

Effectiveness of Percutaneous Ethanol Injection Therapy Compared to Parathyroidectomy in the Management of Secondary and Tertiary Hyperparathyroidism

Abstract

Background: Secondary hyperparathyroidism (SHPT) and tertiary hyperparathyroidism (THPT) are a common complication of chronic renal failure. Percutaneous ethanol injection therapy (PEIT) has been used as alternative to surgery, but its effectiveness is inconsistent. **Objectives:** The objective of the study is to evaluate the effectiveness of PEIT in the management of patients with SHPT and THPT. **Materials and Methods:** Ninety-one patients with chronic renal failure and SHPT or THPT were treated with PEIT ($n = 55$) and surgery ($n = 36$) between January 2006 and July 2015. The medical records, imaging studies, and ablation techniques were reviewed to assess the efficacy of each treatment modality and complications. **Results:** Parathyroid hormone (PTH) level after treatment <160 pg/mL was used to indicate success of treatment. PEIT showed lower effectiveness compared to surgery (1.8% vs. 61.1%). There was no complication in PEIT group. Symptomatic hypocalcemia was found 11.1% in surgery group. **Conclusion:** PEIT in treatment of secondary and THPT was much less effective than surgery due to large nodule sizes, high levels of PTH, and multiple parathyroid nodules.

Keywords: Chronic renal failure, percutaneous ethanol injection therapy, secondary hyperparathyroidism, tertiary hyperparathyroidism

Introduction

Secondary hyperparathyroidism (SHPT) is a common complication of chronic renal failure. The mechanisms involved in hyperparathyroidism can be subdivided into those leading to excessive parathyroid hormone (PTH) synthesis and secretion. Thus, as kidney disease progresses, persistent hyperparathyroidism leads to the development of parathyroid hyperplasia and adenoma.^[1,2]

The initial treatment in SHPT is medical therapy with calcitriol or calcimimetic agent. About 5% of SHPT patients become refractory to medical treatment and need intervention including surgery and alternatively selective percutaneous ethanol injection therapy (PEIT).^[3] Surgical management of SHPT is total parathyroidectomy. The curative rate of total parathyroidectomy in SHPT is as high as 90%–100%.

In patients with tertiary hyperparathyroidism (THPT), intervention treatment is indicated. The success rate after surgery is also high,

over 90%. PEIT is an alternative method to treat SHPT and THPT.^[3]

The indication for selective PEIT includes PTH ≥ 400 pg/mL despite medical treatment with hyperphosphatemia and hypercalcemia and the presence of enlarged gland with suspected nodular hyperplasia confirmed by ultrasonography.^[4]

In our institution, there was no definite guideline or consensus management for patient who developed secondary or THPT. Some patients underwent PEIT, while some underwent parathyroidectomy, which depended on individual clinician. The effectiveness of each treatment options had not been evaluated as well.

This study aim is to evaluate effectiveness and role of PEIT and assess the predictors of treatment success.

Materials and Methods

Patients materials

After the Institutional Review Board approval (No: RAD-2558-03530), this retrospective

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study obtained data from January 2006 to July 2015. The study included 91 patients who had underlying chronic renal failure with biochemical evidence of SHPT (low serum calcium and Vitamin D levels and markedly elevated serum phosphate and PTH levels) or THPT. All patients had serum PTH level ≥ 400 pg/mL despite medical treatment. Patients underwent selective PEIT or parathyroidectomy.

Type of hyperparathyroidism (secondary or tertiary), demographic data, PTH, the first treatment each patient obtained, frequency, and duration of treatment were reviewed by an experienced radiologist (6 years of experience in body interventional radiology).

Successful treatment was defined when follow-up PTH level after treatment was <160 pg/mL, according to the reference long-term target value of PTH from guidelines for selective PEIT for SHPT 2003.^[5] Complications of each treatment were collected.

Radiological evaluation

The presence of enlarged gland was confirmed by ultrasonography. Size and location of parathyroid gland were recorded.

Technique of percutaneous ethanol injection

Selective PEIT was done under ultrasonographic guidance using high-frequency linear transducer (Toshiba, SSA-790A, Japan) as Figure 1. Patient lay on supine position with extended neck. The skin was cleaned with antiseptic solution. Small amount of anesthetic drug was injected locally. A 22G needle was advanced from skin to target parathyroid gland under ultrasonographic guidance. Tip of needle was placed within the gland. About 1 cc of 95% ethanol was slowly injected. The needle was removed. Neck ultrasound was performed to look for hematoma.

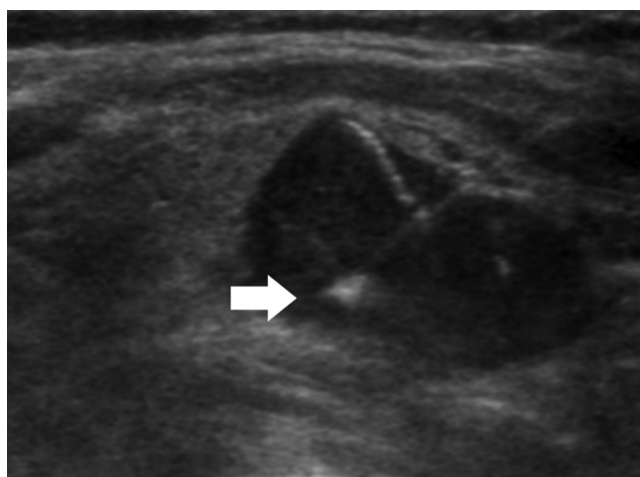


Figure 1: Transverse ultrasound image of the right thyroid gland in a patient with chronic renal failure and secondary hyperparathyroidism showing a round hypoechoic parathyroid nodule (1 cm \times 2.1 cm). The echogenic focus (arrow) at the needle tip represents ethanol injected for ablation. The parathyroid hormone before and after percutaneous ethanol injection therapy was 2542 pg/mL and 1665 pg/mL, respectively

Statistical analysis

Continuous data were reported as mean, maximum, and minimum \pm standard deviation (SD). The categorical data were reported as frequency and percent. Chi-square and odds ratio were used for comparison of two treatment groups. A two-sided $P < 0.05$ was considered statistically significant. Efficacy of treatment was defined into successful treatment and failed treatment, which is reported in frequency and percent. All statistical analysis was performed using IBM SPSS (IBM, Chicago, USA) Statistics version 22.0.

Results

Of the 91 patients in this study, 68 patients (74.7%) were diagnosed as SHPT and 23 patients (25.3%) were diagnosed as THPT. The mean age was 46.2 years (19–78 years).

Tables 1 and 2 demonstrate the demographic data of all patients classified into PEIT and parathyroidectomy groups. Table 3 shows the size of parathyroid glands in PEIT group.

A total of 55 patients underwent PEIT, while 36 patients underwent total parathyroidectomy as their first treatment.

Comparison of age, pretreatment PTH, and sizes of parathyroid glands between the two groups revealed no statistically significant difference.

Table 1: Demographic data of all patients classified into two groups which are the patients who were treated with percutaneous ethanol injection therapy and treated with parathyroidectomy

	PEIT		Surgery	
	n (%)	Mean	n (%)	Mean
Gender				
Male	26 (47.30)		14 (38.90)	
Female	29 (52.70)		22 (61.10)	
All	55		36	
Type of hyperparathyroidism				
Secondary	41 (74.50)		27 (75.00)	
Tertiary	14 (25.50)		9 (25.00)	
PTH level (pg/mL)		1472.79		1564.61
Age (year)		46.33		46.06

PEIT: Percutaneous ethanol injection therapy, PTH: Parathyroid hormone level

Table 2: Characteristic of parathyroid nodules in patients who were treated with percutaneous ethanol injection therapy and treated with parathyroidectomy

	PEIT, n (%)	Surgery, n (%)
Total nodules per case		
One nodule	16 (29.10)	6 (16.70)
Two nodules	26 (47.30)	19 (52.80)
Three nodules	9 (16.40)	8 (22.20)
Four nodules	4 (7.30)	3 (8.30)

PEIT: Percutaneous ethanol injection therapy

All patients have combined treatment including medical therapy with calcitriol or calcimimetic agent and other drugs according to their underlying conditions. The number of PEIT sessions performed and ranged from one to five sessions over a period of 0–53 months [Figure 2].

Follow-up PTH level in all cases immediately after the end of treatment or within 6 months of the last treatment was recorded. The posttreatment PTH of PEIT group ranged from 83.88 pg/mL to 3363.00 pg/mL and the average hormonal level is 1606.96 pg/mL (786.22 SD). The posttreatment PTH of surgery group ranged from 4.1 pg/mL to 5000 pg/mL and the average hormonal level is 517.45 pg/mL (950.83 SD).

The success rate of PEIT was 1.8%, while the success rate of surgery was 61.1% [Table 4].

No complications were reported in the PEIT group, while four patients in the surgical group developed symptomatic hypocalcemia, one patient developed postoperative hematoma, and one patient developed wound infection after surgery.

All patients who were first treated with PEIT and were defined as failure to treatment ($n = 54$) continued other treatments including total parathyroidectomy in 47.3% (26/54) and medication in 50.9% (28/54).

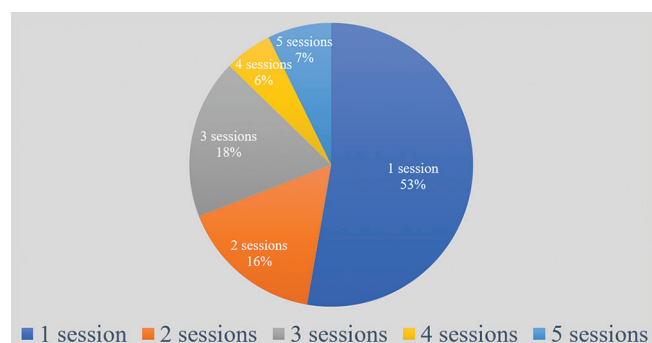


Figure 2: The graph shows the distribution of the percutaneous ethanol injection therapy session and percentage

Table 3: Size of parathyroid nodules of percutaneous ethanol injection therapy group in different locations

Location	Size mm (mean)
RUQ	0.4-2.1 (1.18)
LUQ	0.4-3.8 (1.14)
RLQ	0.4-3.2 (1.31)
LLQ	0.4-2.8 (1.16)

RUQ: Right upper quadrant, LUQ: Left upper quadrant, RLQ: Right lower quadrant, LLQ: Left lower quadrant

Table 4: Successfulness of percutaneous ethanol injection therapy and surgery groups

	PEIT	Surgery	P	OR	95 CI
Successful case, n (%)	1 (1.8)	22 (61.1)	0.000	0.012	0.001-0.970

PEIT: Percutaneous ethanol injection therapy, OR: Odds ratio, CI: Confidence interval

Discussion

Our study revealed very low success rate of PEIT. We did PEIT in 41 patients with SHPT and 14 patients with THPT, only one patient (1.8%) had a PTH level of <160 pg/mL after PEIT. This was lower than previous study by Kakuta *et al.*^[3] who reported that parathyroid function could be maintained within the target range at 1 year in 80.4% of 46 patients with SHPT treated by PEIT.^[3]

The patient who achieved target level of PTH after PEIT in our study was diagnosed SHPT with three parathyroid nodules on the right lower (1.3 cm), left upper (1.1 cm), and left lower (2.0 cm). The PTH level before PEIT was 2558 pg/mL. The patient underwent PEIT three times within 4 months. The PTH level after PEIT was 83.88 pg/mL.

The number of enlarged glands may be a predictor of PEIT success. The Japanese Society for Parathyroid Interventions recommends that PEIT is likely to be ineffective when the number of enlarged parathyroid glands 3 or more because the risk of complications increased with the number of injections. Recently, Koiwa *et al.* demonstrated good results of PEIT when the number of nodules is <2 .^[6] They stated that the risk of PEIT being ineffective in patients with two or more hyperplastic glands was approximately two-fold that for a single gland. This is in contrast to the successful case in our study, which had three enlarged glands. However, PEIT failed in the other 16 patients (29.10%) from 55 patients who had one parathyroid nodule enlargement. Correlation between the number of enlarged glands and success of PEIT in our study could not be assessed due to small number of successful cases.

Prior studies show high effectiveness of PEIT when the parathyroid adenoma is smaller than 0.5 ml. Our study had larger parathyroid nodules. In our institution, the size of parathyroid gland was not measured in volume. We measured in maximum diameter. The mean diameter of the parathyroid nodule in this cohort was larger than 1 cm.

We believe that larger nodule correlates to long-standing disease with high level of PTH. Fumihiko *et al.* reported high level of efficacy for PEIT in patients with PTH <500 pg/mL. This correlates to our study where the mean value of PTH was 1472.79 pg/mL. In case of advance SHPT and IHPT, when glandular destruction and vascular interruption by PEIT are insufficient, parathyroid tissue has a strong proliferative potential may remain and causes ineffectiveness of PEIT.

The reported complications from parathyroid surgery are the risk of injury to the recurrent laryngeal nerve, hematoma, and hypocalcemia. There were no complications following PEIT in our practice. The complications from surgery in our series included symptomatic hypocalcemia in 11.1% of patients. Postoperative neck hematoma and surgical site infection occurred in two patients following the surgery.

This study is limited by its retrospective statistical analysis of small population size and low rate of success.

Conclusion

The study results show that PEIT for SHPT and THPT had a very low success rate of only 1.8%, which is far lower than parathyroid surgery and those reported in the literature. The reasons for the lower success rate of PEIT are likely due to the large nodule sizes, high levels of PTH, and multiple parathyroid nodules.

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Conflicts of interest

There are no conflicts of interest.

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