIONS

Ethics Committee Approval: Approval for the study was granted by the Non-Interventional Studies Ethics Committee of Dicle University Medical Faculty (Date: 14.11.2019, Decision No: 245).

Informed Consent: Because the study was designed retrospectively, no written informed consent form was obtained from patients.

Referee Evaluation Process: Externally peer-reviewed.

Conflict of Interest Statement: The authors have no conflicts of interest to declare.

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Author Contributions: All of the authors declare that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

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