



## CHAPTER I

### INTRODUCTION

Chronic renal failure is a common disease in Thailand. The cause of chronic renal failure may originate from kidney disease itself or may be the complication from other diseases such as hypertension, diabetes mellitus, gouty arthritis etc. When the disease progresses, kidney function in controlling fluid, electrolyte and excretion of the waste products is compromised. The patients require chronic dialysis to prolong their lives. There are two types of chronic dialysis, continuous ambulatory peritoneal dialysis (CAPD) and hemodialysis (HD). In hemodialysis, the patients have to spend time about 4-5 hours per day for 2-3 days per week in the hospital with the hemodialysis machines. In CAPD, the patients can easily change the dialysate fluid in and out their abdominal cavities themselves. Since there are very small number of hemodialysis machines in the government hospital, whereas the number of CAPD patients increased every year. In Chulalongkorn Hospital the number of CAPD patients is about threefold of the hemodialysis cases.

Renal osteodystrophy is one of the important common problem in both hemodialysis and CAPD patients. It is the bone disease observed in the patients of chronic renal failure. In chronic dialysis, renal osteodystrophy may arise from many factors such as hyperparathyroidism, aluminum toxicity, iron overload or some specific uremic toxins (Coburn, and Slatopolsky, 1991).

Secondary hyperparathyroidism was reported as the most common cause of renal osteodystrophy in chronic dialysis (Sherrard et al., 1974 ; Smith et al., 1986). The lesion begins in a mild form and progresses to typical osteitis fibrosa (hyperparathyroid bone disease) . Secondary hyperparathyroidism may be the result of hypocalcemia ,hyperphosphatemia and the deficiency of vitamin D. Hyperphosphatemia can be prevented by oral phosphate binder , aluminum gel or calcium carbonate . The use of aluminum gel is decreased because it is proved that this may cause aluminum toxicity in the long term period and the patients can develop demantia , anemia and osteodystrophy ( Herz et al. 1990 ). Hypocalcemia may come from the low calcium diet or vitamin D deficiency. The deficiency of vitamin D can decrease calcium absorption from the intestine and cause hypocalcemia leading to development of hyperparathyroidism. Some investigators found the definite receptors of calcitriol , one of the active forms of vitamin D in parathyroid cell and suggested that the deficiency of calcitriol can directly stimulate parathyroid hormone secretion (Brumbaugh, et al., 1975).

Active forms of vitamin D are derived from the precursor in diet (vitamin D<sub>3</sub>) . Ultraviolet can also change some precursor of vitamin D to vitamin D<sub>3</sub> too. Vitamin D<sub>3</sub> will further change to many forms and lead to genesis 1,25 dihydroxycholecalciferol ( calcitriol ) in the kidney. Calcitriol is the most potent form of active vitamin D and benefits in suppression of parathyroid hormone ( Coburn, and Slatopolsky, 1991 ).

In cases of overt hyperparathyroid bone disease ( bone erosion, high PTH level, increase alkaline phosphatase) , adequate treatment by vitamin D often leads

to improvement in both continuous ambulatory peritoneal dialysis (CAPD) and hemodialysis patients ( Berl et al., 1978 : Sherrard et al., 1980 ).

In the cases with only high levels of hyperparathyroid hormone are detected , prophylaxis use of vitamin D (calcitriol) in hemodialysis patients is proved to effectively suppress parathyroid hormone and retard the development of osteodystrophy ( Berl et al., 1978; Delmez et al.,1989 ; Gallienti et al., 1992 ). Prophylaxis use of vitamin D in CAPD patients is believed to benefit as in hemodialysis but indeed, there are several differences between CAPD and hemodialysis which can effect renal osteodystrophy. In children, prophylaxis use of vitamin D in CAPD cases is proved to benefit in bone disease and the patients increased growth rate ( Buccianti et al., 1990). In adult patients with CAPD, the effectiveness of prophylactic treatment with 1-alpha hydroxy vitamin D was reported (Watson et al., 1989). However, the study in double blinded controlled trial has not been done.

In Thailand there is no study of renal osteodystrophy in both CAPD and hemodialysis patients. The role of prophylactic treatment of calcitriol in the patients with high levels of parathyroid without other evidences of hyperparathyroid bone disease needs to be proved.

A lot of the exposure to sunlight may produce high levels of vitamin D<sub>3</sub> and leading to increase other active forms of vitamin D. Calcitriol supplementation may not be required. It is possible that high levels of parathyroid hormone may be controlled by dialysis and intensive controlling of hyperphosphatemia.

Calcitriol may not be required due to adequate levels of active compounds metabolized from diet and a lot of sunshine exposure as mentioned. So we intend to use a double-blind randomized controlled trial to prove the benefit of calcitriol in CAPD patients.

Parathyroid hormone, some serum biochemical parameters such as alkaline phosphatase and radiographic features of secondary hyperparathyroidism or osteomalacia will be used as diagnostic tools to identify hyperparathyroidism or hyperparathyroid bone disease.

## OBJECTIVES

The objectives of the study are as follow :

1. To study the effect of calcitriol on parathyroid hormone levels.
2. To study side effects of calcitriol treatment.
3. To study the effect of continuous ambulatory peritoneal dialysis alone on parathyroid hormone levels.
4. To study the progression of hyperparathyroid bone disease in CAPD patients with and without treatment by calcitriol.

## RESEARCH QUESTIONS

### Primary research question

Does the calcitriol reduce the parathyroid hormone level in CAPD patients by 75% of control ?

### Secondary research questions

1. Does the calcitriol treatment increase risk of hypercalcemia or hyperphosphatemia in the patients?
2. Does the calcitriol treatment increase risk of soft tissue calcification in the patients?
3. Does the hyperparathyroid levels significantly increase in patients who do not receive calcitriol treatment?
4. Does the hyperparathyroid bone disease progress in patients who do not receive calcitriol treatment?

### HYPOTHESIS

Calcitriol treatment can reduce the parathyroid hormone level by 75% of control , and the progression of hyperparathyroid bone disease in CAPD patients without the serious side effects.

### EXPECTED BENEFIT AND APPLICATION

There is no study about renal osteodystrophy in Thailand . Most of our patients had financial problems and the cost of calcitriol was rather expensive, so the use of this drug was limited. We expect that our study will clarify the role of this drug as prophylactic use in CAPD patients.

## SUMMARY

In this chapter, an introduction to the problem as well as objectives of the study ,research questions, hypothesis and expected benefit of the study have been presented.