

Percutaneous ethanol injection therapy for advanced renal hyperparathyroidism in Japan: 2004 survey by the Japanese Society for Parathyroid Intervention

Takatoshi Kakuta¹, Masafumi Fukagawa², Masafumi Kitaoka³, Fumihiko Koiwa⁴, Noritaka Onoda⁵, Yasuhiro Tominaga⁶, Tadao Akizawa⁷ and Kiyoshi Kurokawa¹, for the Japanese Society for Parathyroid Intervention

¹Department of Internal Medicine, Tokai University School of Medicine, ²Division of Nephrology and Dialysis Center, Kobe University School of Medicine, ³Public Syowa Hospital, ⁴Department of Internal Medicine Division of Nephrology, Showa University Fujigaoka Hospital, ⁵Sekishinkai Sayama Hospital, ⁶Nagoya Second Red cross Hospital, School of Medicine and ⁷Department of Internal Medicine Division of Nephrology, Showa University School of Medicine

Abstract

Background. Marked hyperplasia of the parathyroid gland (PTG) is a characteristic feature of severe hyperparathyroidism in patients under chronic haemodialysis treatment. Percutaneous ethanol injection therapy (PEIT) is now becoming popular in Japan as a treatment option for secondary hyperparathyroidism (SHPT) and its cost is covered by the National Health Insurance (NHI) System. The Japanese Society for Parathyroid Intervention surveyed its membership in 2004 to revise the guidelines for the use of PEIT.

Methods. The project was approved by the Executive Committee of the Society, and the primary questionnaire was addressed to 3268 centres (departments) affiliated with the Japanese Society for Dialysis Therapy. A follow-up questionnaire was sent to all the centres that responded.

Results. Although the number of centres to which the questionnaire was sent in 2004 was 3268, compared with 2653 in 1998, the number of responses decreased from 1425 (53.7%) in 1998 to 962 (29.4%) in 2004. To the question of whether the centre performed PEIT, 114 (11.9%) answered 'Yes' and 848 (88.1%) answered 'No' in 2004. It was an increase from 1998 when only 83 (5.8%) of 1425 centres answered 'Yes'. In the 1998 survey, 612 patients underwent PEIT at 74 centres, and in 2004, 2098 patients underwent PEIT at 111 centres.

Conclusions. PEIT may become the frequently performed treatment for SHPT patients who become resistant to medical therapy. However, the same problems as in 1998 remain unsolved; that is, recurrent nerve paralysis, difficulty of post-PEIT PTx and lack of evidence showing the long-term effectiveness of PEIT.

Keywords: haemodialysis; nodular hyperplasia; parathyroidectomy (PTx); percutaneous ethanol injection therapy (PEIT); secondary hyperparathyroidism (SHPT)

Introduction

Marked hyperplasia of the parathyroid gland (PTG) is a characteristic feature of severe hyperparathyroidism (HPT) in patients requiring chronic dialysis, and control of secondary hyperparathyroidism (SHPT) is necessary to prevent renal osteodystrophy (ROD) and other complications affecting patients' survival [1–2].

There are several medical therapies, including intravenous pulse infusion of calcitriol and analogue (maxacalcitol) [3–5], but when patients become resistant to drug therapy, hypercalcaemia, hyperphosphataemia and ectopic calcification may develop [6]. For these patients, surgical removal of the enlarged PTG (parathyroidectomy, PTx) is usually necessary to control parathyroid hormone (PTH) secretion [7–10], but recently, in conjunction with developments in imaging technology, some patients have been managed by selective percutaneous ethanol injection therapy (PEIT) in which markedly enlarged glands likely to resist medical treatment (i.e. those with nodular hyperplasia [8–10]) are selectively destroyed and subsequent enlargement is controlled by vitamin D pulse therapy, among other therapies [11–17].

PEIT is now established in Japan as a treatment option for SHPT and its cost is covered by the National Health Insurance (NHI) System. The Japanese Society for Parathyroid Intervention issued guidelines for PEIT in 2003 [18], and conducted questionnaire surveys of the status of PEIT. The Society is now preparing new general guidelines for parathyroid interventions, including PTx, and considered it necessary to confirm the status of PEIT as a treatment option for patients under treatment at dialysis centres across

Correspondence and offprint requests to: Takatoshi Kakuta, Department of Internal Medicine, Tokai University School of Medicine, Bohseidai, Isehara, Kanagawa 259-1193, Japan. Tel: +81-463-93-1121 (Ext: 2350); Fax: +81-463-91-3350; E-mail: kakuta@is.icc.u-tokai.ac.jp

Table 1. Is PEIT used as treatment for secondary hyperparathyroidism in your facility?

	1998 questionnaire, <i>n</i> = 1425 centres (%)	2004 questionnaire, <i>n</i> = 962 centres (%)
1. Yes	83 (5.8)	114 (11.9)
2. No	1342 (94.2)	848 (88.1)
3. Refer to other facility	86 (6.0)	272 (28.3)
4. Would like to offer it if required	419 (29.4)	381 (39.6)
5. Would like to be able to refer to their facility	589 (41.3)	690 (71.7)
6. Long-term maintenance cases		495 (51.5)
7. Cases of PTx after PEIT		195 (20.3)

PEIT, percutaneous ethanol injection therapy; PTx, parathyroidectomy.

Table 2. How many cases of PEIT have been performed at your centre?

	1998 questionnaire, <i>n</i> = 273 centres (%)	2004 questionnaire, <i>n</i> = 185 centres (%)
Number of cases	612 (2.4 ± 10.4)	2098 (8.4 ± 49.8)
Number of centres	74 (27.1)	111 (59.7)

Japan. The results of the questionnaire survey conducted in 2004 are presented as a basis for improving the treatment of SHPT and establishing the indications for PEIT.

Subjects and methods

The project was approved by the Executive Committee of the Society, and the primary questionnaire was addressed to 3,268 centres (departments) affiliated with the Japanese Society for Dialysis Therapy. A follow-up questionnaire was sent to all the centres that responded.

Statistical analysis

In the comparison of the 1998 and 2004 parameter for PEIT, statistical significance was determined by Pearson's chi-square test. Values were considered significant at $P < 0.05$.

Results

Primary questionnaire (Table 1)

Although the number of centres to which the 2004 questionnaire was sent was 3268, compared with 2653 in 1998, the number of responses decreased from 1425 (53.7%) in 1998 to 962 (29.4%) in 2004, respectively. To the question of whether the centre performed PEIT, 114 (11.9%) answered 'Yes', and 848 (88.1%) answered 'No' in 2004. The number of centres that performed PEIT had increased from 1998 when only 83 (5.8%) of 1425 centres answered 'Yes'. The percentage of centres that wished to perform PEIT when necessary and that of centres that would refer the patients had increased from 29.4 to 39.6% and from 41.3 to 71.7%, respectively. There were patients on long-term maintenance in 51.5% of the centres, and in 20.3% of the centres there were patients who had undergone PTx after PEIT.

Table 3. Are you aware that PEIT is included in the National Health Insurance reimbursement price list for 2004?

	PEIT(+), <i>n</i> = 36 centres (%)	PEIT(-), <i>n</i> = 186 centres (%)	Total, <i>n</i> = 222 centres (%)
Yes (already applied)	8 (22.2)	16 (8.6)	24 (10.8)
Yes (have not applied)	19 (52.8)	53 (28.5)	72 (32.4)
No	9 (25.0)	111 (59.7)	120 (54.1)
No answer	0 (0.0)	6 (16.7)	6 (2.7)

Table 4. When choosing PEIT, what risks are you most concerned about? (more than one answer allowed)

	2004 questionnaire, <i>n</i> = 166 centres (%)
Recurrent nerve paralysis	161 (97.0)
Difficulty of PTx after PEIT	120 (72.3)
Not able to perform PTx later	29 (17.5)
Other	11 (6.6)

Apart from PEIT, percutaneous maxacalcitol injection therapy (PMIT) was the most frequent procedure (57.1%), followed by percutaneous calcitriol injection therapy (PCIT) (25%) [19–20].

Follow-up questionnaire

Overall summary. In the 1998 survey, 612 patients underwent PEIT at 74 centres, and in 2004 it was 2098 patients at 111 centres (Table 2).

Approximately half of the valid respondents [75.0% of centres: PEIT (+) and 37.1% of PEIT centres PEIT (-)] knew about the inclusion of PEIT in the NHI reimbursement price list for 2004, and 22.2% of the centres PEIT (+) and 8.6% of centres PEIT (-) had already applied for it (Table 3).

The most worrying complication was recurrent nerve paralysis (97.0%) followed by difficulty of PTx after PEIT (72.3%) (Table 4).

Indications for PEIT. In both the 1998 and 2004 surveys, the PTH level (87.3 versus 50.9%) and size of the PTG (77.0 versus 46.4%) were considered as prescriptive for PEIT (Table 5).

In 2004, intact PTH (iPTH) was used as a parameter to evaluate PTG function in 163 respondent centres, except in 2 centres that each used high sensitive-PTH (HS-PTH) and whole PTH as a parameter, respectively. In 1998, iPTH was the parameter used in 70.3%, HS-PTH in 19.6% and C terminal-PTH (C-PTH) in 12.2% (Table 6). In 2004, the mean intact PTH (iPTH) level in PEIT-treated patients was 598.0 ± 182.7 pg/ml. In 2004, the mean size of the PTG subjected to PEIT was 597.4 ± 423.1 mm³ in the 64 centres that responded to the respective questions. The mean major axis length of the PTG subjected to PEIT was 9.6 ± 2.82 mm in the 134 centres that responded to the respective questions (Table 7).

Table 5. Which reference parameter do you use as indicative for PEIT?

	1998 questionnaire, <i>n</i> = 148 centres (%)	2004 questionnaire, <i>n</i> = 222 centres (%)
PTH level	130 (87.8)	113 (50.9)*
Bone mineral marker	58 (39.2)	57 (25.7)**
Size of PTG	114 (77.0)	103 (46.4)*
Not indicated for PTx	54 (36.5)	57 (25.7)***
Other	38 (25.7)	6 (2.7)

PTG, parathyroid gland; PTH, parathyroid hormone.

**P* < 0.0001.

***P* = 0.006.

****P* = 0.026.

Table 6. Which form of PTH do you use as indicative for PEIT?

	1998 questionnaire, <i>n</i> = 148 centres (%)	2004 questionnaire, <i>n</i> = 222 centres (%)
Intact-PTH	104 (70.3)	161 (72.5)
HS-PTH	29 (19.6)	1 (0.5)*
C-PTH	18 (12.2)	0 (0.0)*
Whole-PTH	0 (0.0)	1 (0.5)*
No answer	7 (4.9)	59 (26.6)

HS-PTH, high sensitive PTH; C-PTH, C terminal PTH.

**P* < 0.001.

Table 7. What size of the PTG do you consider as indicative for PEIT?

	1998 questionnaire	2004 questionnaire
Volume (mm ³)	511.5 ± 218.0 (<i>n</i> = 37)	597.4 ± 4231 (<i>n</i> = 64)
Major axis (mm)	10.59 ± 4.72 (<i>n</i> = 80)	9.60 ± 2.82 (<i>n</i> = 134)

Table 8. How many glands would you subject to PEIT?

Number of PTGs	1998 questionnaire, <i>n</i> = 148 centres (%)	2004 questionnaire, <i>n</i> = 222 centres (%)
1	17 (11.5)	31 (14.0)
2	47 (31.8)	79 (35.6)
3	21 (14.2)	20 (9.0)
>4	32 (21.6)	20 (9.0)

Table 9. Have you had cases of PTx after PEIT?

	1998 questionnaire (%)	2004 questionnaire (%)
Yes, centres	22 (26.8) (<i>n</i> = 82)	31 (14.0) (<i>n</i> = 222)
Cases	22 (8.6) (<i>n</i> = 257)	79 (3.8) (<i>n</i> = 2098)
No, centres	55 (67.1) (<i>n</i> = 82)	20 (9.0) (<i>n</i> = 222)

Regarding the number of PTGs subjected to PEIT, the proportion of one and two glands treated was 49.6% in 67.6% responded centres and that of four or more glands was 18% (Table 8).

Management after PEIT. In 1998, 22 patients at 22 centres underwent PTx following PEIT compared with 79 patients at 31 centres in 2004 (Table 9).

Table 10. What medication do you use after PEIT? (more than one answer allowed)

	2004 questionnaire, <i>n</i> = 115 centres (%)
Oral calcitriol pulse therapy	35 (30.4)
Oral calcitriol maintenance therapy	41 (35.7)
Intravenous calcitriol therapy	52 (45.2)
Intravenous maxacalcitol therapy	53 (46.1)
Falecalcitriol	19 (16.5)
None	13 (11.3)

Table 11. What are your indices of effect of PEIT? (more than one answer allowed)

	2004 questionnaire, <i>n</i> = 96 centres (%)
PTH level	67 (69.8)
Size of PTG on ultrasound	39 (40.6)
Blood flow in PTG on ultrasound	31 (32.3)
Bone mineral marker	42 (43.8)
Other	2 (2.1)

Table 12. What complications have you experienced after PEIT? (more than one answer allowed)

	1998 questionnaire, <i>n</i> = 959 patients (%)	2004 questionnaire, <i>n</i> = 1350 patients (%)
Hoarseness	81 (8.4)	183 (13.6)
Haemorrhage and haematoma	19 (2.0)	22 (1.6)
Pain	92 (9.6)	38 (2.8)
Horner's syndrome	0 (0.0)	2 (0.1)
Other	2 (0.2)	3 (0.2)

As for medical treatment following PEIT, since calcitriol and maxacalcitol for intravenous administration were developed in Japan, these are now used in 45.2 and 46.1% of the centres, respectively, and the percentage of patients maintained with oral calcitriol pulse therapy and conventional oral calcitriol therapy did not vary (Table 10).

The effect of PEIT was evaluated on the basis of PTH level (69.8%), the size of the PTG (40.6%), parathyroid blood flow (32.3%) and bone mineral marker (43.3%) (Table 11).

As for complications, hoarseness was the most frequently observed side effect occurring in 183 (13.6%) patients, and this percentage did not differ from that in 1998 (Table 12).

Technique. The injection volume of ethanol was 69.8 ± 22.3% (*n* = 31) of the gland volume in 1998 and 75.1 ± 22.5% (*n* = 36) in 2004, showing no statistically significant difference between the two surveys.

Discussion

A questionnaire survey of parathyroid interventions performed in Japan was conducted in 2004 to gather

information for a revision of the guidelines, which were last updated in 2003. Although the number of patients had naturally increased since the 1998 survey, the percentage of centres responding to the survey decreased. However, the percentage of centres that wished to perform PEIT increased, which suggests that PEIT may become the frequently performed treatment, despite its well-known demerits such as the possibility of recurrent nerve paralysis, difficulty in performing PTx after PEIT and uncertainty of the duration of its effect (Table 1).

This was reflected in the general interest in its status on the NHI reimbursement price list; 50% of the respondents knew that PEIT was included and 22.2% of the centres that provided PEIT and 8.6% of those that did not had already applied to the NHI. As PEIT was included in the NHI reimbursement price list <1 year ago, information about its inclusion has spread widely, and some of the centres not currently offering PEIT may start to do so in the near future (Table 3).

Problems associated with PEIT

There were two main reasons why centres had hesitated about performing PEIT; namely, (1) the possibility of recurrent nerve paralysis, and that confirmation of recurrent nerve paralysis is difficult in cases of PTx following PEIT (Table 4), (2) because of the presence of adhesions, and it is these problems that cause clinicians to favour PTx as the initial surgical treatment. If PEIT did not cause recurrent nerve paralysis and if PTx after PEIT were not difficult, there would be no reason of not trying selective PEIT first. However, the possibility of recurrent nerve paralysis always exists as long as ethanol is used, and until the efficacy of PMIT and PCIT is not established, it is important to improve the outcome for PEIT by preventing transudation of the drug outside the target PTG and avoid unnecessary procedures.

The following measures should also be taken to prevent the recurrent nerve paralysis: (1) only inject ethanol after confirming that the needle is definitely within the PTG; (2) limit the volume of ethanol to <80% of the volume of the PTG [18]; (3) minimize the amount of ethanol used, while obtaining the maximum therapeutic effect, by using Doppler flow mapping [15–17] and (4) avoid simultaneous PEIT of the right and left PTG [18].

Currently, the measures to prevent post-PEIT adhesions are those mentioned above, as well as performing PTx early if PEIT proves ineffective. It is also necessary to evaluate (1) the results of PTx following PEIT, (2) the time for the development of adhesions after PEIT and (3) the number of times PEIT can be repeated before the adhesions become too severe in each patient treated in each centre.

Indications for PEIT

The Kidney Disease Outcomes Quality Initiative (K/DOQI) issued Clinical Practice Guidelines for Bone Metabolism and Disease in Chronic Kidney Disease [21], in which it is recommended that the level of iPTH should be kept

at 150–300 pg/mL, the serum phosphorus (P) level at 3.5–5.5 mg/dL and the serum calcium (Ca) level within the normal range of laboratory values (8.4–9.5 mg/mL, as close to the lower limit as possible). Supposing, as the K/DOQI guidelines recommend, the upper limits of Ca (<10.2 mg/dL), P (<6.0 mg/dL) and iPTH (<300 pg/mL) are accepted as the appropriate values, parathyroid interventions, including PTx, would be indicated whenever it became impossible to maintain these values with medical treatment. Is it not difficult to immediately perform PTx when maintenance of these values becomes difficult?

Nearly all centres that responded to the 2004 questionnaire used the PTH level, ultrasound findings and bone markers (particularly alkaline phosphatase) as indicators for PEIT (Table 5). In seven centres that used only one factor as an indicator for PEIT, iPTH was the designated parameter. More centres were using HS-PTH (19.6%, 29/148) and C-PTH (12.2%, 18/148) in 1998, which may represent a transition to the unified measurement of iPTH. In the present questionnaire survey, one centre was still using whole PTH (1–84PTH) as the parameter (Table 6). The mean iPTH concentration was 598.0 ± 182.7 pg/ml in 159 centres. Although there was no difference in this value between the present and 1998 surveys, iPTH >500 pg/ml was used as the indication for PEIT in 47% of the centres in 2004, compared with iPTH >600 pg/ml used in 32% of the centres in 1998. Thus, the value of iPTH as an indicator for PEIT had decreased, which indicates a trend towards early PEIT when there is resistance to medical treatment.

It is now widely accepted, whether or not the centre offers PEIT, that the ideal number of glands for PEIT is up to two on ultrasound imaging (Table 8), but it needs to be validated among participating centres that PEIT is more effective for 1–2 affected glands than for 3–4 glands, as verified by ultrasonography, and that longer maintenance is possible in the former, for an effective revision of the guidelines. We can see that patients with single hyperplastic glands of ≥ 0.5 cm³ or no hyperplastic glands of ≥ 0.5 cm³ but with hyperplastic glands of <0.5 cm³ comprise 80% of the effective group, compared with 66% of the ineffective group [22].

Management after PEIT

When selective PEIT, the standard procedure in Japan, is performed, hyperplastic parathyroid glands that are resistant to medical treatment are destroyed and then an adjuvant vitamin D preparation is administered to treat the remaining glands that are responsive to therapy. Medical treatment after PEIT is a lifeline for selective PEIT. Of the 2098 patients who underwent PEIT, 44% have been managed by medical treatment for at least 1 year to date. It has been argued that PEIT on its own is ineffective based on the result that PEIT and PCIT without after treatment produced no effect in study patients with severe SHPT [23].

In 1998, the main after treatment was oral vitamin D pulse therapy, but the predominant trend at present is intravenous administration of calcitriol or maxacalcitol [24]. With the availability of sevelamer and the advent of calcimimetics, it is expected that in the future post-PEIT medical treatment

will become more potent and that the number of patients on long-term maintenance after PEIT will increase.

Conclusion

The 2004 survey results indicate that PEIT is now became widespread as a procedure for the treatment of renal SHPT that is resistant to medical treatment.

However, the same problems as in 1998 remain unsolved, that is, recurrent nerve paralysis, difficulty of post-PEIT PTx and lack of evidence showing the long-term effectiveness of PEIT. It is necessary to further examine the indications for this therapy.

Acknowledgements. We thank all the doctors of a large number of centres who responded to this complicated questionnaire.

Conflict of interest statement. None declared.

References

1. US Renal Data System. *USRDS 2000 Annual Report*. National Institutes of Health, National Institute of Diabetes and Digestive and Kidney Diseases, Bethesda, 2000
2. Patient Registration Committee. Japanese society for dialysis therapy. An overview of regular dialysis treatment in Japan (as of December 2002). *Ther Apher Dial* 2004; 8: 358–382
3. Slatopolsky EA, Weerts C, Thielan J *et al*. Marked suppression of secondary hyperparathyroidism by intravenous administration of 1,25-dihydroxycholecalciferol in uremic patients. *J Clin Invest* 1984; 74: 2136–2143
4. Tsukamoto Y, Nomura M, Marumo F. Pharmacological parathyroidectomy by oral 1,25 (OH)₂D₃ pulse therapy. *Nephron* 1989; 51: 130–131
5. Tsukamoto Y, Hanaoka M, Matsuo T *et al*. Effects of 22-oxacalcitol on bone histology of hemodialyzed patients with severe secondary hyperparathyroidism. *Am J Kidney Dis* 2000 35: 458–464
6. Block GA, Klassen PS, Lazarus JM *et al*. Mineral metabolism, mortality, and morbidity in maintenance hemodialysis patients. *J Am Soc Nephrol* 2004; 15: 2208–2218
7. Tominaga Y. Surgical management of secondary hyperparathyroidism in uremia. *Am J Med Sci* 1999; 317: 390–397
8. Tominaga Y, Tanaka Y, Sato K *et al*. Histology, pathophysiology, and indications for surgical treatment of renal hyperparathyroidism. *Semin Surg Oncol* 1997; 13: 78–86
9. Fukuda N, Tanaka H, Tominaga Y *et al*. Decrease 1,25-dihydroxyvitamin D₃ receptor density is associated with a more severe form of parathyroid hyperplasia in chronic uremic patients. *J Clin Invest* 1993; 92: 1436–1443
10. Fukagawa M, Kitaoka M, Yi H *et al*. Serial evaluation of parathyroid size by ultrasonography is another useful marker for the long-term prognosis of calcitriol pulse therapy in chronic dialysis patient. *Nephron* 1994; 68: 221–228
11. Solbiati L, Giangrand A, Pra LD *et al*. Percutaneous ethanol injection of parathyroid tumors under US guidance: treatment for secondary hyperparathyroidism. *Radiology* 1985; 155: 607–610
12. Kitaoka M, Fukagawa M, Ogata E *et al*. Reduction of functioning parathyroid mass by ethanol injection in chronic dialysis patients. *Kidney Int* 1994; 46: 1110–1117
13. Fukagawa M, Tominaga Y, Kitaoka M *et al*. Medical and surgical aspects of parathyroidectomy. *Kidney Int* 1999; 56(Suppl.73): 65–69
14. Fukagawa M, Kitaoka M, Tominaga Y *et al*. Selective percutaneous ethanol injection therapy (PEIT) of the parathyroid in chronic dialysis patients: the Japanese strategy. *Nephrol Dial Transplant* 1999; 14: 2574–2577
15. Kakuta T, Fukagawa M, Fujisaki T *et al*. Prognosis of parathyroid function after successful percutaneous ethanol injection therapy guided by color Doppler flow mapping in chronic dialysis patients. *Am J Kidney Dis* 1999; 33: 1091–1099
16. Nakamura M, Fuchinoue S, Teraoka S. Clinical experience with percutaneous ethanol injection therapy in hemodialysis patients with renal hyperparathyroidism. *Am J Kidney Dis* 2003; 33: 739–745
17. Tanaka R, Kakuta T, Fujisaki T *et al*. Long-term (3 years) prognosis of parathyroid function in chronic dialysis patients after PEIT guided by colour Doppler ultrasonography. *Nephrol Dial Transplant* 2003; 18(Suppl 3): 51–1
18. Fukagawa M, Kitaoka M, Tominaga Y *et al*. for the Japanese Society for parathyroid intervention: guideline for percutaneous ethanol injection therapy of the parathyroid glands in chronic dialysis patients. *Nephrol Dial Transplant* 2003; 18(Suppl): 31–33.
19. Kitaoka M, Fukagawa M, Fukuda N *et al*. Direct injection of calcitriol into enlarged parathyroid glands in chronic dialysis patients with severe parathyroid hyper function. *Nephrology* 1995; 1: 563–567
20. Shiizaki K, Hatamura H, Negi S *et al*. Percutaneous maxacalcitol injection therapy regresses hyperplasia of parathyroid and induces apoptosis in uremia. *Kidney Int* 2003; 64: 992–1003
21. National Kidney Foundation. K/DOQI (Kidney Disease Outcomes Quality Initiative) Clinical Practice Guidelines for Bone Metabolism and Disease in Chronic Kidney Disease Patients: some therapeutic implications. *Am J Kidney Dis* 2003; 42: S1–202
22. Koiwa F, Kakuta T, Tanaka R *et al*. Efficacy of percutaneous ethanol injection therapy (PEIT) is related to the number of parathyroid glands in haemodialysis patients with secondary hyperparathyroidism. *Nephrol Dial Transplant* 2007; 22: 522–528
23. de Barros Gueiros JE, Cristina M, Gerhard CR *et al*. Percutaneous ethanol (PEIT) and calcitriol (PCIT) injection therapy are ineffective in treating severe secondary hyperparathyroidism. *Nephrol Dial Transplant* 2004; 19: 657–663
24. Tanaka M, Itoh K, Matsushita K *et al*. Combination therapy of intravenous maxacalcitol and percutaneous ethanol injection therapy lowers serum parathyroid hormone level and calcium × phosphorus product in secondary hyperparathyroidism. *Nephron Clin Pract* 2005; 13: 1–7

Received for publication: 25.2.08

Accepted in revised form: 8.3.08