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Research Article

EFFECT OF CALCIUM, ALFACALCIDOL AND HEMODIALYSIS ON SECONDARY HYPERPARATHYROIDISM

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ABSTRACT

Objective: Secondary hyperparathyroidism (SHPT) is the major complication of Chronic Renal Failure (CRF) patients. Our study aimed to evaluate the effect of the calcium carbonate and alfacalcidol with hemodialysis (HD) on SHPT in CRF patients.

Methods: Sixty CRF patients were collected from Center of Renal Diseases and Dialysis of Hodeidah, Yemen. They were diagnosed with SHPT and classified into three groups, the first group was treated by 1800 mg / day of calcium carbonate and 0.25 mcg /day of alfacalcidol with two HD sessions for 6 hours/week. The second group was treated by3600 mg /day of calcium carbonate and 1mcg /day of alfacalcidol with two HD sessions for 6 hours/week with . The third group was treated by 3600 mg /day of calcium carbonate and 1mcg /day of alfacalcidol with HD sessions for 12 hours/week. The biochemical assays of parathyroid hormone (PTH), serum calcium and serum phosphorous levels as indicators effect were carried out.

Results: The results showed after administration of calcium carbonate and alfacalcidol with HD that the PTH, serum calcium and serum phosphorus levels to be significantly different between three groups *($p < 0.05$)*. On the other hand, we observed in the first group significant enhance in PTH and serum phosphorus levels *($p < 0.05$)* while significant decrease *($p < 0.05$)* in serum calcium level *($p > 0.05$)* .We also observed in the second group that the PTH and serum phosphorus levels were not affected while significant decrease *($p < 0.05$)* in serum calcium level. However, the results of the third group showed that significant decrease *($p < 0.05$)* in PTH level and non-significant reduce *($p > 0.05$)* in serum phosphorus level while non-significant increase in serum calcium level *($p > 0.05$)*.

Conclusion: The findings showed high quality of HD therapy (12 hr/ week) lead to reduce of PTH and serum phosphorus levels with increase of serum calcium level .

Keywords : Secondary Hyperparathyroidism , Chronic Renal Failure , Hemodialysis , Calcium Bicrabonate , alfacalcidol , PTH , , Calcium , Phosphorus

INTRODUCTION

Chronic kidney disease (CKD) occurs when one suffers from gradual and usually permanent loss of kidney function over time. This happens gradually, usually over months to years. CKD is divided into five stages of increasing severity. Stage 5 CKD is also referred to as chronic renal failure (CRF) , end-stage kidney disease , wherein there is total or near-total loss of kidney function . [1-4] Also , CRF remains one of the most important public health problem in Yemen . Center of Renal Disease and Dialysis at Hodeidah city , Yemen receives 500 patients with CRF every year. [5]

In addition, the main causes of CRF were recorded in Yemen namely glomerulonephritis (25.4%) , obstructive nephropathy (13.7%), hypertension (11.8%), pyelonephrits (11.8%), diabetic nephropathy (7.8%), arthritis, malaria, vasculitis and postpartum hemorrhage (5.9% each) and Alport's syndrome (3.9%). [6]

On the other hand , CKD is accompanied by progressively impaired metabolism of calcium, phosphorus and vitamin D, eventually leading to secondary hyperparathyroidism (SHPT), a clinical syndrome of abnormal mineral bone metabolism and extra skeletal calcifications that is associated with an increased risk of renal osteodystrophy that is an alteration of bone morphology in renal failure patients .

SHPT is present in about 70% of people starting dialysis. [7-9] Consequently, SHPT in CRF patients require hemodialysis (HD) therapy and supplementation therapy (calcium and vitamin D) for prolonged periods of time.

Therefore, the aim of our study was to demonstrate the effect of different doses of calcium (calcium bicarbonate) and alfacalcidol on PTH level in CRF patients under regular HD with SHPT.

MATERIALS AND METHODS

Standards, chemicals and instruments

The materials of our study included kit of parathyroid hormones assay (Biotinylated Antibody reagent), kit of calcium assay (potassium cyanid with ethanolamine as reagent A , methylthymol blue with hydroxyquinoline as reagent B) , kit of phosphorus assay (diethanolamine with mangasium cholorid as reagent A , 4 – nitrophenylphosphate as reagent B), tube without anticoagulant (QCA Company , Aspain) , sphygmomanometer , Balance , Meter (China Brand), syringe , Tourniquet , lancets , and drugs were used namely calcium carbonate and alfacalcidol . Spectrophotometer (Spectro 23 , USA), Enzyme Linkage Sorbent Assay (ELIZA) of PR 3100 TSC – BioRed (Australia) . HD Machine 4008 (Fresenius Medical Care – Germany). In addition, drug products namely calcium bicarbonate 600 mg tablet, and alfacalcidol 0.25 cmg and 1 mcg were purchased from licensed pharmacy (Hodeidah City).

Study Design and Study Area

One hundreds CRF patients were selected randomly from center of renal disease and dialysis of Hodiedah City , Yemen . The PTH of these patients were assayed by medical laboratory . The results showed sixty SHPT in CRF patients that were used in this study .The personal data , age , sex , blood pressure (BP) , HD duration , drug history and clinical assessment namely muscle weakness , bone pain and back pain were recorded. On the other hand, these patients were classified into three groups. The 1st group: Twenty SHPT in CRF patients were treated with two HD sessions for six hours per week (wk) associated with calcium supplementation in form of calcium carbonate 1800 mg daily and alfacalcidol 0.25 mcg daily for three months. The 2nd group: Twenty SHPT in CRF patients were treated with two HD sessions for six hours per week associated with

calcium supplementation in form of calcium carbonate 3600 mg daily and alfacalcidol 1.0 mcg daily for three months. In the 3rd group : Twenty SHPT in CRF patients were treated with three HD sessions for twelve hours per week associated with calcium supplementation in form of calcium carbonate 3600 mg daily and alfacalcidol 1.0 mcg daily for three months.

The 2nd group: Twenty SHPT in CRF patients were treated with two HD sessions for six hours per week associated with calcium supplementation in form of calcium carbonate 3600 mg daily and alfacalcidol 1.0 mcd daily for three months. In the 3rd group : Twenty SHPT in CRF patients were treated with three HD sessions for twelve hours per week associated with calcium supplementation in form of calcium carbonate 3600 mg daily and alfacalcidol 1.0 mcd daily for three months .

Amount of Dialysis per Week

Amount of dialysis per wk was done by HD Machine and the procedure was as the following : HD time: 6 h/wk. HD bath: calcium 2.5 mEq/L, bicarbonate 35 mEq/L , potassium 2.0 mEq/L , magnesium 1.0 mEq/L , sodium 138 mEq/L and chloride 109.5 mEq/L . Adjust based on weekly measurements of electrolytes, calcium, and phosphorus. [10]

Biochemical Assays Procedures

Sample collection

The whole blood was collected without anticoagulant (serum). After allowing blood to clot , the serum was separated , preferably in a refrigerated centrifuge , and stored at – 20 C° or lower. Serum samples were stored up to 8 hours at 2 - 8 °C. Serum samples frozen at - 20 °C are stable for up to 4 months. Calcium in serum was stable for 10 days at 2 – 8 °C and phosphorus in serum was stable for 7 days at 2 – 8 °C. [11-13]

Parathyroid Hormone Assay

The assay was performed using ELIZA method and calculation was done using ELIZA PR 3100 TSC - Bio- Rad. The DRG Intact PTH measured by a two – site ELISA for the measurement of the biologically of 84- amino acid chain of PTH. One antibody was prepared to bind only the mid-region and C- terminal PTH 39-84 and this antibody was biotinylated . The other antibody was prepared to bind only the N- terminal PTH 1-34 and this antibody was labeled with horseradish peroxidase [HRP] for detection. Streptavidin Well – Biotinylated Anti–PTH (39-84) --- Intact PTH --- HRP conjugated Anti–PTH (1-34). Although mid – region and C-terminal fragments are bound by the biotinylated anti – PTH (39-84), only the intact PTH 1-84 forms the sandwich complex necessary for detection. The capacity of the biotinylated antibody and the streptavidin coated microwell both have been adjusted to exhibit negligible interference by inactive fragments, even at very elevated levels . In this assay , calibrators , controls and patient samples were simultaneously incubated with the enzyme labeled antibody and a biotin coupled antibody in a streptavidin coated microplate well . At the end of the assay incubation, the microwell was washed to remove unbound components and the enzyme bound to the solid phase was incubated with the substrate, tetramethylbenzidine (TMB). An acidic stopping solution was then added to stop the reaction and converts the color to yellow. The intensity of the yellow color was directly proportional to the concentration of intact PTH in the sample. A dose response curve of absorbance unit versus concentration was generated using results obtained from the calibrators. Concentration of intact PTH present in the controls and patient samples were determined directly from this curve. [11, 12]

Serum Phosphate Assay

Inorganic phosphorus in the sample reacts with molybdate in acid medium forming a phosphomolybdate complex that could be measured by spectrophotometry at 340 nm. [13]

Serum Calcium Assay

Total serum calcium concentration was quantified by MTB (Methylthymol Blue) methods. Calcium in the sample reacts with methylthymol blue in alkaline medium forming a coloured complex that could be measured by spectrophotometry. Hydroxyquinoline was included in the reagent to avoid magnesium interference. The absorbance was measured by using spectrophotometer Spectro 23 RS at 610 nm. [14]

Statistical Data Analysis

The differences between three groups were analysed by using descriptive analysis , student's t-test , analysis of variance (ANOVA) test and Chi square at $\alpha = 0.05$ .were used to explore the effect of the calcium, alfacalcidol and HD on CRF patient with SHPT.

RESULTS

Subjects

The background information of the clinical history on the sixty samples in three groups were summarized in table 1 . The personal data namely age, sex, blood pressure (BP), Body Mass Index (BMI) and HD duration were recorded and results showed that the age of the patients included in this study between 19 to 70 years with 2:1 male: female ratio. There was no correlation between age and PTH, phosphorus and calcium blood levels namely coefficient correlation (R^2) less than 0.995 (Table 2) However, the relationship between the gender and these parameters was not observed.. In addition, The BP was not significantly affected by these procedures and the BMI was found to be within normal value.

Table 1: Means of personal data

Parameters	1st group n = 20	2nd group n = 20	3rd group n = 20
Age (Year)	19 – 60	19 – 60	19 – 60
Sex			
• Male	13	12	15
• Female	7	8	5
BMI (Kg/m)	19.59 ± 5.35	19.99 ± 4.62	20.8 ± 5.19
Blood Pressure (mm Hg)			
• Before	179.5 / 85	181/86.5	178.5 / 87.5
• After	179.5 / 85.5	181 / 86	179.5 / 89
Dialysis Duration (Year)	7.75	4.9	5.35

Table 2: Relationship between PTH, serum phosphorus level and serum calcium level with age based on coefficient correlation (R^2)

Parameters	PTH level		Serum phosphorus level		Serum calcium level	
Groups	**Before**	**After**	**Before**	**After**	**Before**	**After**
1st group	0 .0945	0.2537	0.1691	0.0676	0.1591	0.2430
2nd group	0.0436	0.1474	0.2461	0.1562	0.1303	0.1599
3rd group	0.1983	0.0401	0.0258	0.3258	0.0692	0.2604

* (R^2) ≥ 0.995

Biochemical effects

The effect of calcium and alfacalcidol with HD on PTH, serum phosphorus and serum calcium levels were investigated in three groups and summarized in table 3. In the 1st group , the results presented show the mean of the PTH level before calcium and alfacalcidol with HD was 143.75 ± 29.64 pg/ml while the mean of the PTH level after treatment was 264.75± 89.74 pg/ml . The significant increase *(p < 0.05)* in PTH level due to non-response of this group for first protocol (HD sessions for 6 h /wk associated with calcium carbonate 1800 mg daily and alfacalcidol 0.25 mcg daily for three months in comparison with the 2nd and 3rd group (Table 2). On the other hand , we observed in the 1st group significant increase in serum phosphorus level *(p < 0.05)* namely from 5.37 ± 1.25 mg/dl to 6.975 ± 0.913 mg/dl and significant decrease *(p < 0.05)* in serum calcium level from 8.36 ± 0.97 mg/dl to 7.755 ± 0.93 mg/dl.

However, in the 2nd group, according to biochemical assays, we determined the PTH, serum phosphorus and serum calcium levels before and after treatment (HD sessions for 6 h /wk associated with calcium carbonate 3600 mg daily and alfacalcidol 1 mcg daily for three months) and the results proved non-significant decrease (p < 0.05) in PTH level namely from 304 ± 70.3 pg/ml to 299.25 ± 78.82 pg/ml and non-significant increase (p < 0.05) in serum phosphorus level namely 5.72 ± 1.39 mg/dl to 6.03 ± 1.176 mg/dl, while significant decrease *(p > 0.05)* in serum calcium level from 8.995 ± 0.94 mg/dl to 7.82 ± 0.63 mg/dl (Table 2).

While, the PTH, serum phosphorus and serum calcium levels were observed in the 3rd group before treatment and the results were (648.75 ± 208.6 pg/ml), (5.11 ± 1.56 mg/dl) and (8.55 ± 1.182 mg/dl), respectively, while the results were observed after treatment (HD sessions for 12 h /wk associated with calcium carbonate 3600 mg daily and alfacalcidol 1 mcg daily for three months) significant decrease *(p < 0.05)* in PTH level namely 450 .95 ± 201.09 pg/ml, non – significant decrease *(p > 0.05)* in serum phosphorus level namely 4.885 ± 1.454 mg/dl and non – significant increase *(p > 0.05)* in serum calcium level namely 9.135 ± 1.257 mg/dl.

Table 3: Means ± SD of biochemical parameters of patients

Grou *p*s	*P*TH	Serum *p*hos *p*horus	Serum Calcium
1st grou *p*			
• Before	143.75 ± 29.64	5.37 ± 1.25	8.36 ± 0.97
• After	264.75± 89.74	6.975 ± 0.913	7.755 ± 0.93
• *p* value (Intra-group)	*p* < 0.05	*p* < 0.05	*p* < 0.05
2nd grou *p*			
• Before	304 ± 70.3	5.72 ± 1.39	8.99 5 ± 0.94
• After	299.25 ± 78.82	6.03 ± 1.176	7.82 ± 0.63
• *p* value (Intra-group)	*p* > 0.05	*p* > 0.05	*p* < 0.05
3rd grou *p*			
• Before	648.75 ± 208.6	5.11 ± 1.56	8.55 ± 1.182
• After	450 .95 ± 201.09	4.885 ± 1.454	9.135 ± 1.257
• *p* value (Intra-group)	*p* < 0.05	*p* > 0.05	*p* > 0.05
p value (Intergrou *p*s)	*p* < 0.0	*p* < 0.05	*p* < 0.05

Clinical Effect

Change of clinical sym *p*toms among the treated grou *p*s at the start and the end of the study was recorded. In this study as shown in table 4. The clinical sym *p*toms, namely muscle weakness, bone *p*ain and back *p*ain were registered for each *p*atient before and after the *p*rocedure. In the 1stgrou *p*: Only the bone *p*ain was reduced in 10% of *p*atients, this was statistically insignificance *(p > 0.05)*. In 2nd grou *p*, only 15% of *p*atients ex *p*erienced reduction of muscle *p*ain (in significance change *(p > 0.05)*, with a significant reduction *(p > 0.05)* of bone *p*ain that was encountered in 20% of *p*atients while reduction of backache was found in 15% that was insignificant *(p > 0.05)*. Also, in the 3rd grou *p* showed that the treatment success was highest in this grou *p* in com *p*arison with 1st and 2nd that a significant reduction of muscle weakness (50 %), 65 % of bone *p*ain and 65 % of back *p*ain 65 % *(p < 0.05)*.

Table 4: Effect of Calcium, Alfacalcidol and Haemodialysis on clinical sym *p*toms

Clinical sym *p*toms		1st grou *p*	2nd grou *p*	3rd grou *p*	Inter-grou *p*s
Muscle weakness	Before	- 1	- 0	- 3	*p* > 0.05
		+ 19	+ 20	+ 17	
	After	- 1	- 3	- 13	
		+ 19	+ 17	+ 7	
		p > 0.05	*p* > 0.05	*p* < 0.05	
Bone *p*ain	Before	- 0	- 0	- 0	*p* > 0.05
		+ 20	+ 20	+ 20	
	After	- 2	- 4	- 13	
		+ 18	+ 16	+ 7	
		p > 0.05	*p* < 0.05	*p* < 0.05	
Back *p*ain	Before	- 3	- 5	- 0	*p* > 0.05
		+ 17	+ 15	+ 20	
	After	- 3	- 8	- 13	
		+ 17	+ 12	+ 7	
Intragrou *p*		*p* > 0.05	*p* > 0.05	*p* < 0.05	

+ : *P*ain
- : Non *p*ain

Finally, in the Table 2 and 3, the study included observation the effect of calcium and alfacalcidol with HD on biochemical assays and clinical sym *p*toms and the study *p*roved a significant difference between the three grou *p*s *(p < 0.05)*.

DISCUSSION

Minerals are very im *p*ortant for the human body. They have various roles in metabolism and body functions that are essential for the *p*ro *p*er function of cells, tissues and organs. Mineral metabolism disorders are marked by abnormal levels of minerals, either too much or too little, in the blood . [15,16] *P*atients who have severe CKD will eventually develo *p* kidney failure and will require HD. [3]

SH *P*T describes a com *p*lex alteration in bone and mineral metabolism that occurs as a direct result of CKD. [17] SH *P*T to CKD is due to over *p*roduction of *P*TH caused by hy *p*ocalcaemia and hy *p*er *p*hos *p*hatemia. The first changes that usually occur with declining kidney function involve decrease renal excretion of *p*hos *p*hate which will lead to increase *p*hos *p*horus blood level. The body will res *p*ond by several mechanisms to maintain the solubility *p*roduct of calcium and *p*hos *p*horus constant. This with other factors will lead to hy *p*ocalcaemia. On the other hand , the kidneys are the site of activation of vitamin D to the active form, in CKD there will be deficiency of activated vitamin D with subsequent im *p*airment of calcium absor *p*tion. Both decrease calcium and increase *p*hos *p*hate blood level will stimulate *P*TH secretion aiming to increase calcium level by many different mechanisms [18,19].

Hy *p*ocalcaemia,hy *p*er *p*hos *p*hatemia and im *p*aired renal 1,25-dihydroxyvitamin D synthesis with attendant reductions in serum calcitriol concentrations and decreases in vitamin D rece *p*tor ex *p*ression in the *p*arathyroid glands each contribute to excess *P*TH secretion in *p*atients with CRF.[7,19] All re *p*resent targets for thera *p*eutic interventions aimed at *p*reventing the develo *p*ment and controlling the *p*rogression of SH *P*T. [20,15] Des *p*ite the im *p*ortance of controlling *p*hos *p*horus retention and *p*reventing hy *p*er *p*hos *p*hatemia in *p*atients with CRF, current management strategies often are inadequate, *p*articularly in those ingesting diets containing adequate amounts of *p*rotein. [21, 22]

In this study, we aimed to demonstrate the effect of the different clinical measures a *p* *p*lied to treat SH *P*T in CRF *p*atients under regular HD. The various clinical measures include, in the 1st grou *p*, calcium bicarbonate 1800 mg/day , alfacalcidol 0.25 mcg/day and In the 2nd grou *p*, calcium bicarbonate 3600 mg/day, alfacalcidol 1 mcg/day and HD 6 h /wk. In the 3rd grou *p*, calcium bicarbonate 3600 mg/day, alfacalcidol 1 mcg/day and HD 12 hr /wk. There was no relationshi *p* observed between the gender (sex) and biochemical *p*arameters (*P*TH, serum *p*hos *p*horus and serum calcium levels). In com *p*arison with other studies, these relationshi *p* was recorded but it was statistically insignificant different between males and females. [23] Absence of relation between the sex and the *P*TH level may be ex *p*lained by the fact that *P*TH secretion is not controlled by any other endocrine gland. [23]

The relationshi *p* between the age and biochemical *p*arameters (*P*TH , serum *p*hos *p*horus and serum calcium levels) was evaluated and found that there is no correlation between any of these *p*arameters with the age and our results was su *p* *p*orted by *p*revious study [23] . In contrast to other study that re *p*orted an increase of *P*TH levels with the age. [24] Such difference may be attributed to differences in the HD regimens a *p* *p*lied.

Hy *p*ertension in CRF *p*atients on regular HD is known to be either rennin de *p*endent or volume de *p*endent or both. [2] In this study, it was found that the change in hy *p*ertension at the start of the study and by its end was not significant in all studied grou *p*s. This can be ex *p*lained either by insufficient HD hours to deal with volume de *p*endent hy *p*ertension or it is rennin de *p*endent hy *p*ertension. In our study, there was no correlation found between the hy *p*ertension and biochemical *p*arameters (*P*TH, serum *p*hos *p*horus and serum calcium levels), this is su *p* *p*orted by *p*revious study that demonstrated the absence of such correlation. [25] O *p* *p*osite view was re *p*orted in some studies that found a *p*ositive relationshi *p* between *P*TH and severe hy *p*ertension. [26] It is known that cardiovascular diseases (CVD) is consider the major cause of death among End Stage Renal Disease (ESRD) *p*atients , more than 50% of ESRD *p*atients died due to CVD [25]. In addition to traditional risk factor , *p*atients with CKD stage 3 onwards have also non-traditional risk factors mainly increase *P*TH, serum *p*hos *p*horus and serum calcium levels abnormalities that contribute to the *p*rocess of the wide s *p*read accelerated atherosclerosis that *p*lay a major factor in the *p*athogenesis of the different CVD events including hy *p*ertension. The intera- arteriolar atherosclerosis will lead to constriction of the arterioles , this together with high intracellular calcium will increased *p*eri *p*heral resistance that contributed largely in establishment and/or exaggeration of hy *p*ertension. This would ex *p*lain the need for immediate a *p* *p*ro *p*riate measures to control hy *p*er *p*arathyroidism vigorously. [27,25]

Few studies were done to demonstrate the effect of *P*TH on hy *p*ertension among the HD *p*atients and have been done on small scale *p*o *p*ulation and one of these was *p*erformed to assess the effect of *P*TH on the severity of hy *p*ertension among chronic HD *p*atients. [26] It was *p*ublished that ,in *p*atients with chronic high level of *P*TH, there is sustained hy *p*ertension.[28] On the other hand ,an ex *p*erimental study demonstrated the effect of *P*TH on hy *p*ertension in HD *p*atients, hy *p*otension was re *p*orted after acute ra *p*id *p*rescri *p*tion of *P*TH, this was attributed to arterial smooth muscles relaxation induced by *P*TH. [29] There are some re *p*orts indicating the *p*robable role of *P*TH in the genesis of hy *p*ertension in *p*rimary and SH *P*T other than CRF. [30]

In this study, there was no relationshi *p* found between serum calcium and B *P*, this was su *p* *p*orted by other study that demonstrated increased serum calcium and decreased serum *P*TH after oral calcium su *p* *p*lementation but B *P* did not differ, the study concluded that , in subjects with moderate SH *P*T , oral calcium su *p* *p*lementation has no effect on B *P*. [26] The clinical measures giving to *p*atients were aimed to normalize the *P*TH level through su *p* *p*lementation of active Vitamin D to su *p* *p*ress *p*arathyroid gland by feedback mechanism (decrease *P*TH), to increase serum calcium and to decrease serum *p*hos *p*horus [18,19].

In our study, in the 1st grou *p* , the *P*TH level did not decrease and its level was unex *p*ectedly increases that can be ex *p*lained by two com *p*onents: Ineffective inhibition of *P*TH by the feedback mechanism, may be due to the low dose of alfacalcidol given to *p*atient who may have already vitamin D deficiency and the other *p*arameters, namely hy *p*er *p*ho *p*hataemia and hy *p*ocalcaemia continue stimulation of *P*TH secretion. The low calcium level may be attributed to: the increase *p*hos *p*horus level necessitated the decrease of calcium level to kee *p* calcium * *p*hos *p*horus (solubility *p*roduct) constant and the low dose of calcium carbonate given to *p*atients in this grou *p* (1800mg/d) that may be *p*artially consumed as *p*hos *p*hate binder and /or to kee *p* calcium * *p*hos *p*horus *p*roduct constant. In this study, all *p*atients were educated to avoid high *p*hos *p*hate containing diet, some of them were receiving antacid containing aluminum hydroxide in irregular basis but no s *p*ecific measurement was considered in this study to reduce *p*hos *p*horus level .

In the 2nd grou *p*, the decrease in serum calcium was attributed to the mild increase in serum *p*hos *p*horus in attem *p*t to maintain constant *p*roduct (calcium * *p*hos *p*horus). Analysis of the result in the 2nd grou *p* showed: in s *p*ite of increase the calcium dose, yet calcium level did not increase and *p*hos *p*horus did not decrease which mean these two *p*arameters continue stimulation of *P*TH secretion. Com *p*aring the 1st grou *p* and the 2nd grou *p*, the HD *p*arameter was fixed, twice –weekly for both grou *p*s. The other *p*arameters namely calcium and alfacalcidol were given in different doses. It was found, no change in the behavior of calcium and *p*hos *p*horus levels in res *p*onse to increase dosages of alfacalcidol and calcium (in both grou *p*s, *p*hos *p*horus increased and calcium decreased) in contrast, the level of *P*TH was no found to be reduced in the 2nd grou *p*. From the above, we concluded that the initial reduction of *P*TH level (although not significant) was due to *p*artial block of *P*TH secretion by feedback mechanism initiated by Vitamin D Rece *p*tor (VDR) agonist [31,32] , alfacalcidol, when its dosage increased to 1mcg daily. that is a crucial *p*arameter in treating SH *P*T , but dosing needs to be o *p*timized for each *p*atient because the *p*atient res *p*onds in an individualized manner to treatment to su *p* *p*ress and stabilize *P*TH level [33,34].

Careful analysis of the *P*TH levels and the individual res *p*onse to alfacalcidol in the 2nd grou *p*, we believe that VDR agonists effectively treat SH *P*T, but dosing needs to be o *p*timized for each *p*atient because the *p*atient res *p*onds in an individualized manner to treatment to su *p* *p*ress and stabilize *P*TH levels. [33,34,22] Com

*p*aring the 2nd grou *p* and the 3rd grou *p*: two *p*arameters were fixed namely calcium and alfacalcidol dosages given to *p*atients were the same and the only different *p*arameter was the number of HD sessions *p*er wk, where two sessions a *p p*lied to the 2nd grou *p* and three sessions for the 3rd grou *p*.

Regarding the 3rd *p*arameter, calcium su *p p*lementation, there was significant increase re *p*orted in this study. It was re *p*orted that the *p*otential role of exogenous calcium loading as a contributor to the develo *p*ment and *p*rogression vascular calcification argues strongly against the sustained administration of su *p*ra *p*hysiological doses of calcium to *p*atient with little or no residual renal function and to those treated with HD. Finally , the im *p*ortant *p*arameter to take is to lower serum *p*hos *p*horus by different measures the most effective was the thrice-weekly HD, that are considered only marginally adequate to control hy *p*er *p*hos *p*hataemia. This effect was clarified in the 3rd grou *p* where *P*TH secretion was su *p p*ressed and attributed mainly to dialysis induced hy *p*o *p*hos *p*hatemia. Due to the high incidence of ESRD in Yemen, and the limited number of HD machines in the country, the HD regimen is insufficient. For the limitations of current HD strategies, the ongoing use of *p*hos *p*hate binding medications re *p*resents the *p*rimary intervention to manage *p*hos *p*horus retention in *p*atients with ESRD [35,36] From the above, we concluded that the HD duration *p*lays a major role in treatment of SH *P*T. Its effect on these *p*arameters was attributed to HD induced hy *p*o *p*hos *p*hatemia, which reduces *p*arathyroid cell *p*roliferation, *P*TH synthesis and directly decreases its secretion. It does so indirectly through the subsequent increase in serum calcium. [37,38,39,34]

CONCLUSION

CRD has a negative effect on *p*arathyroid gland. It is associated with an increased risk of *P*TH namely SH *P*T. The negative effect on *P*TH level due to the absent of o *p*timum a *p p*lication of K/DOQI guideline and thera *p*eutic for mineral metabolism in HD *p*atients. CRD may induce *P*TH and serum *p*hos *p*horus levels and decreases serum calcium level and these changes cause disorder in metabolism and function of body namely in bone through renal osteodystro *p*hy that is an alteration of bone mor *p*hology in *p*atients with CKD . Su *p p*lementation of VDA rece *p*tor (alfacalcidol 1 mcg) and calcium (calcium bicarbonate 3600 mg) may re *p*lace the body and the HD reduces *P*TH level that *p*lays a major role in treatment of SH *P*T. In brief , HD induces hy *p*o *p*hos *p*hatemia , which reduces *p*arathyroid cell *p*roliferation, *P*TH synthesis and directly decreases its secretion. It does so indirectly through the subsequent increase in serum calcium level.

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