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Comparative Study between Parathyroidectomy and Medical Treatment for Hemodialysis Patients with Secondary Hyperparathyroidism and their Effect on Anemia

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ABSTRACT

Background: One of the most significant complications of chronic renal disease is secondary hyperparathyroidism (SHPT).It is still a debate to determine the treatment regimens of SHPT for every particular patient and the parameters used for follow-up.

Objective: This study aimed to compare parathyroidectomy and medical treatment of SHPT in hemodialysis patients to determine which line of treatment is more effective and to assess the effect of treatment on anemia.

Patients and methods: This cohort retrospective study included 60 patients of end stage renal disease (ESRD) on regular hemodialysis above the age of 18 years old, of both sexes, with duration of hemodialysis more than one year, duration of treatment more than 6 months and intact parathyroid hormone (iPTH) more than 800 pg/ml. Patients were classified into three equal groups: Group 1 (parathyroidectomy group), group 2 who were on cinacalcet medical treatment and group 3 who were on conventional medical treatment vitamin D analogues.

Results: In 12 months- post- management, there were comparable findings between the groups at calcium levels. However, phosphorus, iPTH and alkaline phosphatase levels were substantially elevated in vit D analogues group and lower in parathyroidectomy group. Hemoglobin levels were substantially elevated in both parathyroidectomy and cinacalcet groups when compared with vit D analogues group at 12 months post-management.

Conclusions: Parathyroidectomy is more effective than medical treatment for hemodialysis patients with SHPT.

Keywords: Anemia, Hemodialysis, Parathyroidectomy, Secondary hyperparathyroidism.

INTRODUCTION

One of the leading global health concerns with major consequences, the prevalence of ESRD and the need for frequent hemodialysis is increasing annually. In their 9th Annual Report, the Egyptian Society of Nephrology and Transplantation (ESNT) reported that the incidence of ESRD in Egypt had risen to 483 cases per million people. Hemodialysis is the primary therapy for ESRD, a major health concern in Egypt [(1)].

Secondary hyperparathyroidism (SHPT) is a significant complication associated with CKD and ESRD. CKD leads to phosphate retention owing to impaired excretion in the proximal tubules, and the kidneys are incapable of converting vitamin D into its biologically active form. These in addition to hypocalcemia lead to overproduction of parathyroid hormone as a result of parathyroid gland hyperstimulation [(2)].

Management helps to enhance the outcome and lower the consequences; SHPT is linked with risk of high bone turnover, which results in bone mineral disorders, vascular calcification, risk of fracture, cardiovascular morbidities and death [(3)]. Treatment of SHPT follow these options: Control of hyperphosphatemia by diet restriction of phosphate or phosphate binders, control of PTH by using vitamin D analogues or calcimimetics and after failure of pharmacotherapy parathyroidectomy is the last line [(4)].

There is still a debate to determine the therapeutic regimens for SHPT for every particular patient and the parameters used for follow up. Controversy about the choice of active vitamin D and calcimimetics to lower PTH level due to their side effects, which may limit their long use but both of them are effective to decrease PTH [(5)].

One of the major and frequent side effects of regular hemodialysis in patients is anemia, which results from many causes including decreased synthesis of erythropoietin (EPO), resistance to EPO and shorter half-life of RBCs through accumulation of high level of PTH [(6)].

Treatment of SHPT among hemodialysis patients using either calcimimetics, vitamin D receptor activators or parathyroidectomy will improve anemia [(7)]. Calcimimetics improves the effect of EPO stimulating agents and decrease the resistance by decreasing bone marrow fibrosis [(8)]. Either enhanced EPO production or response improvement, parathyroidectomy as a line of therapy for SHPT in ESRD reduces anemia and uses of exogenous EPO. Therefore, refractory ESRD-related anemia indicated to be a sign for parathyroidectomy [(9)].

This work aimed to compare parathyroidectomy and medical treatment of SHPT to determine which line of treatment in SHPT is more effective on laboratory parameters and clinical symptoms and to assess the management effect of SHPT on anemia.

PATIENTS AND METHODS

This retrospective cohort research included 60 patients over 18 years of age, of both genders, who were diagnosed with ESRD and undergoing regular hemodialysis for over one year, with a treatment

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duration exceeding six months and S iPTH levels more than 800 pg/ml.

Exclusion criteria: hemodialysis duration less than one year, patients undergoing peritoneal dialysis, a therapy duration of less than six months, patients with advanced or decompensated liver disease, and those with malignancy or active severe persistent infections throughout the trial period.

Patients were categorized into three equal groups: Group 1 (parathyroidectomy group), group 2 who were treated with cinacalcet and group 3 who received traditional medical therapy with vitamin D analogues.

All patients had comprehensive history taking and laboratory investigations, including CBC, serum phosphorus, calcium, iPTH, alkaline phosphatase, albumin, ferritin, transferrin saturation, and CRP. Serum phosphorus, calcium, albumin, alkaline phosphatase, transferrin saturation, and C-reactive protein were analyzed using the Beckman Coulter AU480 semi-automated chemistry analyzer. Complete blood count was performed with the automated cell counter Micros 60 by Horiba, USA. Serum iPTH and serum ferritin were analyzed using the Tosoh AIA 900, Tokyo, Japan.

Ethical approval: The research was conducted following approval from The Ethical Committee of Tanta University Hospitals, Tanta, Egypt. The research was executed in compliance with the Declaration of Helsinki. The patients duly signed informed consent forms. This work has been carried out in accordance with The Code of Ethics of the World Medical Association (Declaration of Helsinki) for studies involving humans.

Statistical analysis

Statistical analysis was performed utilizing SPSS version 26 (IBM Inc., Chicago, IL, USA). The means and standard deviations of quantitative variables were compared among the three groups utilizing ANOVA, succeeded by a Tukey post hoc test. The qualitative variables were examined using the Chi-square test and reported as frequency and percentage (%). A two-tailed P value ≤ 0.05 was deemed as statistically significant.

RESULTS

The mean of duration of dialysis of included patients was 11 ± 5.7 (years) and as regards the underlying cause of CKD diabetes mellitus was the most common cause (25%) (Table 1).

Table (1): Demographic data for studied patients

		N=60
Age (years)		47.83±11.68
Sex	**Male**	33(55.0%)
	Female	27(45.0%)
Duration of dialysis (years)		11±5.71
Cause of CKD	**DM**	15 (25.0%)
	HTN	12 (20.0%)
	Obstructive uropathy	6 (10.0%)
	Glomerular diseases	9 (15.0%)
	Lupus nephritis	5 (8.3%)
	ADPKD	3 (5.0%)
	Drug induced (interstitial)	2 (3.3%)
	Alport syndrome	1 (1.7%)
	Uncertain cause	7 (11.6%)

Data are presented as mean ± SD or frequency (%). CKD: chronic kidney disease, DM: diabetes mellitus, HTN: hypertension, ADPKD: Autosomal dominant polycystic kidney disease.

In terms of pre-management, serum calcium levels were markedly elevated in the Parathyroidectomy group compared to the remaining groups ($P<0.05$). PO_4^{3-}, serum albumin, CBC, serum ferritin, Tsat, and CRP were comparable between the parathyroidectomy group and the cinacalcet group. The iPTH and ALP levels in the parathyroidectomy group exhibited no significant change when compared to the cinacalcet group. Nonetheless, the levels of iPTH and ALP in the parathyroidectomy group were markedly elevated compared to the vit D analogues group. Upon comparison of all groups, iPTH and ALP levels were markedly elevated in the parathyroidectomy group ($P<0.05$) (Table 2).

Table (2): Comparison of laboratory investigations among the three groups pre-management

	Parathyroidectomy (n= 20)	**Cinacalcet (n= 20)**	**Vit. D analogues (n= 20)**	**Test of sig.**	**P**
S. Calcium (mg/dL)	9.58±0.5	9.31±0.81	8.74±0.94	F=6.165	**0.004***
	P1=0.515, **P2=0.003*,** P3=0.059				
PO_4 (mg/dL)	5.59±0.92	5.35±1.07	5.01±1.07	F=1.625	**0.206**
	P1=0.739, P2=0.181, P3=0.548				
iPTH (pg./mL)	2111.75±68.82	1907.9±83.19	1217.05±220.64	F=14.96	**<0.001***
	P1=0.465, **P2<0.001*, P3<0.001***				
Alkaline phosphatase activity (U/L)	775.85±31.32	580.15±15.39	466.85±67.16	F=5.225	**0.008***
	P1=0.116, **P2=0.006*,** P3=0.475				
Albumin(g/dL)	4.03±0.15	3.90±0.16	3.97±0.26	F=1.145	0.268
	P1=0.197, P2=0.231, P3=0.961				
Hb (g/dL)	9.14 ± 1.06	9.21 ± 1.09	9.17 ± 1.13	F=0.0206	0.979
	P1=0.978, P2=0.996, P3=0.993				
WBCs (cells/µL)	5.37 ± 1.5	6.31 ± 1.86	6.27 ± 1.43	F=2.186	0.122
	P1=0.163, P2=0.189, P3=0.997				
Platelets (K/µL)	263.25 ± 62.64	284.05 ± 56.7	293.05 ± 76.12	F=0.5677	0.57
	P1=0.749, P2=0.556, P3=0.947				
Ferritin (ng/mL)	154.2 ± 13.32	180.2 ± 41.85	180.8 ± 33.72	F=0.1901	0.827
	P1=0.858, P2=0.852, P3=1.235				
Tsat (%)	21.25 ± 8.52	23.57 ± 9.9	17.32 ± 7.21	F=2.6907	0.077
	P1=0.673, P2=0.326, P3=0.07				
C- reactive protein(mg/L)	6.54 ± 1.94	6.04 ± 1.26	7.05 ± 1.53	F=0.238	0.789
	P1=0.938, P2=0.935, P3=0.77				

Data are presented as mean ± SD. * significant p value <0.05, P1: Parathyroidectomy versus Cinacalcet, P2: Parathyroidectomy versus Vit. D analogues, P3: Cinacalcet versus Vit. D analogues, f: ANOVA test, S: serum, PO_4^{3-}**:** phosphorus, iPTH: intact parathyroid hormone, Hb: hemoglobin, WBCs; white blood cell, Tsat: transferrin saturation.

Six months post-management, serum calcium, phosphate, iPTH, and ALP levels were considerably lower in the parathyroidectomy group compared to the other groups (P<0.05). Serum albumin and CBC were comparable across groups in all comparisons. T.sat was markedly reduced in the vit D analogues group compared to the other groups (P<0.05) (Table 3).

Table (3): Comparison of laboratory investigations among the three groups 6 months post-management

	Parathyroidectomy (n= 20)	**Cinacalcet (n= 20)**	**Vit. D analogues (n= 20)**	**Test of sig.**	**P**
S. Calcium (mg/dL)	7.83 ± 0.78	8.53 ± 0.9	9 ± 0.81	F=10.026	**<0.001***
	P1=0.03*, **P2<0.001*,** P3=0.18				
PO_4 (mg/dL)	3.67±1	5.29±1.16	5.67±1.17	F=18.223	**<0.001***
	P1<0.001*, P2<0.001*, P3=0.53				
iPTH (pg./mL)	130.9 ± 7.74	1387 ± 16.7	962.05±78.31	F=44.434	**<0.001***
	P1<0.001*, P2<0.001*, P3=0.008*				
Alkaline phosphatase activity (U/L)	187.95 ± 25.02	441.5 ± 291.49	330.75±64.48	F=7.595	**0.001***
	P1<0.001*, P2=0.08, P3=0.215				
Albumin(g/dL)	3.99±0.146	3.90±0.264	3.93±0.192	F=1.145	0.371
	P1=0.174, P2=0.325, P3=0.704				
Hb (g/dL)	10.07 ± 0.23	10.04 ± 0.67	9.54±0.99	F=0.0206	0.09
	P1=0.993, P2=0.123, P3=0.153				
WBCs (cells/µL)	5.6 ± 1.62	6.3 ± 1.3	5.76±1.43	F=0.811	0.449
	P1=0.449, P2=0.954, P3=0.619				
Platelets (K/µL)	262.6 ± 7.84	298.25±22.15	277.05±64.75	F=0.79	0.459
	P1=0.429, P2=0.869, P3=0.739				
Ferritin (ng/mL)	167.4±15.67	178.35±14.55	161.65±12.16	F=0.097	0.908
	P1=0.957, P2=0.988, P3=0.902				
Tsat (%)	24.7±5.94	24.3 ± 5.24	17.96 ± 4.2	F=4.296	**0.02***
	P1=0.987, **P2=0.03*, P3=0.04***				
C- reactive protein(mg/L)	6.63 ± 1.42	4.38 ± 1.08	4.88 ± 1.18	F=1.486	0.235
	P1=0.237, P2=0.414, P3=0.929				
	P1=0.1, P2=0.09, P3=0.99				

Data are presented as mean ± SD. * Significant p value <0.05, P1: Parathyroidectomy versus Cinacalcet, P2: Parathyroidectomy versus Vit. D analogues, P3: Cinacalcet versus Vit. D analogues, f: ANOVA test, S: serum, PO_4: phosphorus, iPTH: intact parathyroid hormone, Hb: hemoglobin, WBCs; white blood cell, Tsat: transferrin saturation.
After 12 months of treatment, s ca^{2+} and albumin levels exhibited no significant differences between the groups. The PO_4^{3-} level was markedly elevated in the vit D analogues group compared to the cinacalcet group (P < 0.001). The iPTH level was markedly elevated in the cinacalcet and vit D analogues groups compared to the parathyroidectomy group (P<0.001). Nevertheless, no substantial difference was seen between the cinacalcet and vit D mimics groups. The ALP level was markedly elevated in the cinacalcet and vit D analogues groups compared to the parathyroidectomy group (P < 0.001) (Table 4).

Table (4): Comparison of laboratory investigations among the three groups 12 months post-management

	Parathyroidectomy (n= 20)	**Cinacalcet (n= 20)**	**Vit. D analogues (n= 20)**	**Test of sig.**	**P**
S. Calcium (mg/dL)	8.86 ± 0.69	8.61 ± 0.93	9.3 ± 1.14	F=2.7729	0.07
	P1=0.68, P2=0.31, P3=0.06				
PO_4 (mg/dL)	4.01 ± 1.01	5.22 ± 1.06	6.62 ± 1.31	F=26.52	**<0.001***
	P1=0.004*, P2<0.001*, P3<0.001*				
iPTH (pg./mL)	81.24 ± 5.07	950.9 ± 84.37	1030.6±29.06	F=51.8	**<0.001***
	P1<0.001*, P2<0.001*, P3=0.72				
Alkaline phosphatase activity (U/L)	97.15 ± 4.19	286.1 ± 16.3	375.25±29.51	F=14.37	**<0.001***
	P1=0.002*, P2<0.001*, P3=0.22				
Albumin(g/dL)	4.06 ± 0.22	3.90 ± 0.19	4.01 ± 0.23	F=0.992	0.377
	P1=0.924, P2=0.247, P3=0.21				
Hb (g/dL)	10.94 ± 0.65	10.92 ± 0.72	9.88 ± 0.98	F=11.6	**0.001***
	P1=0.997, **P2<0.001*, P3<0.001***				
WBCs (cells/µL)	5.23 ± 1.33	5.84 ± 1.9	5.94 ± 1.11	F=0.901	0.41
	P1=0.54, P2=0.43, P3=0.98				
Platelets (K/µL)	257.3±6.91	264.55±13.43	315±8.6	F=2.776	0.07
	P1=0.96, P2=0.09, P3=0.15				
Ferritin (ng/mL)	183.9±13.51	235.2±16.5	188.1±16.93	F=0.588	0.56
	P1=0.59, P2=0.99, P3=0.64				
Tsat (%)	29.4±3.58	29.07±3.13	21.17±1.01	F=5.798	**0.005***
	P1=0.99, **P2=0.01*, P3=0.01***				
C- reactive protein (mg/L)	6.78±2.11	4.33±1.48	4.24±1.52	F=3.01	0.06
	P1=0.1, P2=0.09, P3=0.99				

Data are presented as mean ± SD. * Significant p value <0.05, P1: Parathyroidectomy versus Cinacalcet, P2: Parathyroidectomy versus Vit. D analogues, P3: Cinacalcet versus Vit. D analogues, f: ANOVA test, S: serum, Po_4: phosphorus, iPTH: intact parathyroid hormone, Hb: hemoglobin, WBCs; white blood cell, Tsat: transferrin saturation.

Regarding pre-management, itching, bone discomfort, fractures, blood transfusions, EPO per week and anemic symptoms, the parathyroidectomy and cinacalcet groups revealed comparable findings. The parathyroidectomy group had a significantly higher itching than the vit. D analogues group (P= 0.04).

With P< 0.05, bone discomfort was considerably higher in both groups than in the vit. D mimics group (P<0.05). Regarding six months after care, itching was much higher in the vit D analogues group than in the parathyroidectomy group (P < 0.001) and much higher in the cinacalcet group (P = 0.047). For bone pain, fractures, blood transfusions, EPO dose per week or anemic symptoms, the three groups showed no significant variations (Table 5).

Table (5): Comparison between the three groups regarding clinical data pre- management and 6 months post-management

	Parathyroidectomy (n= 20)	**Cinacalcet (n= 20)**	**Vit. D analogues (n= 20)**	**Test of sig.**	**P**
Pre- management					
Itching (No of pts%)	9 (45%)	4 (20%)	3 (15%)	X^2=5.284	0.07
	P1=0.09, **P2=0.04*,** P3=0.677				
Bone pain (No of pts%)	13 (65%)	14 (70%)	6 (30%)	X^2=7.677	**0.02***
	P1=0.739, **P2=0.03*, P3=0.01***				
Fractures (No of pts%)	3 (15%)	3 (15%)	0 (0%)	X^2=3.333	0.189
	P1=1, P2=0.07, P3=0.07				
Blood transfusion (No of pts%)	5 (25%)	4 (20%)	4 (20%)	X^2=0.196	0.907
	P1=0.705, **P2=0.705,** P3=1				
Epo (wk.- dose per week)	2.85 ± 0.49	2.9 ± 0.45	2.8 ± 0.62	F=0.181	0.835
	P1=0.951, P2=0.951, P3=0.819				
Anemia symptoms	12 (60%)	6 (30%)	9 (45%)	X^2=3.636	0.162
	P1=0.057, P2=0.342, P3=0.327				
6 months post- management					
Itching (No of pts%)	0 (0%)	4 (20%)	10 (50%)	X^2=14.161	**<0.001***
	P1=0.035*, P2<0.001*, P3=0.047*				
Bone pain (No of pts%)	7 (35%)	8 (40%)	7 (35%)	X^2=0.144	0.931
	P1=0.744, P2=1, P3=0.744				
Fractures (No of pts%)	0 (0%)	1 (5%)	0 (0%)	X^2=2.034	0.362
	P1=0.311, P2=--, P3=0.311				
Blood transfusion (No of pts%)	1 (5%)	1 (5%)	3 (15%)	X^2=1.745	0.418
	P1=1, P2=0.292, P3=0.292				
Epo (wk.- dose per week)	2.5 ± 0.89	2.5±0.76	2.65±0.88	F=0.2099	0.811
	P1=1, P2=0.841, P3=0.841				
Anemia Symptoms	4 (20%)	4 (20%)	5 (25%)	X^2=0.196	0.907
	P1=1, P2=0.705, P3=0.705				

Data are presented as mean ± SD or frequency (%). * Significant p value <0.05, P1: Parathyroidectomy versus Cinacalcet, P2: Parathyroidectomy versus Vit. D analogues, P3: Cinacalcet versus Vit. D analogues, f: ANOVA test, x2: qui square test. No of pts: Number of patients, Epo: erythropoietin, wk: week.

Regarding 12 months post-management, bone discomfort, itching, EPO dose per week, and anemic symptoms, the vit D analogues group had notably higher than the parathyroidectomy group and cinacalcet group (P<0.05). For fractures or blood transfusions, there were no significant variations among the groups (Table 6).

Table (6): Comparison between the three groups regarding clinical data 12 months post- management

	Parathyroidectomy (n= 20)	**Cinacalcet (n= 20)**	**Vit. D analogues (n= 20)**	**Test of sig.**	**P**
Itching (No of pts%)	0 (0%)	3 (15%)	14 (70%)	X^2=26.76	**<0.001***
	P1=0.07**, P2<0.001*, P3<0.001***				
Bone pain (No of pts%)	1 (5%)	4 (20%)	12 (60%)	X^2=15.92	**<0.001***
	P1=0.15, **P2<0.001*, P3=0.009***				
Fractures (No of pts%)	1 (5%)	0 (0%)	1 (5%)	X^2=1.034	0.59
	P1=0.31, P2=1, P3=0.31				
Blood transfusion (No of pts%)	0 (0%)	0 (0%)	2 (10%)	X^2=4.138	0.1263
	P1=--, P2=0.15, P3=0.15				
Epo (wk.- dose per week)	1.1±1.07	1.25±1.25	2.55±1	X^2=10.29	**<0.001***
	P1=0.905, **P2<0.001*, P3<0.001***				
Anemia Symptoms	0 (0%)	1 (5%)	7 (35%)	X^2=12.40	**0.002***
	P1=0.31, **P2=0.004*, P3=0.02***				

Data are presented as mean ± SD or frequency (%). * Significant p value <0.05, P1: Parathyroidectomy versus Cinacalcet, P2: Parathyroidectomy versus Vit. D analogues, P3: Cinacalcet versus Vit. D analogues, X^2: qui square test. No of pts: Number of patients, Epo: erythropoietin, wk: week.

In parathyroidectomy group, serum calcium, PO_4^{3-}, iPTH and ALP were significantly higher in pre-management evaluation than in 6 months post-management evaluation. S ca^{2+} was significantly increased in 12 months post-management evaluation compared to the 6-month assessment (P <0.001). PO_4^{3-}, iPTH, ALP were insignificantly different at 6- and 12-months post-management evaluation. PO_4^{3-} was significantly decreased when compared to post-management and pre-management group. ALP levels were consistently higher in the pre-group when assessing all time points. Serum albumin, WBCs, Plt, s. ferritin and CRB were insignificantly different between both groups. Hb levels were significantly higher in the 6-month post-management evaluation than in pre-management evaluation and in 12 months than in 6 months. T.sat was significantly higher in 12 months post-management than in pre-management (P=0.01) and did not exhibit significant differences between groups at any time point (Table 7).

Table (7): Comparison of laboratory investigations of time data in parathyroidectomy group

	Pre-management	**6 months**	**12 Months**	**Test of sig.**	**P**
S. Calcium (mg/dL)	9.58 ± 0.5	7.83 ± 0.78	8.86 ± 0.69	F=34.78	**<0.001***
	P1<0.001*, P2=0.003*, P3<0.001*				
PO_4 (mg/dL)	5.59 ± 0.92	3.67 ± 0.1	4.01 ± 1.01	F=21.97	**<0.001***
	P1<0.001*, P2<0.001*, P3=0.52				
iPTH (pg./mL)	2111.75±46.82	130.9±7.74	81.24±5.07	F=352.17	**<0.001***
	P1=0.009*, P2=0.02*, P3=0.84				
ALP activity (U/L)	775.85±31.32	187.95±25.02	97.15±4.19	F=64.04	**<0.001***
	P1<0.001*, P2<0.001*, P3=0.35				
Albumin(g/dL)	4.03 ± 0.15	3.99 ± 0.14	4.06 ± 0.22	F=0.665	**0.518**
	P1=0.48, P2=0.66, P3=0.25				
Hb (g/dL)	9.14 ± 1.06	10.07 ± 0.83	10.94 ± 0.65	F=21.75	**<0.001***
	P1=0.003*, P2<0.001*, P3=0.007*				
WBCs (cells/µL)	5.37±1.5	5.6±1.62	5.23±1.33	F=0.3152	0.73
	P1=0.88, P2=0.95, P3=0.71				
Platelets (K/µL)	263.25±7.64	262.6±7.84	257.3±6.91	F=0.0424	**0.96**
	P1=1.07, P2=0.96, P3=0.97				
Ferritin (ng/mL)	154.2±13.32	167.4±15.67	183.9±13.51	F=0.2455	0.78
	P1=0.95, P2=0.76, P3=0.92				
Tsat (%)	21.25 ± 4.52	24.7 ± 4.94	29.4 ± 5.58	F=4.441	**0.01***
	P1=0.43, **P2=0.01*,** P3=0.21				
CRP (mg/L)	6.54±1.94	6.63±1.42	6.78±1.11	F=0.014	0.99
	P1=0.99, P2=0.98, P3=0.99				

Data are presented as mean ± SD. * Significant p value <0.05, P1: Pre versus 6 months, P2: P Pre versus 12 Months, P3: 6 months versus 12 Months, f: ANOVA test, S: serum, PO_4: phosphorus, iPTH: intact parathyroid hormone, ALP: alkaline phosphatase, Hb: hemoglobin, WBCs; white blood cell, Tsat: transferrin saturation, CRP: C- reactive protein.

In cinacalcet group, s. Ca^{2+} and iPTH level were significantly higher in pre-management evaluation than 6- and 12-months post management, while no significant difference between 6- and 12-month evaluation. PO_4^{3-} and serum albumin were insignificantly different between subsequent time points. ALP was insignificantly different between in pre-management evaluation and 6 months post-management and between 6- and 12-months post-management, while was significantly higher in pre-management evaluation than in 12 months post-management (P<0.05). Hb levels were significantly higher in the 6-month post-management evaluation than in the pre-management levels (P = 0.008). At 12 months, it was significantly higher than in 6-month post-management and comparing all time points (P<0.001) (Table 8).

Table (8): Comparison of laboratory investigations of time data in cinacalcet group

	Pre-management	6 months	12 Months	Test of sig.	P
S. Calcium (mg/dL)	9.31±0.81	8.53±0.9	8.61±0.93	F=4.7396	**0.01***
	P1=0.02*, P2=0.04*, P3=0.96				
PO_4 (mg/dL)	5.35 ± 1.07	5.29 ± 1.16	5.22 ± 1.06	F=0.0703	**0.93**
	P1=0.98, P2=0.93, P3=0.98				
iPTH (pg./mL)	1907.9±73.19	1387±16.7	950.9±44.37	F=10.115	**<0.001***
	P1=0.046*, P2<0.001*, P3=0.11				
ALP activity (U/L)	580.15±15.39	441.5±21.49	286.1±16.3	F=5.823	**0.005***
	P1=0.25**, P2=0.003*,** P3=0.18				
Albumin(g/dL)	3.90±0.16	3.90±0.26	3.90±0.20	F=0.004	0.996
	P1=0.94, P2=1.00, P3=0.94				
Hb (g/dL)	9.21 ± 1.09	10.04 ± 0.67	10.92 ± 0.72	F=20.355	**<0.001***
	P1=0.008*, P2<0.001*, P3=0.005*				
WBCs (cells/µL)	6.31 ± 1.86	6.3 ± 1.3	5.84 ± 1.9	F=0.35	0.71
	P1=0.79, P2=0.75, P3=0.75				
Platelets (K/µL)	284.05±16.7	298.25±22.15	264.55±13.43	F=0.4377	0.65
	P1=0.92, P2=0.85, P3=0.62				
Ferritin (ng/mL)	180.2±6.85	178.35±4.55	235.2±7.5	F=0.8884	0.42
	P1=0.99, P2=0.49, P3=0.47				
Tsat (%)	23.57 ± 5.9	24.3 ± 5.24	29.07 ± 4.13	F=2.47	0.09
	P1=0.96, P2=0.11, P3=0.19				
CRP (mg/L)	6.04 ± 1.26	4.38 ± 1.08	4.33 ± 1.48	F=1.4297	0.25
	P1=0.33, P2=0.31, P3=1.01				

Data are presented as mean ± SD. * Significant p value <0.05, P1: Pre versus 6 months, P2: P Pre versus 12 Months, P3: 6 months versus 12 Months, f: ANOVA test, S: serum, PO_4: phosphorus, iPTH: intact parathyroid hormone, ALP: alkaline phosphatase, Hb: hemoglobin, WBCs; white blood cell, Tsat: transferrin saturation, CRP: C- reactive protein.

In Vit. D analogues group, s.ca^{2+}, ALP, Albumin, CBC, CRP, T.sat and s. ferritin were insignificantly different among the groups. PO_4^{3-} levels were insignificantly different in the pre-management and 6 months post-management, while was significantly higher in 6 months post-management than pre-management and in 6 months post-management than in 12 months post-management (P<0.05). iPTH was significantly higher in pre-management than in 6- and 12-months post management (Table 9).

Table (9): Comparison of laboratory investigations of time data in vit. D analogues group

	Pre-management	6 months	12 Months	Test of sig.	P
S. Calcium (mg/dL)	8.74 ± 0.94	9 ± 0.81	9.3 ± 1.14	F=1.659	0.19
	P1=0.68, P2=0.17, P3=0.59				
PO_4 (mg/dL)	5.01 ± 1.07	5.67 ± 1.17	6.62 ± 1.31	F=9.2915	**<0.001***
	P1=0.19, **P2<0.001*, P3=0.04***				
iPTH (pg./mL)	1217.05±20.64	962.05±78.31	1030.6±89.06	F=6.37	**0.003***
	P1=0.003*, P2=0.04*, P3=0.63				
ALP activity (U/L)	466.85±27.16	330.75±14.48	375.25±29.51	F=2.03	0.14
	P1=0.13, P2=0.38, P3=0.79				
Albumin(g/dL)	3.97 ± 0.26	3.93 ± 0.19	4.01 ± 0.23	F=1.014	0.369
	P1=0.97, P2=0.22, P3=0.21				
Hb (g/dL)	9.17 ± 1.13	9.54 ± 0.99	9.88 ± 0.98	F=2.3516	0.104
	P1=0.997, **P2<0.001*, P3<0.001***				
WBCs (cells/µL)	5.23 ± 1.33	5.84 ± 1.9	5.94 ± 0.11	F=0.901	0.41
	P1=0.49, P2=0.09, P3=0.56				
Platelets (K/µL)	293.05 ± 6.12	277.05 ± 4.75	315 ± 8.6	F=1.347	0.27
	P1=0.77, P2=0.61, P3=0.24				
Ferritin (ng/mL)	180.8 ± 13.72	161.65±12.16	188.1±16.93	F=0.148	0.86
	P1=0.92, P2=0.99, P3=0.86				
Tsat (%)	17.32 ± 4.21	17.96 ± 4.2	21.17 ± 1.01	F=1.2516	0.29
	P1=0.97, P2=0.31, P3=0.44				
CRP (mg/L)	7.05 ± 1.53	4.88 ± 1.18	4.24 ± 0.52	F=2.153	0.13
	P1=0.29, P2=0.13, P3=0.86				

Data are presented as mean ± SD. * Significant p value <0.05, P1: Pre versus 6 months, P2: P Pre versus 12 Months, P3: 6 months versus 12 Months, f: ANOVA test, S: serum, PO_4: phosphorus, iPTH: intact parathyroid hormone, ALP: alkaline phosphatase, Hb: hemoglobin, WBCs; white blood cell, Tsat: transferrin saturation, CRP: C- reactive protein.

In parathyroidectomy group, itching, bone pain, blood transfusion, EPO dosage per week (Epo/wk.), and anemia symptoms showed significant differences between the pre-management evaluation and subsequent evaluations at 6 and 12 months. In cinacalcet group, itching, fractures, blood transfusions, and anemia symptoms were insignificantly different in all time points. Epo/wk and bone pain were significantly higher in the pre-management evaluation compared to the 6-month and 12-month post-management evaluations (P < 0.05) (Table 10).

Table (10): Comparison between the three groups regarding clinical data in parathyroidectomy, Cinacalcet group

	Pre-management	**6 months**	**12 months**	**Test of sig.**	**P**
Parathyroidectomy group					
Itching (No of pts%)	9 (45%)	0 (0%)	0 (0%)	X^2=21.18	**<0.001***
	P1<**0.001***, **P2<0.001***, P3=--				
Bone pain (No of pts%)	13 (65%)	7 (35%)	1 (5%)	X^2=15.82	**<0.001***
	P1=0.06, **P2<0.001*, P3=0.02***				
Fractures (No of pts%)	3 (15%)	0 (0%)	1 (5%)	X^2=3.75	0.15
	P1=0.07, P2=0.29, P3=0.31				
Blood transfusion (No of pts%)	5 (25%)	4 (20%)	4 (20%)	X^2=0.196	**0.02***
	P1=0.08, **P2=0.02*,** P3=0.31				
Epo (wk.- dose per week)	2.85 ± 0.49	2.5 ± 0.89	1.1 ± 1.07	F=23.63	**<0.001***
	P1=0.402, **P2<0.001*, P3<0.001***				
Anemia symptoms	12 (60%)	4 (20%)	0 (0%)	X^2=19.09	**<0.001***
	P1=0.009*, P2<0.001*, P3=0.04*				
Cinacalcet group					
Itching (No of pts%)	4 (20%)	4 (20%)	3 (15%)	X^2=0.223	0.89
	P1=1, P2=92, P3=0.92				
Bone pain (No of pts%)	14 (70%)	8 (40%)	4 (20%)	X^2=10.317	**0.006***
	P1=0.06, **P2=0.001*,** P3=0.17				
Fractures (No of pts%)	3 (15%)	1 (5%)	0 (0%)	X^2=3.75	0.15
	P1=0.57, P2=0.19, P3=0.0.59				
Blood transfusion (No of pts%)	4 (20%)	1 (5%)	0 (0%)	X^2=5.673	0.06
	P1=0.36, P2=0.11, P3=0.59				
Epo (wk.- dose per week)	2.9 ± 0.45	2.5 ± 0.76	1.25 ± 1.25	F=18.97	**<0.001***
	P1=0.33, **P2<0.001*, P3<0.001***				
Anemia Symptoms	6 (30%)	4 (20%)	1 (5%)	X^2=4.23	0.12
	P1=0.77, P2=0.11, P3=0.36				

Data is presented as frequency (%) or mean ± SD. * Significant p value <0.05, P1: Pre versus 6 months, P2: P Pre versus 12 Months, P3: 6 months versus 12 Months, f: ANOVA test, X^2: qui square test, no of pts: Number of patients, Epo: erythropoietin, wk: week.

In vit. D analogues group, itching increased from 15% in the pre-management phase to 50% after 6 months and 70% after 12 months. As regards all points of time, itching significantly increased (p=0.001). Bone pain and anemia symptoms, fractures and blood transfusions and Epo/wk. were insignificantly different in all time points (Table 11).

Table (11): Comparison between the three groups regarding clinical data in Vit. D analogues group

	Pre-management	**6 months**	**12 months**	**Test of sig.**	**P**
Itching (No of pts%)	3 (15%)	10 (50%)	14 (70%)	X^2=12.525	**0.001***
	P1=0.06, **P2=0.002*,** P3=0.43				
Bone pain (No of pts%)	6 (30%)	7 (35%)	12 (60%)	X^2=5.011	0.12
	P1=0.94, P2=0.16, P3=0.29				
Fractures (No of pts%)	0 (0%)	0 (0%)	1 (5%)	X^2=2.034	0.36
	P1=1, P2=0.2, P3=0.32				
Blood transfusion (No of pts%)	4 (20%)	3 (15%)	2 (10%)	X^2=0.784	0.65
	P1=0.68, P2=0.38, P3=0.63				
Epo (wk.- dose per week)	2.8 ± 0.62	2.65±0.88	2.55±1	F=0.44	0.65
	P1=0.84, P2=0.62, P3=0.93				
Anemia Symptoms	9 (45%)	5 (25%)	7 (35%)	X^2=1.758	0.42
	P1=0.42, P2=0.81, P3=0.79				

Data are presented as mean ± SD or frequency (%). * Significant p value <0.05, P1: Pre versus 6 months, P2: P Pre versus 12 Months, P3: 6 months versus 12 Months, f: ANOVA test, X^2: qui square test. No of pts: Number of patients, Epo: erythropoietin, wk: week.

DISCUSSION

The most prevalent problems that might influence the life quality for CKD patients were SHPT and anemia [10]. In the current study, regarding laboratory investigations 6 months after management among the three groups, we found that comparing all groups, s.Ca^{2+} and PO_4^{3-} were considerably higher in the vitamin D analogues group. While, when comparing all groups, iPTH and ALP were considerably higher in the cinacalcet group. Meanwhile, in comparison between the three groups regarding laboratory investigations 12 months after management, there was a comparable s.Ca^{2+} levels between the three groups. Comparing all groups, PO_4^{3-}, iPTH and ALP were notably higher in the vit. D analogues group. These outcomes are in agreement with **Koh *et al.*** [11] who found that mean serum calcium levels were similar in parathyroidectomy and calcimimetics groups for treatment of SHPT during follow-up. Furthermore, **Alvarado *et al.*** [12] declared in patients underwent parathyroidectomy and patients took cinacalcet for SHPT, mean PTH in cinacalcet group was higher than in parathyroidectomy group.

In our study according to complete blood count investigations 6 months after management, no significant differences were observed. While, according to evaluations 12 months after management, there was a considerable improvement in Hb level in both parathyroidectomy and cinacalcet groups when compared with vitamin D analogues group. In line with our results, **Conzo *et al.*** [13] found that in the surgical group, none exhibited iron shortage, external hemorrhage, or mild to moderate anemia.. Concerning twelve-month Hb levels, 26 out of 30 patients (86.6%) exhibited a substantial rise, and 5 (19.2%) of them exhibited a Hb level above 12 g/dl. In line with our results about symptoms 6- and 12-months post-management, **Conzo *et al.*** [13] found that in surgical group, Concerning the postoperative ESA dose, 27 out of 30 patients (90%) required no pharmacological intervention, whereas 3 out of 30 patients (10%) necessitated a reduced dosage. No notable perioperative or postoperative complications were detected. Eighteen patients (60%) need intravenous postoperative therapy of calcium gluconate owing to hypocalcemia, which was sometimes severe.

In parathyroidectomy group, serum calcium, PO_4^{3-}, iPTH and ALP was significantly higher in pre-management evaluation than 6 months post-management evaluation. S. Ca^{2+} was significantly increased in 12 months post-management evaluation compared to the 6-month assessment ($P < 0.001$). PO_4^{3-}, iPTH, ALP was insignificantly different at 6- and 12-months post-management evaluation. PO_4^{3-} was significantly decreased in levels when compared to post-management and pre-management group. ALP levels were consistently higher in the pre- group when assessing all time points. Serum albumin, WBCs, Plt, s. ferritin and CRB were comparable between both groups. Hb levels were significantly higher in the 6-month post-management evaluation than in pre-management evaluation and in 12 months than in 6 months. T.sat was significantly higher in 12 months post-management than in pre-management ($P=0.01$) and did not exhibit significant differences between groups at any time point. In cinacalcet group, s.ca and iPTH level were significantly higher in pre-management evaluation than in 6- and 12-months post management, while no significant difference between 6- and 12-month evaluations. PO_4^{3-} and serum albumin were insignificantly different between subsequent time points. ALP was insignificantly different between in pre-management evaluation and 6 months post-management and between 6- and 12-months post-management, while was significantly higher in pre-management evaluation than in 12 months post-management ($P<0.05$). Hb levels were significantly higher in the 6-month post-management evaluation than in the pre-management levels ($P = 0.008$). At 12 months, it was significantly higher than in 6-months post-management and comparing all time points ($P<0.001$).

In vit. D analogues group, s.Ca^{2+}, ALP, Albumin, CBC, CRP, T.sat and s. ferritin were insignificantly different among the groups. PO_4^{3-} levels were insignificantly different in the pre-management and 6 months post-management, while was significantly higher in 6 months post-management than pre-management and in 6 months post-management than in 12 months post-management. iPTH was significantly higher in pre-management than in 6- and 12-months post management. Our study agrees with **Chen *et al.*** [14] who observed a significant decrease in iPTH and Ca^{2+} levels following Parathyroidectomy. Particularly, iPTH levels decreased from 2273.97 ± 273.96 to 390.96 ± 693.72 (pg/ml), and Ca^{2+} levels decreased from 2.49 ± 0.25 to 1.88 ± 0.32(mmol/l) from the postoperative 1st month. Also, **Huang *et al.*** [15] revealed that The mean baseline intact PTH level in the parathyroidectomy group was significantly greater than in the non-parathyroidectomy group ($p=0.043$). A decrease in the mean iPTH, calcium, and phosphorus levels was seen in the parathyroidectomy group. On the other hand, **Qiu *et al.*** [16] showed that no substantial disparity existed in Hb levels between preoperative and postoperative assessments at various time intervals. Also, **block *et al.*** [17] found that in 138 patients received cinacalcet, there was a reduction in PTH concentrations of more than 50%. On the other hand, there were some differences in the specifics of our findings with **Tanaka *et al.*** [18] who reported a moderate decline in serum phosphorus after cinacalcet initiation, with a mean serum phosphate of 5.80 ±1.32 mg/dL at baseline.

Tanaka *et al.* [6] found that in the cinacalcet initiators, the use of cinacalcet for 6 months was associated with a 1.1-fold increase in the odds of achieving the target Hb level of ≥10 g/dL Odds ratio was 1.13, with a 95% CI [1.09, 1.17], $p < 0.001$. The mean variation in Hb level for every subsequent 6-month period of cinacalcet use was +0.064 g/dL [0.047, 0.081]. **Varim *et al.*** [19] sought to find out how paricalcitol, alphacalcidol, vit D analogues affected individuals with

CRF. Revealed inadequate reduction of parathormone levels in CRF patients treated with Vit D analogues as compared with untreated patients. Furthermore, there was
a significant higher (p=0.018) phosphorous levels in alp hacalcidol treated patients than in untreated individuals.

In consistence with our results about symptoms of time data in parathyroidectomy group, **Chen *et al.*** [14] reported significant improvements in symptoms after parathyroidectomy, including reduced EPO usage, skin itching, and bone pain. As well, **Trunzo *et al.*** [8] exhibited a reduction in EPO needs at 12 months postoperatively after parathyroidectomy. Opposing to our results, about symptoms of time data in cinacalcet group , **Tanaka *et al.*** [6] found that in the cinacalcet initiators EPO use was in 955 (71.4%) patients and iron supplement use was in 263 (19.7%) patients. In agreement to our study with our results symptoms of time data in vit. D analogues group , **Varim *et al.*** [19] found that the groups who got vit D analogues had comparable values for biochemical indicators before and after therapy, including erythropoiesis-stimulating agent (ESA) dosage.

LIMITATIONS

The study's limitations were limited sample size. The research was conducted at a single center. So, we recommend that future multicenter studies with larger sample size and participants followed for longer periods of time are needed. We argue that randomized controlled trials are necessary.

CONCLUSION

Both parathyroidectomy and cinacalcet proved effectiveness in managing SHPT and reducing serum calcium levels, phosphorus, intact parathyroid hormone, alkaline phosphatase, clinical symptoms, frequency of EPO stimulating agents use, and anemia symptoms when compared to vitamin D analogues. Parathyroidectomy demonstrated superiority on cinacalcet as regards laboratory investigations especially on iPTH, PO_4 and ALP, which reached normal values post-operative.

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