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A prospective randomized study on intermittent post-dialysis dose regimen of Cinacalcet, single center experience

Mohammad Hannon Alsodani [1], Kasem Hamza Merza [2] , Shathah Hussain Ali [3]

[1] Assistant Prof., Dr., Consultant Nephrologist, College of Medicine-Baghdad University, Iraq

[2] B.Sc., Ministry of Higher Education and Scientific Research, Iraq

[3] Prof., Dr., Clinical Biochemistry, College of Pharmacy- Baghdad University, Iraq

ABSTRACT

Background: Treatment of secondary hyperparathyroidism (SHPT) is important in management of patients with end-stage kidney disease on hemodialysis (HD). cinacalcet provides an option for the control of SHPT in patients who fail traditional therapy, It may not have optimal results in non-compliant patients.

Aim of the study: The aim of this study is to evaluated effectiveness of post-dialysis dosing of cinacalcet (three time \week),tolerability and adherence as compared to daily home administration.

Methods: prospective randomized controlled clinical trial carried out in Iraqi center of dialysis of Baghdad teaching hospital – medical city complex during the period from March 2020 to January 2021. forty two patients with end-stage renal disease on hemodialysis (HD) with secondary hyperparathyroidism (SHPT),group (A) treated with daily dose of cinacalcit taking by patients at home and group (B) treated with post dialysis dosing of Cinacalcet(three times per week)were given to patients at the dialysis center. Intact parathyroid hormone (i-PTH), serum calcium, phosphorus,albumin and alkaline phosphatase were followed every two weeks for two month and compared to baseline values in both groups.

Results: A significant decline in i-PTH levels were detected in group (A) ($p = 0.001$)at two months therapy as compared to a non significant drop in group(B) ($p=0.1$)

Conclusions: The effectiveness of daily dosing of Cinacalcet is higher effectiveness than intermittent dosing of Cinacalcet in treatment of patients with secondary hyperparathyroidism., no significant difference is recorded between daily dosing of Cinacalcet and intermittent dosing of Cinacalcet regarding need for phosphate binders tablets, alfacalcidol tablet and side effects.

Introduction

1-Chronic kidney Disease

1-1-Definition

According to the Kideny Disease Improving Global Outcome (KDIGO)2012 clinical practice guideline for evaluating and managing Chronic kidney Disease(CKD), CKD is defined as aberration in kidney structure or function for more than three months. These aberration may be seen as endurance markers of kidney damage or a GFR of less than 60 mL/minute/ 1.73 m^2 .[(1)]

1-2-End-stage kidney disease (ESKD)

End-stage kidney disease (ESKD) , also referred as end-stage renal failure, corresponds to the last stage of chronic kidney disease (stage 5), when the kidneys' function is no longer sufficient to sustain life (GFR <15 mL/ min/ 1.73m2) and kidney replacement therapy (dialysis or transplant) is needed.(2)

1-3-CKD-Related Complications:

Progressive CKD is related to multi dilemma with higher prevalence and intensity at last stages of kidney function, which interact with each. These dilemma contributen to high morbidity and mortality and low quality of life. Some of these dilemma can be readily defined and quantified (cardiovascular disease, hypertension, anemia, mineral bone disorder, volume overload, electrolytes, and acid-base abnormalities) and may need a certain higher management form , for example, the prescription of erythropoiesis stimulating agents to correct anemia[(3)]

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1-3-1-Hypertension:

Hypertension is a crucial risk factor for cardiovascular and kidney disease. Conversely, chronic kidney disease (CKD) is the most common cast of secondary hypertension and ascend evidence suggests it is an independent risk factor for cardiovascular morbidity and mortality[(4).]

1-3-2-Cardiovascular complications:

Cardiovascular disease (CVD) considers the major cause of mortality in CKD patients, and the prevalence and saddle of this complication increases with decreasing kidney function For example, the risk of mortality from CVD is 8.1-fold higher in a patient with CKD stage **5(**eGFR < 15 ml/min per 1.73) than in a hint population with normal kidney function [. (3)]

1-3-3. Anemia:

Anemia is a prevalent complication during the later stages of CKD. When present, it may cause symptoms such as fatigue and shortness of breath. The pathogenesis of anemia in chronic kidney disease is complex, but a main cause is a relative deficit of erythropoietin. New information has explained the critical function of the hypoxia-sensing system in mediating erythropoietin synthesis and release. Iron deficiency is a second important factor in the anemia of chronic kidney disease [(5)]

1-3-4. CKD-related mineral bone disorder:

Bone-mineral metabolism aberrations , which the (KDIGO)2006 guidelines newly defined as chronic kidney disease-mineral and bone disorder (CKD-MBD), have been distinctly implicated not only in the development of secondary hyperparathyroidism (SHPT) and renal osteodystrophy, but have also been related to the evolution of CKD and its complications, including cardiovascular complications, and they eventually contribute significantly to an increase in morbidity and mortality rates in patients with CKD[(6).]These

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modifications constitute a systemic disorder that is characterised by aberrations calcium, phosphorous, parathyroid hormone (PTH), and vitamin D metabolism, which, along with to affecting the skeletal system, is related to the demeanor of cardiovascular and soft tissue calcifications that orderly are associated with cardiovascular pathologies in patients with CKD[.(7-10)..]

1-3-5. Salt and Water Retention

In CKD stages 4 to 5, and perhaps in CKD stage 3, there is reduction of defense against high sodium and low sodium. In clinical practice, high sodium with fluid retention is commonnly, although the prevalence has not been defined. While the extracellular fluid volume may be high, the sodium equilibrium appears to be relatively well-maintained till end-stage renal disease[(11).]high sodium and fluid donate not only edema, which may negatively affect quality of life, but also hypertension and thereby CVD (specifically concentric left ventricular hypertrophy, which can result in diastolic dysfunction). The mainstay of therapy is adherence to simple fluid balance (intake vs. output) concepts, decrease of dietary salt intake, and use of natriuretic drugs (which may be less effective in the more late stages of CKD). [(3)]

1-3-6. Metabolic acidosis and electrolyte disorder

the kidneys play a main role in the maintain of body fluids, electrolytes and acid-base balance, CKD and ESKD expected result in multiple disorders including hyperkalemia, metabolic acidosis and hyperphosphatemia which, orderly, lead to dangerous complications consisting muscle wasting, bone-mineral disorder, vascular calcification and mortality. Although, in patients with ESKD, some disorders can be treated by the renal replacement therapy, existing dialysis modalities are remote from ideal[.(12)]

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1-3-7- Uremic Symptoms*:*

The syndrome of uremia contains a multi of symptoms including : anorexia, fatigue, cachexia, pruritus, nausea, restless leg syndrome, sleep disturbances, and sexual dysfunction[.(13).] .Pruritus is common and can negatively affect quality of life. The causes are inadequately understood but are likely to contain the buildup of specific uremic

toxins in the skin. differentiating uremic itching from others caused by other conditions is essential because the treatment may be various. Topical treatment and antihistamines are convenient to LMIC. Other drugs, such as gabapentin and opioid receptor modulators, are likely to be of more restricted availability . [3]

1-4-Cinacalcet

1-4-1-Chemical description

Cinacalcet HCl is described chemically as N-[1-(R)-(-)-(1-naphthyl)ethyl]-3-[3-(trifluoromethyl)phenyl]-1-aminopropane hydrochloride and has the following structural formula[14]

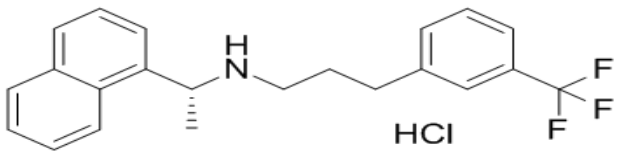

Figure 1-1: Cinacalcet structure

1-4-2-Pharmacology

Cinacalcet is a type II calcimimetic agent with unique mechanism of action(15, 16). It binds to the transmembrane zone of the calcium-sensing receptor, which leads to a various structural form that is more sensitive to serum calcium. dissimilar vitamin D sterols, cinacalcet does not increase serum

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calcium levels; therefore, adverse effects related to hypercalcemia can be evaded.[16]

Aim of the study

The aim of this study is to
1-compare the two dosage regimen of cinacalcet drug in haemodialysis patients .
2- evaluate tolerability
3- evaluate adherence as compared to daily home administration of cinacalcet .

Chapter two

Patients and Methods

2-Setting and Study Design

This study prospective randomized controlled study parallel design was accomplished at the Iraqi Dialysis Center of Baghdad Teaching Hospital in Medical City complex – Baghdad from March 2020 to January 2019.

2-1-Patients

Sixty one patients treated in Iraqi Dialysis Center who have included in the study. The patients have regular schedule for haemodialysis three time per week , four hours session.

2-2-Inclusion and exclusion criteria:

2-2-1-Inclusion criteria:-

The patients included in this study should have the following criteria,

A- Patients on haemodialysis for at least 3 months

B-age of patients are≥ 18 years,

C- Severe SHPT with i-PTH >300 pg/L,

D- Corrected serum Ca × PO4 product > 55mg\dl,

E-patients with negative recent cardiovascular disease.

2.2.2-Exclusion criteria

The patients were excluded if:

A- i-PTH <300 pg/mL,

B- Corrected Ca <8.4mg/Dl

C- patients with recent(<6 months) cardiovascular disease such as (myocardial infarction or arrhythmia),

D-patients on regular haemodialysis Used drugs inhibit cytochrome p450(CYP3A4) such as azole group and macrolide group or drugs induce cytochrome p450(CYP3A4) in last 3 weeks,

E-patients with Parathyroidectomy.

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Patients and Methods
2-3-Procedure:

Sixty one patients included in this study were divided randomly into two groups (A & B):-

Group (A)-Thirty one patients given cinacalcit tablet daily at home , while

Group (B)- Thirty patients given cinacalcit tablet[three time weekly] post dialysis in Dialysis Center.

In Group (**A**)-number of patients complete the study (21) and (10) patients withdrawal from the study , due to

- ✓ Adverse event (n=3)
- ✓ death(n=1)
- ✓ Noncompliance with with study (n=2)
- ✓ Lost to follow-up (n=3)
- ✓ Other (n=1)

In Group (**B**)-number of patients complete the study (21) and (9) patients withdrawal from the study, due to

- ✓ Adverse event (n=5)
- ✓ death(n=1)
- ✓ Noncompliance with with study (n=3)
- ✓ Lost to follow-up (n=0)
- ✓ Other (n=0).

2-3-1-Collection of blood sample and preparation

The five milliliter blood sample draw from patients included in study before dialysis session, blood serum of sample are collected in plain tube for measuring (parathyroid hormone, calcium, phosphorus, albumin and alkaline phosphtase). This procedure repeated every two weeks for two

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months ,then compare between results at baseline and after two months between two groups.

After one month of study, gastrointestinal tolerability was evaluated for each group . for gastrointestinal tolerability, the Gastrointestinal Symptom Rating Score (GSRS) [17] was used as an measurment method. The five(5) groups of symptoms included reflux, pain in abdomin, diarrhoea, dyspepsia, and constipation. It consists of a Likerttype scale of seven (7) points.

Adherence to medicines was estimated at the beginning interventional group A of using the Morisky -Green test[18]. It estimate if the patient fosters a right manner regarding medicines. To be believe best adherence,the response to all questions should sufficient. At the end of group B, adherence to medicines was estimated by calculating the number of tablets giving to patient.

2.4-Statistical analysis

The data of patients were analyzed by application of Microsoft excel program and Statistical Package for Social Sciences (SPSS) version 23.

Outcomes of analysis were arranged in scales variables (means & standard deviation) and in categorical variables. Chi square test was used for comparison between categorical data (Fishers exact test applied whenexpected variable was less than 20% of total). Independent sample t-test was used to compare between two means. The level of significance (p value) was set as ≤ 0.05.

Results

This study included 42 patients with secondary hyperparathyroidism (SHPT) divided into two groups according to treatment regimen with Cinacalcet. No significant differences were observed between group A SHPT patients and group B SHPT patients regarding age and gender. All these findings are shown in table(3-1).

Table (3-1): Distribution of Demographic Characteristics According To Study Groups.

Variable	Group A		Group B		P
Age	51.28±14.46		47.8±13.8		0.5*^{NS}
Gender	Group A		Group B		0.7**^{NS}
	No.	%	No.	%	
Male	15	71.4	14	66.7	
Female	6	28.6	7	33.3	

*Fishers exact test, **Chi-square test, NS=Not significant.

Group A = 21 patients treated with daily dose of Cinacalcet, Group B =21 patients treated with intermittent post-dialysis dose of Cinacalcet.

overweight was significantly associated with group A patients . longer dialysis duration were significantly common for group B patients. No significant differences were observed between group A and group B regarding CKD etiology . All these findings were presented in table(3-2)

Table (3-2): Distribution of BMI Values , Duration of Dialysis and CKD etiology Characteristics According To Study Groups.

Variable	Group A		Group B		P
	No.	%	No.	%	
BMI (Kg/m ^{2})[19]					0.01*S
Underweight(<18.5) Kg/m ^{2} Kg/m ^{2}	2	9.5	2	9.5	
Normal(18.5-24.9))Kg/m^2)	3	14.3	12	57.1	
Overweight(25-29.9)	13	61.9	4	19.0	
Obese(≥30)	3	14.3	3	14.3	
Duration of dialysis					0.01*S
<1 year	6	28.6	0	-	
1-2 years	7	33.3	6	28.6	
>2 years	8	38.1	15	71.4	
CKD etiology					0.5*NS
Hypertesion(HT)	8	38.1	4	19.0	
DM	4	19.0	5	23.8	
Polycystic kidney	1	4.8	0	9.5	
Renal stone	2	9.5	0	-	
Systemic lupuserymatosus (SLE)	1	4.8	2	9.5	
Unknown	2	9.5	2	9.5	
HT and DM	2	9.5	1	4.8	
Renal congenital anomalies	1	4.8	1	4.8	
Herbal drugs	0	-	1	4.8	
Glomerulonephritis	0	-	1	4.8	
Drugs (meropenem)	0	-	2	9.6	

*Fishers exact test, S=Significant, NS=Not significant

Mean Dialysate Ca of both study groups was similar (1.25). Mean baseline Alfacalcidol tablet 1microgram (mcg) was (0.62) for group A and (0.77) for group B were with no significant difference between study groups. Mean baseline Calcium carbonate (CaCo3) tablets 500 milligram (mg) was (2.5) for group A and (2.7) for group B with no significant difference between both study groups . Furthermore,no significant differences were observed between group A patients and group B patients regarding baseline Sevelemar 800 mg tablets , baseline PTH , baseline of serum Calcium (Ca) and baseline of Phosphuors(Po4) . All these findings were shown in **table- (3-3)**.

Table (3-3): Distribution of Baseline Measures According To Study Groups

Variable	Group A	Group B	P
	Mean±SD	Mean±SD	
Dialysate Ca(1.25mmol\L)	1.25±0.00	1.25±0.00	-
Active vitaminD(1mcg)	0.62±0.39	0.77±0.36	0.3*^{NS}
CaCo3 tablet (500mg)	2.5±0.73	2.7±0.46	0.3*^{NS}
Sevelemar tablet (800mg)	8.4±11	3.2±1.6	0.3*^{NS}
Serum PTH (pg/ml)	722.8±299.4	832.1±495.9	0.2*^{NS}
Serum Ca (mg/dl)	9±0.56	8.9±0.38	0.6*^{NS}
Serum Po4(mg/dl)	4.6±1.4	4.37±1.5	0.5*^{NS}

* Independent sample t-test, NS=Not significant

Mean weekly dose of Cinacalcet for group A was (400 mg) which was significantly higher than (322.8 mg) mean dose of Cinacalcet received by group B . All these findings were shown in table- **(3-4).**

Table (3-4): Distribution of Cinacalcet dose according to study groups.

Variable	**Group A**	**Group B**	**P**
	Mean±SD	**Mean±SD**	
Mean Weekly dose of Cinacalcet(mg)	400±131.2	322.8±118.8	**0.05***^{S}

* Independent sample t-test, S=Significant.

After two months, The dose of Caco3 tablet with meals was stopped in high proportion of patients of both study groups . The dose of Sevelemar tablet with meals stopped in 5 patients of group A, same dose in 2 group B patients and increased in 2 patients from group B with no significant difference between two study groups . No significant differences were observed between group A patients and group B patients regarding alphacalcidol tablets . All these findings were shown in table (3-5).

Table (3-5): Distribution of calcium carbonate, sevelemer and alfacalcidol drugs after two months according to study groups.

Variable	**Group A**		**Group B**		**P**
	No.	**%**	**No.**	**%**	
Dose of calcium carbonate(500mg) tablet with meals					0.3*^{NS}
No treatment before and	6	28.6	6	28.6	

Stop treatment	15	71.4	12	57.1	
Same dose	0	-	2	9.5	
Increased dose	0	-	1	4.8	
Dose of sevelemer tablet(800mg)					0.1*^{NS}
No treatment before and	15	71.4	16	76.2	
Stop treatment	5	23.8	1	4.8	
Same dose	1	4.8	2	9.5	
Increased dose	0	-	2	9.5	
Dose alfacalcidol tablet(1mcg)					0.5*^{NS}
No treatment before and	6	28.6	8	38.1	
Stop treatment	6	28.6	3	14.3	
Same dose	6	28.6	5	23.8	
Increased dose	3	14.3	5	23.8	

** Fishers exact test, NS=Not significant.*

Mean PTH for group A at baseline was (722.8), while after 2 months treatment, a significant decline to (329.5) of PTH . Mean Albumin (Alb), Mean Alkaline phosphatse (ALP) and Mean serum (Ca). for group A patients at baseline was not significantly different after two months treatment . Mean serum(Po4)of group A patients at baseline was (4.6), while after 2 months treatment, mean PO4 of group A patients was (4) with a significant decline . Mean PTH of group B patients was (832.1), while after two months of treatment, mean PTH of group B patients was (681.7) with no significant decline in PTH for group B patients . Mean(Alb), Mean (ALP), Mean serum (Ca), Mean serum (PO4). for group B patients at baseline was not significantly different after two months treatment All these findings were shown in table(3 -6) .

Table (3-6): Distribution of Means for Outcome Measures at Baseline and After 2 Months For Both Study Groups.

Variable	**Baseline**	**After 2 months**	**P**
	Mean±SD	**Mean±SD**	
Group A			
PTH (pg/ml)	722.8±299.4	329.5±474.9	**<0.001***^{S}
ALB(g/dl)	4.17±0.38	3.8±0.84	0.1*^{NS}
ALP (u/l)	185.9±165.2	135.2±97.4	0.2*^{NS}
Ca (mg/dl)	9±0.56	8.7±0.88	0.1*^{NS}
PO4 (mg/dl)	4.6±1.4	4±0.94	**0.05***^{S}
Group B			
PTH(pg/ml)	832.1±495.9	681.7±614.5	0.1*^{NS}
ALB(g/dl)	4±0.9	4±0.68	0.7*^{NS}
ALP(u/l)	185.7±109.5	162.5±336.2	0.7*^{NS}
Ca (mg/dl)	8.9±0.38	8.5±0.7	0.06*^{NS}

PO4 (mg/dl)	4.37±1.5	4.33±1.6	0.8*^{NS}

** Independent sample t-test, S=Significant, NS=Not significant.*

No significant differences were observed between group A patients and group B patients regarding post-treatment pain, heartburn, acid reflex nausea, rumblimg, bloating , burping , flatus , constipation , diarrhea , loose stool and hard stool. Although no significant difference between group A and group B SHPT patients regarding hunger pain , the hunger pain was higher among group A SHPT patients. A significant association was observed between post-treatment urgent bowel movement side effect and group A SHPT patients . Although there were no significant difference between group A and group B SHPT patients regarding no complete emptying bowel , this side effect was higher among group A patients. All these findings were presented in table (3-7).

Table- (3-7): Distribution of post-treatment side effects according to study groups.

Variable	Group A		Group B		P
	No.	%	No.	%	
Pain	7	33.3	6	28.6	0.7*^{NS}
Heartburn	4	19.0	2	9.5	0.3**^{NS}
Acid reflux	8	38.1	5	23.8	0.3*^{NS}
Hunger pain	5	23.8	1	4.8	0.07**^{NS}
Nausea	8	38.1	10	47.6	0.5*^{NS}
Rumbling	8	38.1	8	38.1	1.0*^{NS}
Bloating	11	52.4	6	28.6	0.1*^{NS}
Burping	7	33.3	4	19.0	0.2*^{NS}
Flatus	10	47.6	10	47.6	1.0*^{NS}
Constipation	6	28.6	6	28.6	1.0*^{NS}
Diarrhea	6	28.6	2	9.5	0.1**^{NS}
Loose stool	3	14.3	1	4.8	0.2**^{NS}
Hard stool	3	14.3	5	23.8	0.4**^{NS}
Urgent bowel	6	28.6	1	4.8	**0.03**^{**S}
Not completely emptying bowel	3	14.3	0	-	0.07**^{NS}

** Chi-square test, **Fishers exact test, ***Independent sample t-test, S=Significant, NS=Not significant.*

No significant differences were observed between group A patients and group B patients regarding adherence score and GSRS . All these findings were shown in table (3-8).

Table (3-8): Distribution of Morisky scale GSRS measures according to study groups.

Variable	Group A		Group B		P
	No.	%	No.	%	
Morisky adherence score					0.07*^{NS}
Yes	18	85.7	21	100.0	

No	3	14.3	0	-	
GSRS					0.1**^{NS}
Mean±SD	8.9±7		6±5.4		

**Fishers exact test, **Independent sample t-test, NS=Not significant.*

Discussion

The secondary hyperparathyroidism involves parathyroid hyperplasia and continuous high plasma levels of parathyroid hormone which accompanying chronic kidney disease [(20)]. The Cinacalcet therapy improved the Kidney Disease Outcomes Quality Initiative treatment targets among dialysis patients as compared to conventional therapy [(21)].

In present study, mean PTH for group A SHPT patients was significantly declined after two months treatment (p<0.001), with no significant change in PTH mean for group B SHPT patients after two months (p=0.1). These findings are similar to results of Haq et al [(22)] study in United Arab Emirates two groups of SHPT patients; first group with intermittent post-dialysis dosing of Cinacalcet and second group with daily home administration of Cinacalcet which found no significant decline in PTH after 16 weeks for first group as compared to significant decline in PTH for second group. Our study findings are inconsistent with results of a study conducted by Al-Hwiesh et al [(23)] in Saudi Arabia on 29 patients with end stage renal disease and SHPT on hemodialysis treated for one year with daily dose of Cinacalcet that shifted after one year into intermittent dosing and found no significant change in PTH levels between two treatment periods although rise in phosphorus level after intermittent treatment and finally they concluded that intermittent dosing of Cinacalcet is effective and cost effective in treatment of post-dialysis SHPT. This inconsistency might be attributed to fact that our study selected two patients groups in same duration, while the Saudi Arabian selected same group of patients in two different durations [(23)]. Although no significant decline in PTH among SHPT patients with intermittent dosing of Cinacalcet, the PTH dose was decreased from (832.1) to (681.7) after two months, but this decrease was not statically significant. Many authors continuing the survey on finding new agents suppress the PTH with no hyperphosphatemia or hypercalcemia.

The calcium-sensing receptors (CaSR) located on parathyroid cells are responsible in regulation of PTH secretion in addition to calcium homeostasis .[(24)] Additionally, the PTH level could be also regulated by extracellular calcium [(25)]. The calcimimetics are agents which theoretically rising sensitivity of the calcium-sensing receptors located on parathyroid gland to calcium [(26)]**.** The cinacalcet is now the common public calcimimetic. Many researchers documented that selection of cinacalcet as available treatment regimens increases the percentage of patients who are able to attain K/DOQI end-points related to PTH, calcium, and phosphate levels, and the calcium phosphorous product [(25, 26)]. Many literatures found that patients on maintenance hemodialysis with mild to severe hyperparathyroidism have a reduced levels of plasma PTH levels with a reduction in the levels of calcium and phosphate after administration of the calcimimetics [(21, 27)].

Current study showed a significant decline in Phosphorus level after two months treatment with daily Cinacalcet dose (p=0.05), while no significant decline in Phosphorus level was observed after intermittent dosing of Cinacalcet (p=0.8). This finding is consistent with results of Zitt et al [(28)] study carried out in Western European countries on 1865 dialysis patients which reported that PTH was the key predictor of Phosphorus level after Cinacalcet addition to treatment and a significant decline in PTH level was associated with a significant decline in Phosphorus level. Peter et al [(29)] study in USA used Renal Data System data with data from a large dialysis organization found that short-term treatment of PTH levels with Cinacalcet is not a profound surrogate for longer-term improvements in cardiovascular or survival risk, however, the

Phosphorus levels were significantly declined after short term Cinacalcet treatment [29]. Present study showed no significant differences were observed between group A SHPT patients and group B SHPT patients regarding need for calcium carbonate tablet, Sevelemar tablet and alphacalcidol tablets. Many literatures like Torres et al (30)study in Spain and Rozhinskaya et al(31) study in Russia reported the importance of Phosphate binders in increasing effectiveness of Cinacalcet role in controlling SHPT among dialysis patients. Shopit et al (32) study in Yemen found that need of alphacalcidol tablet is not significantly different according to dosing of Cinacalcet among SHPT patients post dialysis.

In current study, no significant differences were observed between group A SHPT patients and group B SHPT patients regarding most of post-treatment side effects. These findings are in agreement with results of Al-Hilali et al [33] study in Kuwait included 27 patients on hemodialysis with SHPT resistant to conventional therapy who were categorized into two groups (one group with daily dose of Cinacalcet and another dose with intermittent dosing of Cinacalcet) and found no significant differences between two groups regarding iPTH, calcium phosphate, alkaline phosphate and post treatment side effects. Different meta-analysis studies proved the effectiveness of calcimimetic therapy in patients with SHPT post dialysis and improve the proposed outcomes [34]. Other authors reported the important role of cinacalcet for prevention of parathyroidectomy and hypercalcemia [35,36], however, all these researches detected many side effects related to cinacalcet like nausea, vomiting and hypocalcemia [37]. For that, these side effects together with PTH decline are regarded the goal of Nephrologists in treating SHPT post dialysis [38]. Simo et al [39] study in Spain revealed the significant role of post-dialysis use of calcimimetic in secondary hyperparathyroidism control, gastrointestinal tolerability improvement and increasing patients' satisfaction. Our study showed a significant association between post-treatment urgent bowel movement side effect and group SHPT patients on daily dose of Cinacalcet in comparison to SHPT patients on intermittent dosing of Cinacalcet (p=0.03). This finding is inconsistent with results of Gojaseni et al [40] study in Thailand which found no significant difference in gastrointestinal post treatment side effects between SHPT patients on low dose of Cinacalcet and SHPT patients on daily dose of Cinacalcet. This inconsistency might be due to significantly higher weekly Cinacalcet doses administered for SHPT patients daily cinacalcit dosing in comparison to SHPT on intermittent Cinacalcet dosing.

In current study, no significant differences were observed between group A SHPT patients and group B SHPT patients regarding treatment adherence. This finding is consistent with result Simo et al [39] study in Spain which found intermittent dosing of cinacalcit to be beneficial in determined patients with poor treatment compliance.

Conclusion

- The effectiveness of daily dosing of Cinacalcet is higher than effectiveness intermittent dosing of Cinacalcet in treatment of patients with secondary hyperparathyroidism.
- Although difference in effectiveness, no significant difference is recorded between daily dosing of Cinacalcet and intermittent dosing of Cinacalcet regarding need for phosphate binders(sevelamer tablet,calcium carbonate), and alfacalcidol tablet.
- Although difference in effectiveness, no significant difference is recorded between daily dosing of Cinacalcet and intermittent dosing of Cinacalcet regarding post-treatment side effects.
- Urgent bowel movement was the common side effect for daily dosing of Cinacalcet in comparison to intermittent dosing of Cinacalcet.
- Although difference in effectiveness, no significant difference is recorded between daily dosing of Cinacalcet and intermittent dosing of Cinacalcet regarding adherence.

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