Surgical verification of percutaneous maxacalcitol injection therapy on enlarged parathyroid glands in chronic dialysis patients

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Abstract

Selective percutaneous ethanol injection therapy (PEIT) has been used to control parathyroid function in patients with secondary hyperparathyroidism (2HPT) when one or more parathyroid gland (PTG) progresses to the nodular hyperplasia stage. However, PEIT can have adverse side effects, such as nerve paralysis and adhesion, because the ethanol is destructive. Intraparathyroid injection of a vitamin D analogue has been designed as a treatment to control parathyroid function without destruction of the PTG or causing adhesions to the surrounding tissue, and the present study aimed to verify the effect of percutaneous maxacalcitol (22-oxacalcitriol) as the vitamin D analogue. The study group comprised two haemodialysis patients who needed parathyroidectomy for uncontrolled 2HPT. The treatment began with an ultrasonographically guided injection of 10 mg of maxacalcitol solution into the largest PTG and, 1 week later, parathyroidectomy was performed to examine the effect of the maxacalcitol injection both macroscopically and microscopically. The injected glands were swollen and inflamed, and adhesions made it difficult to remove them. There was macroscopic and microscopic evidence of haemorrhagic necrosis and adhesions to the surrounding tissue. Direct vitamin D analogue injection should not be performed as a primary treatment option because the adverse side effects are not overcome by this technique.

Keywords: chronic renal failure; haemorrhagic necrosis; hyperparathyroidism; maxacalcitol; parathyroid gland

Introduction

Secondary hyperparathyroidism (2HPT), characterized by high turnover bone disease and hyperplasia of the parathyroid gland (PTG), is a common complication in chronic dialysis (CD) patients [1]. Supplementation with vitamin D analogues is a useful treatment to suppress serum parathyroid hormone (PTH) secretion and to prevent parathyroid enlargement [2], but it is difficult to control 2HPT, even with vitamin D pulse therapy, when one or more PTGs progress to the nodular hyperplasia stage [3]. Recently, selective percutaneous ethanol injection therapy (PEIT) has been used to control parathyroid function in patients with 2HPT prior to parathyroidectomy [4], but there are adverse side effects such as pain and nerve paralysis. Moreover, it is difficult to perform parathyroidectomy after PEIT because of the inflammation around the injected PTG, which causes adhesions. Intraparathyroid injection of a vitamin D analogue is designed to be a treatment without these adverse effects [5], and it has been suggested that this treatment can control parathyroid function without destruction of the PTG or causing adhesions to the surrounding tissue. We aimed to verify the effect of percutaneous maxacalcitol (22-oxacalcitriol), as the vitamin D analogue, injection therapy (PMIT) into enlarged PTGs.

Subjects and methods

We examined two haemodialysis patients who needed parathyroidectomy for uncontrolled 2HPT. Their intact PTH level had not decreased to less than 1000 pg/ml, although they had been treated with intravenous maxacalcitol injection therapy for >6 months. Ultrasonography revealed four enlarged PTGs in the neck, with the maximal PTG diameter >20 mm in each patient. The treatment was commenced with an ultrasonography-guided injection of 10 μg of maxacalcitol solution (5 μg/ml oxarol, Chugai, Tokyo, Japan) into the largest PTG. Parathyroidectomy was performed 1 week...
later in order to examine the effect of the maxacalcitol injection both macroscopically and microscopically.

**Results**

The injected glands of both patients were swollen and inflamed, and adhesions made it difficult to remove the parathyroid glands. Macroscopic examination of the injected PTG showed haemorrhagic changes, and the microscopic findings were degeneration of the parathyroid cells and haemorrhage (Figure 1).

**Discussion**

In the clinical setting, we often observe 2HPT patients with enlarged PTGs >10 mm in diameter who are resistant to vitamin D treatment [6]. Parathyroid hyperplasia progresses from diffuse to nodular in 2HPT. The density of vitamin D receptors and calcium-sensing receptors in the parathyroid cells in nodular hyperplasia is significantly lower than in diffuse hyperplasia [7]. In such cases, conventional vitamin D administration, including intravenous pulse therapy, ceases to be beneficial, and up till now surgical parathyroidectomy was considered the only treatment for these advanced cases [8]. Recently, selective PEIT of the PTG has become an established strategy [4] and is a powerful adjunct to medical therapy [9]. It uses ethanol to destroy all glands with nodular hyperplasia selectively, followed by conventional therapy to control the remaining glands exhibiting diffuse hyperplasia. However, PEIT is not always safe, as the ethanol is destructive, and adverse side effects, such as pain, nerve paralysis and adhesion, can occur.

The technique of increasing the concentration of vitamin D in selectively enlarged PTGs (i.e. PMIT) may be useful as it acts specifically on the mechanisms of 2HPT and does not destroy tissue, which makes it different from and safer than PEIT, while still using direct injection into the PTG.

In the present study, we carried out PMIT for two 2HPT patients who were scheduled for parathyroidectomy.

![Fig. 1.](https://example.com/fig1.jpg) (a) Macroscopic view of the parathyroid glands that did not receive maxacalcitol injection. (b) Macroscopic findings in the parathyroid glands following maxacalcitol injection; note the haemorrhagic changes. (c) Microscopic findings in the parathyroid glands following maxacalcitol injection. Parathyroid cells show degeneration with haemorrhage (H&E, x400).
in order to observe the macroscopic and microscopic effects of direct vitamin D analogue injection. The intact PTH concentration had not decreased 1 week after PMIT because we only injected maxacalcitol into one enlarged PTG in each patient. We proceeded with parathyroidectomy 1 week after PMIT, and the operative findings were greatly different from our expectation. The PTGs were swollen, and inflammation had caused adhesions, making the parathyroidectomy difficult. Macroscopically and microscopically there was haemorrhagic necrosis of the PTGs in both patients, which indicates that PMIT may have other mechanisms of tissue destruction, such as local stimulation of vitamin D receptors. It is generally believed that vitamin D analogues do not destroy the PTG and that its direct injection is a safe treatment for 2HPT; however, haemorrhagic necrosis occurred in the PTGs, and the adverse effects of PMIT were significant in both the PTG and the surrounding tissue.

We conclude that direct vitamin D analogue injection should not be performed as a primary treatment option. Further research of this procedure is required.

References