



**Comparison Effect of Loading Calcitriol and Titrating Calcitriol Treatment to Control Hypocalcemia after Parathyroidectomy in Chronic Kidney Disease; Randomized Control Trial, Open labeled**

Sathit Niramitmahapanya MD\*, Chadsuphar Sirirachta MD\*, Benjawan L. Niramitmahapanya MD\*\*, Chaicharn Deerochanawong MD\*, Udom Krairitichai MD\*\*, Pornake Athipan MD\*\*\*

\*Endocrinology Unit, Department of Internal Medicine, Rajavithi Hospital, Rangsit University, Bangkok, Thailand

\*\*Nephrology Unit, Department of Internal Medicine, Rajavithi Hospital, Rangsit University, Bangkok, Thailand

\*\*\*Department of Otolaryngology-head and neck, Rajavithi Hospital, Rangsit University, Bangkok, Thailand

**BACKGROUND :** Postoperative hypocalcemia in patients with renal hyperparathyroidism is common problems after parathyroidectomy(PTX). Transient hypocalcemia was observed in 83% of the patients (2). On the contrary, the presence of postoperative hypocalcemia is not a guarantee of surgical cure. (10) With renal hyperparathyroidism, Jofre and colleagues (3) observed that 20% of their patients had hungry bone syndrome necessitating longer hospitalization, which was defined as calcium levels below 8.0 mg/dl for more than 8 days. In addition to biochemical values, the presence or absence of hypocalcemic symptoms has also been taken into consideration in many studies. Comparisons are further complicated by the fact that a low serum calcium level does not always predict the development of symptoms or signs of hypocalcemia.

Oral calcium and active vitamin D supplements may be sufficient in some patients. On the other hand, intravenous calcium administration is often necessary if severe or symptomatic hypocalcemia develops. "Need for intravenous calcium" has been used as an indicator of the magnitude of hypocalcemia. Vitamin D usually takes two days to increase intestinal uptake of calcium. Preoperative vitamin D treatment is recommended, even in patients who are hypercalcemia. As aforementioned, intravenous calcium administration remains most straightforward to restore serum calcium levels rapidly. Cozzolino et al. (1) proposed an algorithm to start calcium infusion when a steep fall in calcium levels is noted. However, it might be better to prevent hypocalcemia altogether.

**Material and Method :**

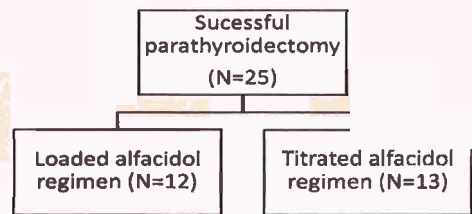
Study design From August 2009 to September 2010, thirty patients referred to underwent parathyroidectomy for symptomatic hyperparathyroidism at our institute during this time. Among them, 5(16.67%) patients were excluded from the study because of primary hyperparathyroidism and no patient had persistent disease after surgery (postoperative intact PTH >300 pg/dl). Remained 25 patients were chronic kidney disease stage 5 who underwent successful PTH were randomized in this study.

Before surgery, serum levels of calcium, phosphorus, alkaline phosphatase (ALP), blood urea nitrogen (BUN) and creatinine were measured routinely using standard auto-analytical techniques. Intact PTH (1-84) was measured by the two-site immunoradiometric assay (ELSA-PTH; CIS Bio International, Gif-sur-Yvette, France) with a normal range is 10 to 65 pg/ml. All patients underwent dialysis the day before operation. Preoperative imaging of the parathyroid glands was not routinely used. Bilateral cervical exploration was performed in all patients to identify four parathyroid glands. Our goal was to control intact PTH to the target range of 150 to 300 pg/ml, as recommended by K/DOQI guidelines(9).

**METHODS :**

A; Titrated dose regimen was defined by supplemented calcitriol with titrated against serum calcium level (started at 1mcg/d, alfalcidol (250 mcg) 2\*2 per day) with constant dose of oral calcium carbonate(1 grams of calcium carbonate by 3\*3 per day) but the amount of intravenous calcium gluconate was titrated against serum calcium when reached indicated(Table1).

B; loaded dose regimen was defined by supplemented calcitriol with loaded against serum calcium level (started dose at 4mcg/d, alfalcidol (250 mcg) 4\*4 per day) with constant dose of oral calcium carbonate tablet (1 grams of calcium carbonate by 3\*3 per day) but the amount of intravenous calcium gluconate was titrated against serum calcium when reached indicated as below in Table1.



**Trial profile**

Vitamin dose (Loading regimen)	Strategies
Step1 Vitamin 1-α 4X4 (2 days)	Continue dose if corrected calciums7.5 mg/dl, if corrected calcium <7mg/dl *
Step2 Vitamin 1-α 4X3 (2 days)	Continue dose if corrected calciums7.5 mg/dl, if corrected calcium <7mg/dl *
Step3 Vitamin 1-α 4X2 (2 days)	Continue dose if corrected calciums7.5 mg/dl, if corrected calcium <7mg/dl *
Step4 Vitamin 1-α 3X2 (2 days)	Continue dose if corrected calciums7.5 mg/dl, if corrected calcium <7mg/dl *
Step5 Vitamin 1-α 2X2 (2 days)	Continue dose if corrected calciums7.5 mg/dl, if corrected calcium <7mg/dl *
Vitamin dose (Titrating regimen)	Strategies
Step1 Vitamin 1-α 2X2	Increase dose to next step if corrected calciums7.5 mg/dl, if corrected calcium <7mg/dl *
Step2 Vitamin 1-α 3X2	Increase dose to next step if corrected calciums7.5 mg/dl, if corrected calcium <7mg/dl *
Step3 Vitamin 1-α 4X2	Increase dose to next step if corrected calciums7.5 mg/dl, if corrected calcium <7mg/dl *
Step4 Vitamin 1-α 4X3	Increase dose to next step if corrected calciums7.5 mg/dl, if corrected calcium <7mg/dl *
Step5 Vitamin 1-α 4X4	Increase dose to next step if corrected calciums7.5 mg/dl, if corrected calcium <7mg/dl *

Table 1 of strategies to control hypocalcemia in postoperative parathyroidectomy

**RESULTS :**

Table 2 Clinical outcome of postparathyroidectomy

Characteristic	Successful Parathyroidectomy (n=25)		p-value
	Titrated (n=13)	Loaded(n=12)	
Amount of alfalcidol(tab)	57.75±75.28	59.17±22.73	0.95
Calcium gluconate treatment (%)	58.33%	25%	0.10
Amount of calcium gluconate (iv)	7.58±8.96	3.00±6.18	0.16
Hypocalcemia (%)	83.33%	75%	0.63
Duration of hospitalization(day)	9.50±4.83	8.25±3.11	0.46
Mean change of calcium level in the first 7 days post surgery	2.68±2.16	0.33±0.99	0.036*

**CONCLUSION :** Based on our results, we introduced preventive strategies approach to started loading calcitriol dose regimen immediately after surgery in patients because this regimen can reduced incidence of postoperative hypocalcemic parathyroidectomy from 83 to 75% and loading regimen can ameliorated the mean reduction of day 7 post-operative serum calcium level better than titrating regimen.

