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ORIGINAL ARTICLE

Evaluation of Cholecalciferol Efficacy in the Management of Secondary Hyperparathyroidism in Hemodialysis Patients

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ABSTRACT

The deficiency of vitamin D is public among hemodialysis (HD) patients and is a key factor in the development of secondary hyperparathyroidism (SHPT). Secondary hyperparathyroidism is currently accomplished by lowering circulating phosphate levels with parathyroid hormone (PTH), vitamin D analogs, and oral binders. The current study aim was to assess the efficacy of cholecalciferol in the management of secondary hyperparathyroidism in hemodialysis patients with concomitant vitamin D deficiency/insufficiency. A total of 53 patients were taken with25 male and 28 female patients. After treating patients with cholecalciferol, serum PTH levels improved significantly, with mean pre-treatment levels of 486.99±191.10, which had decreased to a mean post-treatment level of 301.66±201.08. Serum Vitamin D levels also improved significantly, with mean pre-treatment levels of 10.86±4.98, which increased to a mean post-treatment level of 29.98±17.24. Patients treated with cholecalciferol had no significant change in phosphorous and calcium levels.

Keywords: Parathyroid Hormone; Cholecalciferol; Vitamin D; Secondary Hyperparathyroidism; hemodialysis; Pakistan

INTRODUCTION

Until the end of the twentieth century, vitamin D, one of the fat-soluble vitamins, was thought to be a precursor of endocrine agents, regulating calcium and bone mineral homeostasis. Secondary hyperparathyroidism (SHPT) is the organism's adaptive maladaptive response to the concerned homeostasis of phosphorus, calcium metabolism and vitamin D instigated by falling renal function in many cases (Toussaint and Damasiewicz, 2017; Omrani and Daraizade, 2018).

Dysregulation of minerals (Ca, P) homeostasis results in increased levels of the serum phosphorus and phosphatonin fibroblast growth factor 23 (FGF23) while decreased calcitriol synthesis and renal phosphorus excretion. Due to a reduction in glomerular filtration rate (GFR), the bone disease and pathophysiology of secondary hyperparathyroidism caused which reduces phosphate excretion and retention, stimulating PTH production and parathyroid gland growth (Yuen et al., 2016). Reduction in ionized calcium levels can also cause PTH creation due to the lessening of vitamin D in spoiled kidneys, as well as phosphate retention (Jones, 2007; Dusso et al., 2011)). A reduction in the level of vitamin D can also cause hyperparathyroidism by causing hypocalcemia or a direct effect on PTH gene transcription (Drüeke and Massy, 2015; Cozzolino et al., 2016).

Hyperparathyroidism in renal disease patients causes osteitis fibrosa cystica and bone turnover which is considered by a variety of indicators such as immune dysfunction, renal osteodystrophy, anemia, bone fragility, spartan vascular calcifications, pain, modifications in cardiovascular construction and role, syndromes due to compressive possessions of resistance and cysts in erythropoietin. These all-adverse effects may lead to the failure of the kidney which badly affects the blood supply to the body and even during severe situations causes cardiovascular mortality and morbidity in renal failure patients.

SHPT is a public ailment in patients who are facing chronic kidney disease (CKD) that is branded by high serum parathyroid hormone (PTH) levels, minerals (calcium and phosphorus) metabolism imbalance, and high production of parathyroid hyperplasia. SHPT appears early in the course of CKD and worsens as kidney function deteriorates (Foley RN, Parfrey, 1997; Rix et al., 1999; Jones et al., 1998; Fineman et al., 1999). Calcitriol is currently used in hemodialysis patients to luxury vitamin D shortage and prevent its related complications by lowering parathormone plasma concentrations over a 3-6 months course of treatment (Nasuto et al., 2016; Suki and Moore, 2016; Hamano and Fukagawa, 2017). The current study was conducted to evaluate the cholecalciferol efficacy in the management of SHPT in hemodialysis patients.

METHODOLOGY

Study Area: The current study was conducted in District Headquarters (DHQ) hospital Dera Ismail Khan (D.I. Khan) Division of Khyber Pakhtunkhwa province from June 2020 to December 2020. D.I. Khan is the 37th largest city and 5th largest province of Pakistan located on the west bank of the Indus River. t is 300 and 230 kilometers south of the provincial capital Peshawar, KPK, and northwest of Multan, Punjab, respectively. The total population of D.I. Khan is 217,457.

Patients: Around 53 patients (25 males, 28 females) with vitamin D deficiency (lower than 20 mg/ml) and hyperparathyroidism (PTH >300 mg/ml) were included in this clinical trial. The age of the patients was in between 30-85 years which was referred to DHQ hospital and included in this study. Written permission was gained from hospital administration and patients. After consent, samples of blood were collected to determine the 25-hydroxy vitamin D, intact PTH, and minerals like calcium, and phosphorus in the blood. Patients with less than 20 mg/ml vitamin level and improved than 300 g/mL PTH level were arbitrarily allocated to one of two (2) groups. First and two both groups were given calcium carbonate tablets containing 1500-1000 mg/d. 1st group was given cholecalciferol (50 000 units, 3 times/week), while 2nd group was given calcitriol (0.25 g, 1 time/day), both of which were manufactured by a company. After three months, blood samples from collected from the first and two groups and reanalyzed using the laboratory indices.

RESULTS AND DISCUSSION

Calcium, phosphorus, and parathyroid hormone (PTH) abnormalities cause chronic kidney disease (CKD) and mineral and bone disorder (MBD), which are linked to poor results in patients on care dialysis. Long-established cornerstones of SHPT therapy, doxercalciferol, and paricalcitol effectively reduce PTH in maximum SHPT patients but frequently result in higher phosphorous and calcium levels, a thoughtful barrier to their use (Palmer et al., 2007; Vervloet et al., 2010; Tentori et al., 2015).

HTH is an illness considered by the extreme discharge of parathyroid hormone (PTH) as a result of a phosphocalcic metabolic illness triggered by hyperphosphatemia and hypocalcemia. PTH secretion can be minimized by the use of vitamins such as D. The excessive secretion of PTH can directly or indirectly affect kidneys, bones, intestines, and minerals like calcium and phosphorus, etc (Silver and Levi, 2005). Vitamin D

cannot be converted by the kidney into the physiologically active 1,25-cholecalciferol. Reduced intestinal calcium absorption results in low serum calcium and elevated phosphate due to the kidney's failure to excrete phosphate, which increases parathyroid hormone secretion (Tentori et al., 2015; Lau et al., 2018; Steinl and Kuo, 2021). Osteosclerosis is characterized by enlarged bone density, mainly in the axial skeleton which weakens the bone (Mizobuchi et al., 2019; Rodríguez-Ortiz and Rodríguez, 2020). SHPT brown tumour caused by bigger osteoclastic action and fibroblast production (Van Der Plas et al., 2020; Komaba et al., 2017; Ballinger et al., 2014; Cunningham et al., 2011).

Table 1: Demographic features of patients.

Gender	Number	Percentage
Male	25	47.16
Female	28	52.83
Age		
30-45	13	24.52
46-60	24	45.28
61-85	16	30.18
Diabetes Mellitus		
Yes	20	37.73
No	33	62.26

Table 1 shows the demographic characteristics of patients admitted in the hospitals on maintenance hemodialysis. Total 53 patients were included in this clinical trial and out of the total, 25 (47.16%) and 28 (52.83%) were males and females, respectively. Another study was conducted in Karachi, Pakistan by Asif et al. (2020) to evaluate the vitamin D efficacy in the form of cholecalciferol for the control of SPTH in patients admitted to hospitals. In their study, a total of 42 patients was involved and among them, investigated that serum PTH levels improved significantly with the pre-treatments of vitamins D in cholecalciferol form and reduced with post-treatments but calcium and phosphorus levels decreased.

Table 2: Pre-treatment and post-treatment laboratory parameters

	Pre	Post	p-value
	Mean±SE	Mean±SE	
Serum Ca	8.53±0.85	8.92±0.64	0.245
Serum Po4	4.88±0.43	4.96±0.63	0.382
Serum PTH	486.99±191.10	301.66±201.08	0.000
Vitamin D3	10.86±4.98	29.98±17.24	0.000

p-value ≤ 0.05 is considered a significant

Vitamin D is necessary for calcium and phosphorus balance regulation. It is produced in the skin but is also found in the diet. 1,25 dihydroxy vitamin D is the active form. Its primary action is to rise the accessibility of calcium and phosphorus for the creation of new bone. Recent research has also revealed that vitamin D has important actions in a variety of other tissues. Vitamin D increases calcium and phosphorus serum levels by improving intestinal absorption (Bosworth and de Boer, 2013; Guo and Yuan, 2015; Matias et al., 2010).

Table 3: Mean comparison of pre and post-treatment of cholecalciferol administration according to vitamin D3 level

Vitamin D		Pre	Post	p-value
		Mean±SE	Mean±SE	
≤ 15	Serum Ca	9.02±0.32	7.66±0.27	0.312
	Serum Po4	3.99±2.89	3.98±0.61	0.309
	Serum PTH	618.13±28.45	301.32±200.01	0.000
	Vitamin D3	6.75±2.54	26.67±10.84	0.000
≥ 15	Serum Ca	7.88±0.55	7.54±0.33	0.444
	Serum Po4	4.53±0.54	4.01±0.65	0.675
	Serum PTH	397.11±164.71	401.51±200.01	0.116
	Vitamin D3	18.64±2.90	43.33±11.19	0.000

p-value≤0.05, considered significant

Overall mean comparison of pre and post treatments of cholecalciferol administration according to vitamin D3 level is given in table 3. Injections of active vitamin D have been linked to improved survival in patients undergoing chronic hemodialysis.

CONCLUSION

While our understanding of vitamin D metabolism grows, many critical aspects of vitamin D levels and treatment regimens must be defined. In the management of SHPT in ESRD patients on hemodialysis, monthly administration of cholecalciferol appears to be simple, effective, and inexpensive, with no adverse effects. However, more randomized, controlled, large sample size studies are needed to well define the character of cholecalciferol in the treatment of SHPT in ESRD patients.

Conflict of interest: The authors have no conflict of interest.

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