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EFFECT OF CINACALCET ON CALCIUM AND PHOSPHOROUS LEVELS IN PATIENTS HAVING CHRONIC KIDNEY DISEASE WITH SECONDARY HYPER PARATHYROIDISM

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Keywords:

Chronic Kidney disease , secondary hyper parathyroidism, Calcium , Phosphorous , Parathyroid hormone, Cinacalcet

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ABSTRACT

Chronic kidney disease (CKD) is a worldwide epidemic and escalating problem. Approximately 20 million adults in the United States are in various stages of CKD, with >400,000 individuals with end-stage kidney disease and >300,000 individuals requiring maintenance hemodialysis. Secondary hyperparathyroidism (SHPT) is an adaptive response to chronic kidney disease (CKD) that results in elevated serum parathyroid hormone (PTH) levels due to increased production and secretion of intact PTH (iPTH) by hyperplastic parathyroid gland chief cells.Calcimimetics agents are potential candidates for reducing secondary hyperparathyroidism. Calcimimetics agents act by increasing sensitivity of calcium sensing receptor in Parathyroid gland.Secondary hyperparathyroidism (SHPT) is a common complication among long-term dialysis patients.The present review is aimed on to study the effect of cinacalcet on calcium and phosphorous levels on patients having CKD with SHPT.The ability of cinacalcet to reduce PTH secretion, along with reductions inthe serum calcium, phosphorus, and calcium–phosphorusproduct provide an alternative to the traditional treatment regimen, and should be a newer treatment regimen to therapeutic strategy in the management of SHPT.

INTRODUCTION

Chronic kidney disease (**CKD**), also known as **chronic renal disease**, is progressive loss in kidney function over a period of months or years. The symptoms of worsening kidney function are not specific, and might include feeling generally unwell and experiencing a reduced appetite[1].Often, chronic kidney disease is diagnosed as a result of screening of people known to be at risk of kidney problems, such as those with high blood pressure or diabetes and those with a bloodline relative with CKD[2]. This disease may also be identified when it leads to one of its recognized complications, such as cardiovascular disease, anemia, pericarditis or renal osteodystrophy . CKD is a long-term form of kidney disease; thus, it is differentiated from acute kidney disease (acute kidney injury) in that the reduction in kidney function must be present for over 3 months[3]. CKD is an internationally recognized public health problem affecting 5–10% of the world population . With loss of kidney function, there is an accumulation of water, waste, and toxic substances in the body that are normally excreted by the kidney. Loss of kidney function also causes other problems such as anemia, high blood pressure, acidosis (excessive acidity of body fluids), disorders of cholesterol and fatty acids, and bone disease.Stage 5 chronic kidney disease is also referred to as kidney failure, end-stage kidney disease, or end-stage renal disease, wherein there is total or near-total loss of kidney function. There is dangerous accumulation of water, waste, and toxic substances, and most individuals in this stage of kidney disease need dialysis or transplantation to stay alive.

Secondary hyperparathyroidism is a frequently encountered problem in the management of patients with chronic kidney disease (CKD)[4]. Its pathophysiology is mainly due to hyperphosphatemia and vitamin D deficiency and resistance. This condition has a high impact on the mortality and morbidity of dialysis patients. Early diagnosis of secondary hyperparathyroidism is crucial in the management of patients with CKD. The treatment remains a challenge for patients and their clinicians. It should include a combination of dietary phosphorus restriction, phosphate binders, vitamin D analogues, and calcimimetics[5].Secondary hyperparathyroidism is the leading cause of renal osteodystrophy and bone disease. Renal osteodystrophy[6] is sometimes called "the silent crippler"; affected patients may be completely asymptomatic. Symptoms, including bone and joint pain and bone deformation and fractures, are more frequent during the late stages of the disease[7]. Osteitis fibrosa cystic[8], the classic and former most common osteodystrophy, is mainly caused by high bone turnover secondary to high levels of circulating PTH[9]. The excessive suppression of PTH can lead to adynamic bone disease (currently the most common osteodystrophy), mainly because of low bone turnover.

Cinacalcet hydrochloride, a first-in-class calcimimetic agent, offers a new therapeutic approach to the treatment of SHPT[10].Cinacalcet puts forth its action by binding to the parathyroid Ca sensing receptor (CaSR). Cinacalcet is effective for the reduction of parathyroid hormone, serum calcium, phosphorus, and calcium-phosphate[11] product levels. Cinacalcet is available as a once-daily oral therapy. Adverse effects are generally mild.Cinacalcet is indicated for the treatment of secondary hyperparathyroidism[12] in patients with Chronic Kidney Disease on dialysis and for the treatment of hypercalcemia in patients with parathyroidcarcinoma.Cinacalcet[13] lowers serum calcium, and therefore patients should be carefully monitored for the occurrence of hypocalcemia. Potential manifestations of hypocalcemia include paresthesias, myalgias, cramping, tetany, and convulsions.

MATERIALS AND METHODS

STUDY DESIGN

Prospective experimental study

STUDY POPULATION

Patients diagnosed with chronic kidney disease.

SAMPLE SIZE

60 patients.

$(Z^2_{1-\alpha/2})\ (1-p)\ p$ where p: Expected proportion

$\zeta^2\ p$ ζ: Relative precision

$1-\alpha/2$: Desired confidence level

STUDY SITE

Nephrology department of Pushpagiri Medical College Hospital and Pushpagiri College of Pharmacy, Thiruvalla

STUDY PERIOD : 6 months

INCLUSION CRITERIA

- Patients with Chronic kidney disease.
- Secondary hyperparathyroidism patients.
- Both male and female patients.
- OP/IP

EXCLUSION CRITERIA

Patient not willing to participate in the study.

ETHICAL CONSIDERATION:

The study was conducted after the approval from institutional ethics committee. Informed signed consent was collected from all patients who met the inclusion criteria .

A prospective experimental study on 'effect of cinacalcet on serum calcium and phosphorous levels in patients having CKD with secondary hyperparathyroidism' was conducted at Pushpagiri Medical College Hospital , Thiruvalla. Study was done after getting approval from institutional ethics committee and informed consent from the patients. Patients data collection form was used for recording the demographic details of the patients. Patients was recruited based on the inclusion and exclusion criteria. The duration of the study was 6 months.Calcium and phosphorous level were analysed from residual blood samples of patients collected from the laboratory by using semi autoanalyzer in the Pushpagiri college of pharmacy.Residual blood is the blood remaining after the blood routine analysis in the lab. Blood was not withdrawn directly from the patient and any financial burden was not imposed on the patient. iPTH level was obtained from the patients medication record.Safety and efficacy was assessed by determining the clinical outcome and determining the percentage of patients with control of calcium, phosphorous and iPTH level after use of cinacalcet and detecting their side effects. Medication adherence of the patient was evaluated using MMAS 4 scale.

Procedure to find out Calcium:

Blank : Pipetted out 1000 microlitre of the reagent R_1 to a test tube.

Standard : Pipetted out 1000 microlitre of R_1, 25 microlitre of thecalibrater to a test tube.

Sample : Pipetted out 1000 microlitre of R_1, 25 microlitre of the patient sample to a test tube.

Mix well and incubate at room temperature for 5 minutes.

Measured at 650 nm in the semiautomatic analyser.

R_1 :Arsenazo 3 reagentCalibrater : Calcium standard 10 mg/dl

Procedure to find out Phosphorous :

Blank : Pipetted out 1000 microlitre of the reagent R_1 to a test tube.

Standard : Pipetted out 1000 microlitre of R_1 , 20 microlitre of the calibrater to a test tube.

Sample : Pipetted out 1000 microlitre of R1 , 20 microlitre of the patient sample to a test tube.

Mix well and incubate at room temperature for 5 mts.

Measured at 340 nm.

RESULTS AND DISCUSSION

- **AGE**

In this study majority of the study population belongs to the age group 46-55. The mean age of the study was found to be 55.15.

- **GENDER**

In this study, majority of patients were malesfollowed by females .From these 35 (58%) male patients followed by 25 (42%) female patients.

- **FAMILY HISTORY**

In this study majority of the patients having family history of chronic kidney disease.50(83.3%) patients having family history and 10 (16.7 %) patients having no family history of chronic kidney disease.

- **SOCIAL HABITS**

Out of 60 patients, 55.0 % having no social habits. Majority of the patients having no social habits.

SIDE EFFECTS

Out of 60 patients , 30 (50 %) patients had side effects .The most prominent side effect were vomiting(21.7%) followed by nausea(20%).And majority of the patients having no side effects.

EFFECT OF CINACALCET ON CALCIUM

The mean value of calcium after drug use is 9.16 and the P value is< 0.001 which is significant. Since P < 0.001 , the calcium level was significantly decreased..

EFFECT OF CINACALCET ON PHOSPHOROUS

The mean value phosphorous after drug use is 4.65 and the P value is < 0.001 which is significant.Since P < 0.001 the phosphorus level was significantly decreased .

EFFECT OF CINACALCET ON INTACT PARATHYROID HORMONE

The mean value of iPTH after drug use is 217.41 and the p value is < 0.001 . Which is significant. Since P< 0.001 the iPTH level was significantly decreased.

MEDICATION ADHERENCE

In this study, medication adherence was found to significantly increase after patient counselling with a P value of P < 0.001. MMAS 4 was used for determining medication adherence.

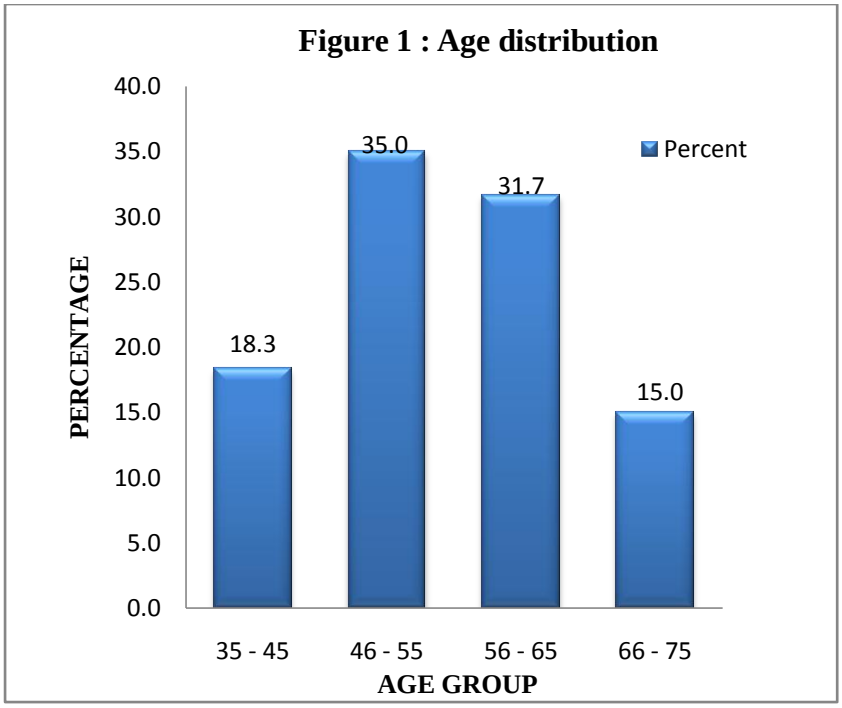


Figure 1 : Age distribution
40.0
35.0
30.0
25.0
20.0
15.0
10.0
5.0
0.0
PERCENTAGE
Percent
18.3
35.0
31.7
15.0
35 - 45
46 - 55
56 - 65
66 - 75
AGE GROUP

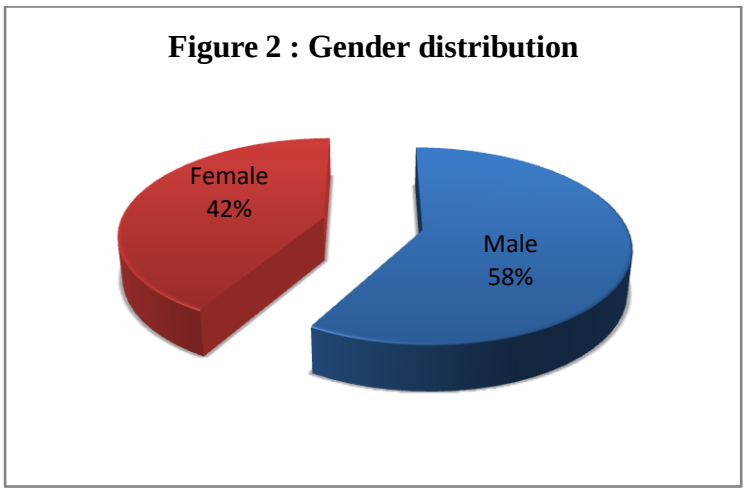


Figure 2 : Gender distribution
Female
42%
Male
58%

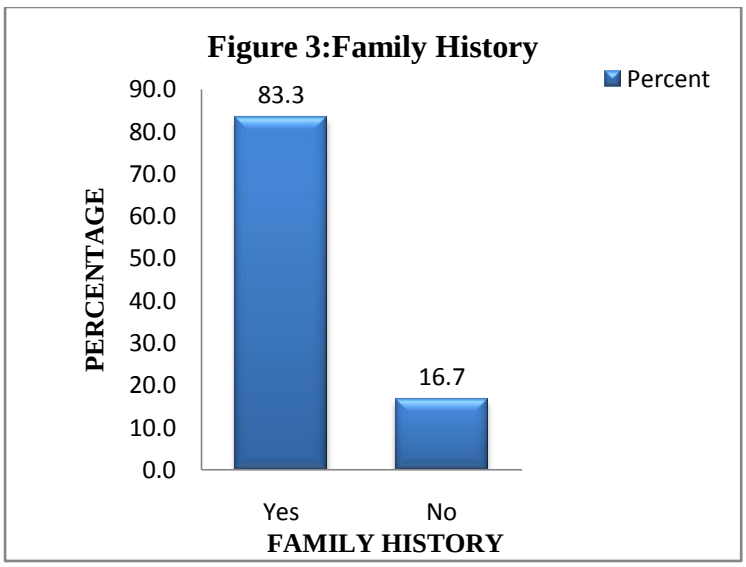


Figure 3:Family History
Percent
90.0
80.0
70.0
60.0
50.0
40.0
30.0
20.0
10.0
0.0
PERCENTAGE
83.3
16.7
Yes
No
FAMILY HISTORY

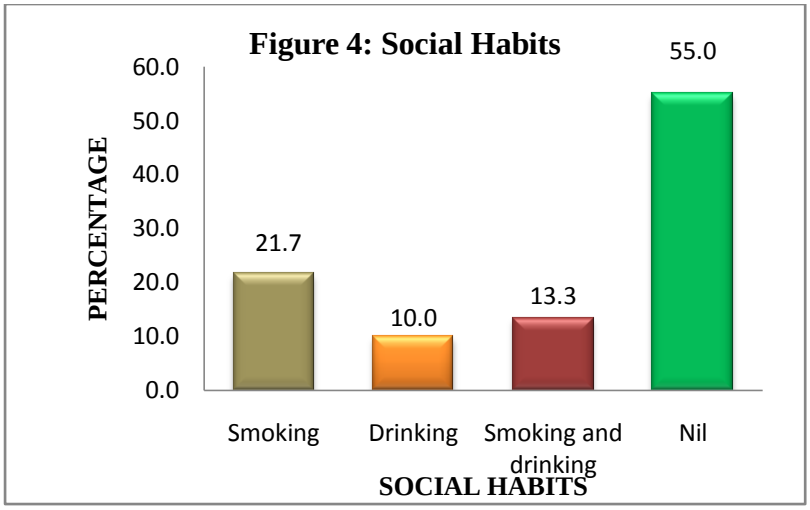


Figure 4: Social Habits
PERCENTAGE
60.0
50.0
40.0
30.0
20.0
10.0
0.0
21.7
10.0
13.3
55.0
Smoking
Drinking
Smoking and drinking
Nil
SOCIAL HABITS

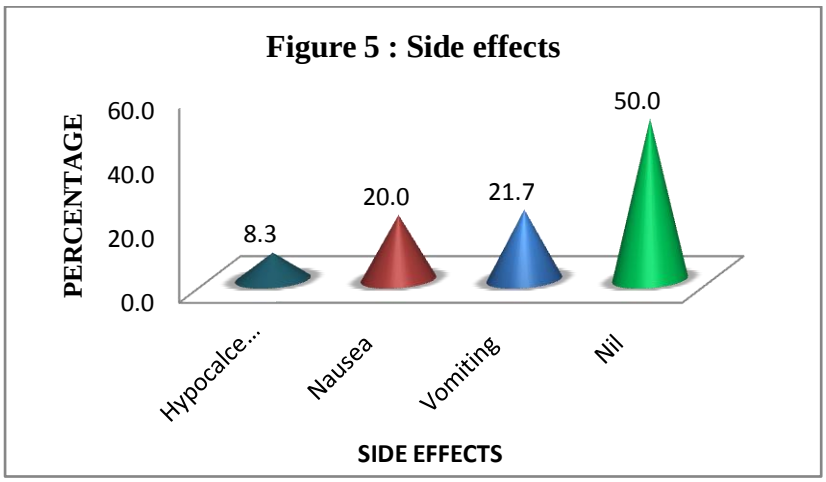


Figure 5 : Side effects
PERCENTAGE
60.0
40.0
20.0
0.0
8.3
20.0
21.7
50.0
Hypocalce...
Nausea
Vomiting
Nil
SIDE EFFECTS

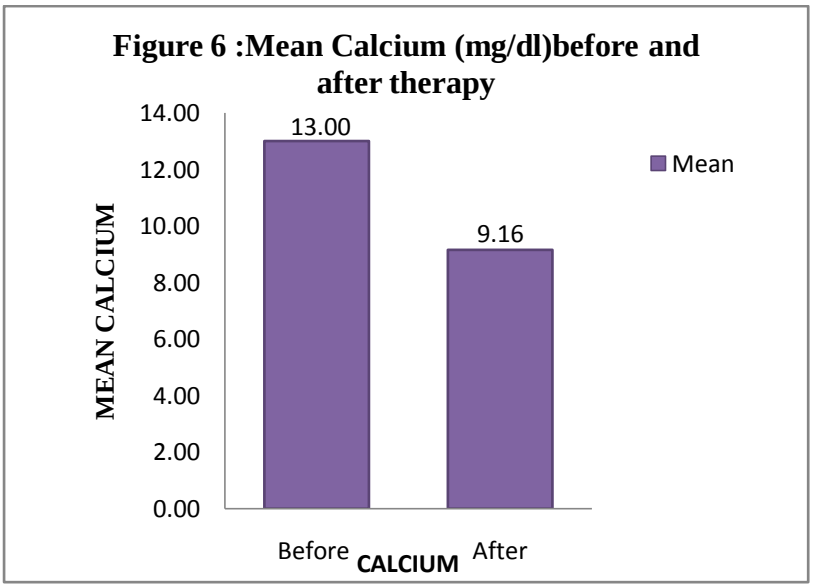
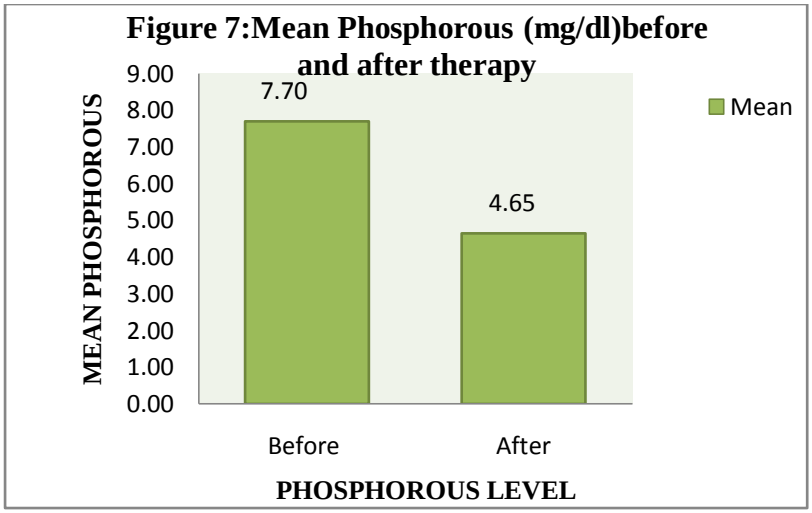


Figure 6 :Mean Calcium (mg/dl)before and after therapy
MEAN CALCIUM
14.00
12.00
10.00
8.00
6.00
4.00
2.00
0.00
13.00
9.16
Mean
Before
After
CALCIUM



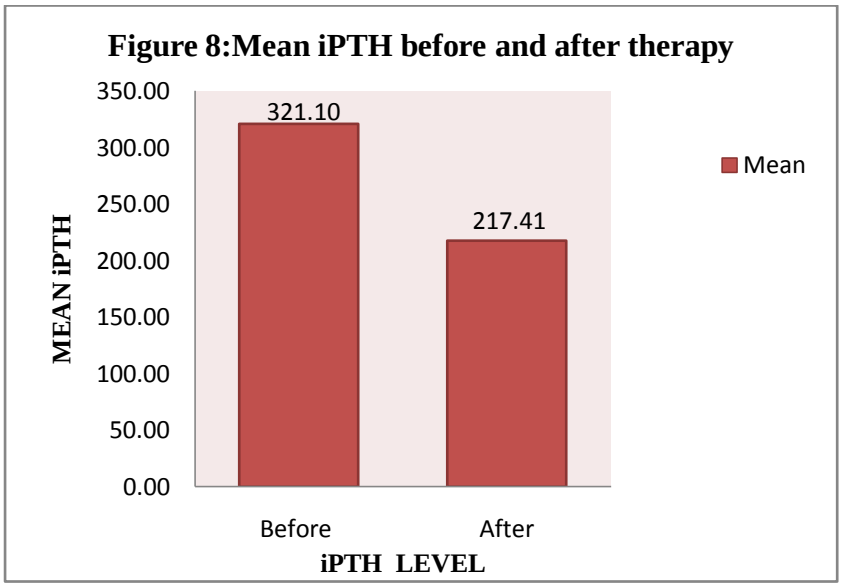
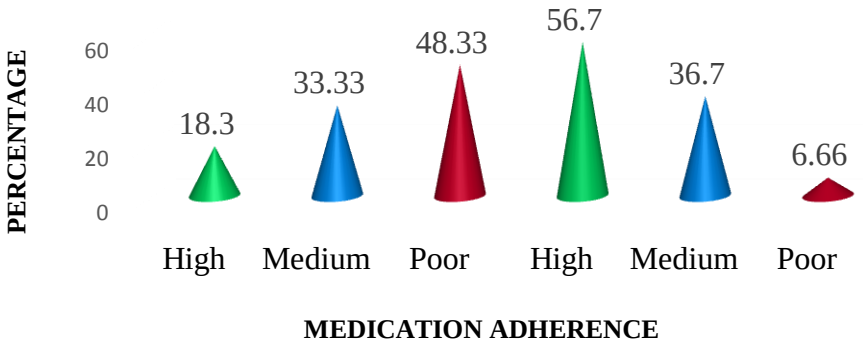


Figure 9:Medication adherence



CONCLUSION

Chronic kidney disease (CKD) is an increasingly common clinical problem that raises a patient's risk for developing several life-threatening medical conditions, including end stage renal diseaseand cardiovascular disease .Secondary hyperparathyroidism (SHPT) is a common consequence of chronic kidney disease (CKD).Secondary hyperparathyroidism (SHPT) is an adaptive response to chronic kidney disease (CKD) that results in elevated serum parathyroid hormone (PTH) levels due to increased production and secretion of intact PTH (iPTH) by hyperplastic parathyroid gland chief cells.Cinacalcet is the calcimimetic used for the treatment of secondary hyperparathyroidism in chronic kidney disease patients.Cinacalcet is the only available calcimimetic, licensed for use in chronic kidney disease patients stage 5.The aim of treatment of secondary hyperparathyroidism is to lower levels of PTH, calcium, and phosphorus in the blood, in order to prevent progressive bone disease and the systemic consequences of disordered mineral metabolism. From this study on 'Effect of Cinacalcet on calcium and phosphorous levels in patients having chronic kidney disease with secondary hyperparathyroidism' it can be concluded that cinacalcetsignificantly decreases the amount of calcium , phosphorous and iPTH .Cinacalcet have mild side effects and higher safety and efficacy . So the drug is effective in the treatment of secondary hyperparathyroidism. .A close monitoring of serum calcium , phosphorous and iPTH level are necessary.Due to the impact of clinical pharmacist interventions , themedication adherence was found to significantly increase after patient counselling . 34 patients were highly adherent 22 patients were medium adherent and 4 patients were moderate adherent after patient counselling.

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