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Medical management after parathyroid intervention

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Abstract

Vitamin D or vitamin D analogues pulse therapy is seldom effective in patients with at least one parathyroid gland with nodular hyperplasia, and surgical parathyroidectomy or parathyroid intervention is indicated. In parathyroid interventions, especially in selective percutaneous ethanol injection therapy (PEIT), the enlarged parathyroid gland(s) with nodular hyperplasia is selectively destroyed by ethanol injection, while other glands with diffuse hyperplasia are managed by medical therapy. Thus, medical management, e.g., use of appropriate dose of vitamin D or vitamin D analogues after the PEIT procedure, is as important as the destruction of the hyperplastic tissue itself. Recent studies showed that the combination of PEIT and intravenous vitamin D pulse therapy lead to reduce serum PTH level and calcium-phosphorus products in haemodialysis patients. In this article, we focus on the importance of medical therapy after PEIT, and review the efficacy of the combination of PEIT and intravenous vitamin D pulse therapy for haemodialysis patients with secondary hyperparathyroidism.

Keywords: haemodialysis; intravenous vitamin D therapy; percutaneous ethanol injection therapy (PEIT); secondary hyperparathyroidism

Introduction

Secondary hyperparathyroidism with marked parathyroid hyperplasia is one of the most important complications in chronic dialysis patients [1]. Elevated serum phosphorus and calcium–phosphorus products and secondary hyperparathyroidism are associated with substantially high incidences of cardiac, visceral and peripheral vascular calcification in dialysis patients [2,3]. Cardiovascular disease accounts for nearly 50% of all deaths in dialysis patients, and the incidence of cardiovascular death in these patients is markedly higher than in the general population [4]. There is growing recognition that abnormal mineral metabolism and secondary hyperparathyroidism together play a key role in the morbidity and mortality in haemodialysis patients.

Percutaneous ethanol injection therapy (PEIT) is widely used in Japan as an alternative treatment for secondary hyperparathyroidism [5–8]. However, a few studies showed that PEIT was ineffective in severe secondary hyperparathyroidism in haemodialysis patients [9]. In this article, we focus on the importance of medical therapy after PEIT, and review the efficacy of the combination of PEIT and intravenous vitamin D pulse therapy for haemodialysis patients with secondary hyperparathyroidism.

Parathyroid size as a marker for refractory hyperparathyroidism

Parathyroid glands with the volume of 0.5 cm^3 or diameter of 1 cm are considered critical for the diagnosis of nodular hyperplasia 10), 11). Vitamin D or vitamin D analogues pulse therapy is seldom effective in patients with even one gland diagnosed as nodular hyperplasia, and surgical parathyroidectomy or parathyroid intervention is indicated in such cases.

Recently, Vulpio *et al*. [12] reported that patients with moderate secondary hyperparathyroidism had a single enlarged parathyroid gland, whereas patients with severe secondary hyperparathyroidism exhibited more than one enlarged gland. They concluded that the ultrasonographic findings correlated with the severity of secondary hyperparathyroidism and therapeutic outcome. Thus, routine evaluation of the size and number of enlarged parathyroid glands assists in the selection of therapy for secondary hyperparathyroidism.

The theoretical basis of PEIT (Figure 1)

The theoretical basis of PEIT is that enlarged parathyroid gland(s) with nodular hyperplasia is destroyed 'selectively' by ethanol injection, while other glands with diffuse hyperplasia are managed by medical therapy, such as intravenous vitamin D analogues. Thus, medical management after the PEIT procedure is as important as the destruction of the hyperplastic tissue itself. In this respect, 'selective PEIT' is no longer an alternative to surgical parathyroidectomy, but rather has become a powerful adjunct to medical therapy.

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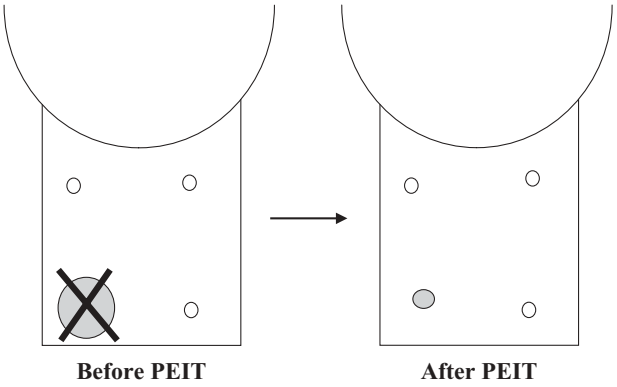

Fig. 1. Schematic representation of the concept of percutaneous ethanol injection therapy (PEIT). The size of the enlarged parathyroid gland diminishes after PEIT with a resultant improvement of resistance to medical therapy including vitamin D analogues. Thus, it is essential to use an appropriate dose of vitamin D analogue soon after PEIT.

As shown in Figure 1, the size of enlarged parathyroid gland was reduced after the PEIT procedure, which also improved resistance to medical therapy including vitamin D analogues.

Difference between parathyroid intervention and parathyroidectomy

Parathyroid intervention, i.e., surgical parathyroidectomy and direct injection therapy, should be reserved for refractory hyperparathyroidism associated with nodular hyperplasia. There are three surgical approaches: total parathyroidectomy with or without autotransplantation; subtotal parathyroidectomy and minimally invasive surgery [13,14]. In general, total parathyroidectomy with forearm autograft is preferred as a procedure for secondary hyperparathyroidism, especially in patients who would require long-term haemodialysis, because recurrently enlarged autograft can be easily removed from the forearm [13]. Direct injection therapy, such as PEIT, percutaneous calcitriol injection therapy (PCIT) and percutaneous maxacalcitol injection therapy (PMIT), is also an effective treatment for refractory hyperparathyroidism [15–17]. The main difference between parathyroidectomy and direct injection therapy is the selection of target glands. In total parathyroidectomy with autograft, all glands are surgically removed and fragments from the smallest gland are transplanted in the forearm, while in direct injection therapy, an enlarged gland with nodular hyperplasia is selectively destroyed by ethanol or other vitamin D compounds, while other glands with diffuse hyperplasia are managed by medical therapy. Thus, it is essential to use an appropriate dose of vitamin D analogue soon after direct injection therapy [8]. In a recent clinical study, patients with one hyperplastic gland responded well to PEIT as demonstrated by the efficacy rate, remission period and risk of relapse [18]. Thus, patients with one enlarged gland are the best indication for PEIT as recommended by the JSDT guidelines [19]. The selection of an optimal method for parathyroid intervention should be determined by the number and location of enlarged glands, as well as the presence of ectopic glands.

Importance of medical therapy after PEIT procedure

Several studies showed that PEIT is an effective treatment for refractory secondary hyperparathyroidism [5–8]. However, a few studies also demonstrated that PEIT was an ineffective treatment for severe secondary hyperparathyroidism in haemodialysis patients [9]. With respect to the number of enlarged glands and intensive medical therapy after PEIT, previous studies did not always select one enlarged gland and did not use an appropriate dose of vitamin D soon after PEIT. This might be a key point in securing appropriate outcome by PEIT for secondary hyperparathyroidism.

Based on the theoretical basis of PEIT, intensive medical therapy should be applied immediately after PEIT. We previously reported that the combination of intravenous maxacalcitol therapy and selective PEIT results in suppression of PTH secretion, regression of parathyroid hyperplasia and the control of calcium-phosphorus products and demonstrated the importance of medical therapy after PEIT [8].

Based on these evidences, we believe that the efficacy of PEIT depends on the number and location of enlarged glands, and the appropriate dose of vitamin D treatment after PEIT.

Conclusions

Disturbance in mineral and bone metabolism is one of the most important causes of increased cardiovascular mortality in chronic renal diseases. According to recent clinical guidelines, the control of parathyroid function in such patients should be achieved without the risk of vascular calcification. Parathyroid intervention should be reserved for patients with nodular hyperplasia to avoid prolonged and potentially even harmful medical therapy. Moreover, intensive medical therapy should be applied immediately after PEIT. Further studies are required to elucidate whether this combination therapy can improve the long-term prognosis of patients with secondary hyperparathyroidism.

Conflict of interest statement. None declared.

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