COMPARISON BETWEEN INTERMITTENT ORAL AND INTRAVENOUS ALFACALCIDOL IN MANAGEMENT OF RENAL OSTEODYSTROPHY


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ABSTRACT

Renal osteodystrophy (ROD) represents a relevant and frequent complication of chronic renal failure; although the spectrum of ROD is broad secondary hyperparathyroidism remains its most commonly encountered histological pattern. Alfacalcidol, taken orally or administered intravenously, is known to reverse the complication of chronic renal failure induced osteodystrophy (ROD).

In this study (29) Endstage renal disease (ESRD) patients, who were on dialysis (19 on hemodialysis and 10 on peritoneal dialysis) for longer than six months and having serum parathormone (PTH) levels at least four times normal and serum calcium less than 2.1 mmol/L, were randomly allocated to treatment with oral or intravenous (i.v.) alfacalcidol for a period of one year.

There were nine patients on hemodialysis (HD) and six on peritoneal dialysis (PD) in the oral treatment group, while in the i.v. group there were ten on hemodialysis and four on peritoneal dialysis. Clinical and serial biochemical assessments showed no statistically significant difference between the orally and i.v. treated patients in terms of suppressing secondary hyperparathyroidism and osteodystrophy. However, patients with features of mild ROD on bone histology which is repeated after 12 months of treatment showed significant improvement, also the dual photon study and quantitative CT revealed improvement of bone mineral density in both treatment groups.
In conclusion, both oral and i.v. alfalcaldol, administered intermittently, were able to equally suppress secondary hyperparathyroidism in dialysis patients. This was shown by improvement in PTH levels as well as improvement in bone histomorphometry and bone density.

We further support the use of intermittent oral alfalcaldol in chronic renal failure patients because of easy administration, convenience, and cost-effectiveness in addition to the potency regarding the control of the hyperparathyroid status of the patients with (ESRD).

**Introduction**

The osteodystrophic uraemic syndrome is a disabling bone disease caused by the osseous effects of excessively increased circulating TH.(1)

For several years vitamin D supplements have constituted the main pillar of medical treatment of this syndrome.(2,3)

It is now evident that hyperparathyroidism develops early in the course of progressive chronic renal failure. Absolute or relative deficiency of 1,25 dihydroxycolecalciferol represents one of the major factors in the genesis of renal failure.(4) As renal failure reduces the decrease in functional mass and hyperphosphataemia in a decrease in the renal 1α-xylase activity, thus decreasing calcium sensitivity of parathyroid cells, reduces pre-proPTH mRNA decreasing transcription and inhibits parathyroid cell proliferation.(5,6) Indirectly, calcitriol increases calcium intestinal absorption and diminishes skeletal resistance to the calcaemic action of PTH.(7)

The aim of our study is to compare the efficacy of oral and i.v. Vitamin D (α-calcidol) administration on renal osteodystrophy (ROD) in 2 groups of patients with end stage renal failure (ESRF) on maintenance dialysis replacement, with emphasis on the associated biochemical and bone changes.

**Patients and Methods**

Patients; 29 end stage renal failure patients (ESRF) on maintenance dialysis were enrolled into the study, there were 16 males and 13 females their ages ranged between 15-54 years with mean of 37.3±14.5. 19 patients (12 males and 7 females) were on maintenance dialysis, 10 patients (4 males and 6 females) were on intermittent peritoneal dialysis twice weekly for mean duration 75.3±23.6 months.

The etiology of ESRF was: glomerulonephritis (8 patients), diabetes mellitus (2 patients), interstitial nephritis (7 patients), hypertension (4 patients), unknown (6 patients).

The inclusion criteria for study patients were: age less than 60 years, duration on dialysis (HD or PD) more than six months, serum PTH levels elevated to at least 6 times the normal and S. Ca levels less than 2.1 mmol/L.

Exclusion criteria included: history of sensitivity to alfalcaldol, persistent hypercalcaemia (S. Ca > 2.8 mmol/L), calcium-phosphorus product > 6, evidence of aluminium toxicity (serum Al > 50 µmol/L), and/or previous parathyroidectomy.

Methods: the patients were randomly divided into 2 groups; the 1st group included 15 patients (9 HD and 6 PD) who received oral alfalcaldol. The 2nd group of 14 patients (10 HD and 4 PD) received i.v. Alfalcaldol. For the first 2 weeks, all patients received 1 µg alfalcaldol 3 times/week. Subsequently, the dose was increased to 2 µg thrice weekly for 3 weeks and later to 3 µg thrice weekly for 3 weeks; eventually the dose was ad-
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Methods: the patients were randomly divided into 2 groups; the 1st group included 15 patients (9 HD and 6 PD) who received oral alfacalcidol. The 2nd group of 14 patients (10 HD and 4 PD) received i.v. Alfacalcidol. For the first 2 weeks, all patients received 1 μgm alfacalcidol 3 times/week. Subsequently, the dose was increased to 2 μgm thrice weekly for 3 weeks and later to 3 μgm thrice weekly for 3 weeks; eventually the dose was adjusted to maintain S. Ca level around 2.5 mmol/L. patients were maintained on that dose for a total period of 12 month. The patients on HD received alfacalcidol after dialysis session and Kt/V was aimed at > 1.2 in both groups. Dialysate calcium concentration was 1.7 mmol/L in both HD and PD solutions. When hypercalcaemia (S. Ca) > 2.7 mmol/L occurred, treatment with vitamin D was held until returning to normal range with subsequent adjustment of the dose between 0.5 to 3 μgm. None of the study patients were on aluminum-containing drugs. Follow-up involved:

- Detailed clinical assessment.
- Weekly determination of S. Ca, phosphorus, albumin, bicarbonate and alkaline phosphatase levels. The PTH and aluminum levels were checked monthly and 3-monthly respectively by radioimmunoassay.
- All patients had skeletal surveys, dual photon or quantitative CT study for bone mineral density (figure 1 & 2, curve 1) and bone biopsy (figure 3 & 4), which was performed once at the beginning of the study and again after 12 months of treatment.

Tetracycline labeling was done by the following protocol: 250 mg tetracycline twice daily for two days, discontinuation for one week and readministration for 4 days, transiliac trephine bone biopsies.