



A PROSPECTIVE OBSERVATIONAL STUDY ON THE EFFECT OF PHOSPHATE BINDERS ON SERUM LEVELS OF CALCIUM & PHOSPHOROUS AMONG CHRONIC KIDNEY DISEASE PATIENTS UNDERGOING MAINTENANCE HAEMODIALYSIS - A PILOT STUDY

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ABSTRACT:

BACKGROUND: This prospective observational pilot study was conducted in hyperphosphatemic chronic kidney disease patients undergoing maintenance haemodialysis aimed at determining the effect of phosphate binders on serum levels of calcium & phosphorous, to seek Knowledge Attitude & Practice and Medication Adherence of the patients. The possible factors for non-adherence and impact of patient counselling in the participants were also assessed.

METHODOLOGY: Pre Hemodialysis results of calcium and phosphorous were analysed over 3 months. KAP scores were assessed by using KAP questionnaire and adherence was assessed using Adherence to Refills and Medication Scale.

RESULTS: A total of 10 patients were taken for this pilot study. Out of this 9 were male and 1 female. All the patients got effective hyperphosphatemic management with phosphate binders which altered the serum calcium and phosphorous levels except on patient who was on calcitriol. The knowledge, attitude and practice of the patients were assessed separately and improved with proper education. Similarly adherence is improved after giving patient counselling. Some of the possible factors for non-adherence were also assessed like availability, size, price etc.

CONCLUSION: In conclusion, all patients receive proper effect of the drug, most patients have good knowledge of phosphate binders and have positive attitude & practice since most of them were literate. A structured health education approach and counselling sessions remain essential for enhancing patient knowledge, shifting attitudes within a targeted demographic, and promoting treatment adherence, particularly among young and employed individuals.

KEYWORDS: CKD, Haemodialysis, Phosphate Binders, Hyperphosphatemia.

INTRODUCTION

CHRONIC KIDNEY DISEASE

Chronic Kidney Disease is a progressive loss of function of kidney over several months to years characterized by the presence of kidney damage or an estimated Glomerular Filtration Rate (eGFR) less than 60ml/min persisting for 3 months or more, irrespective of cause, resulting in the need for renal replacement therapy (Dialysis/Transplantation).^[4]

STAGES OF CHRONIC KIDNEY DISEASE (CKD):

KIDNEY DAMAGE STAGES	DESCRIPTION	eGFR (ml/min/1.73m²)
0	With risk factors for CKD	>90
1	With evidence of kidney damage	>90
2	Mild decrease in GFR	60-89
3	Moderate decrease in GFR	30-59
4	Severe decrease in GFR	15-29
5	Kidney Failure	<15

ETIOLOGY:

In CKD, the progressive loss or damage to functioning nephrons as a function of time is the result of a primary disorder or disease of the kidney, a secondary complication of certain systemic diseases (e.g., diabetes mellitus or hypertension), or an acute injury to the kidney that results in irreversible kidney damage.^[1]

In 2008, the leading causes of ESRD in newly diagnosed patients were

- Diabetes Mellitus (44%)
- Hypertension (28%)
- Chronic glomerulonephritis (7%)^[1]

The remaining cases of ESRD can be attributed to a variety of other pathologies include ^[1]

- Polycystic kidney disease
- Congenital malformations of the kidneys
- Nephrolithiasis
- Interstitial nephritis
- Renal artery stenosis
- Renal carcinoma, and
- Human Immunodeficiency Virus– associated nephropathy ^[1]

HEMODIALYSIS

Hemodialysis is the most common type of dialysis and the one most people are aware of. At dialysis centres, this is usually carried out 3 days a week, with each session lasting around 4 hours. ^[20]

The main function of haemodialysis is to reduce the volume of uremic toxins in the blood, especially small and medium sized molecules, through diffusion. It also decreases the patient's fluid volume via ultrafiltration and manages metabolic disturbances. ^[18]

This is achieved by a dialysis machine, which takes blood from the patient and pumps it towards the semi-permeable membrane. The dialysate is pumped from the opposite direction (counter current flow) to create a larger concentration gradient. ^[18]

Without dialysis, lack of kidney function will result in metabolic acidosis as the body fails to excrete excess acid and uses its serum bicarbonate to neutralize the pH. Therefore the dialysate needs to have a high bicarbonate concentration, which ensures a concentration gradient is present to allow bicarbonate to pass into the blood. Dialysis aims to move the patient from a state of mild metabolic acidosis to mild metabolic alkalosis, which prevents the acidosis from getting too severe between dialysis sessions. ^[18]

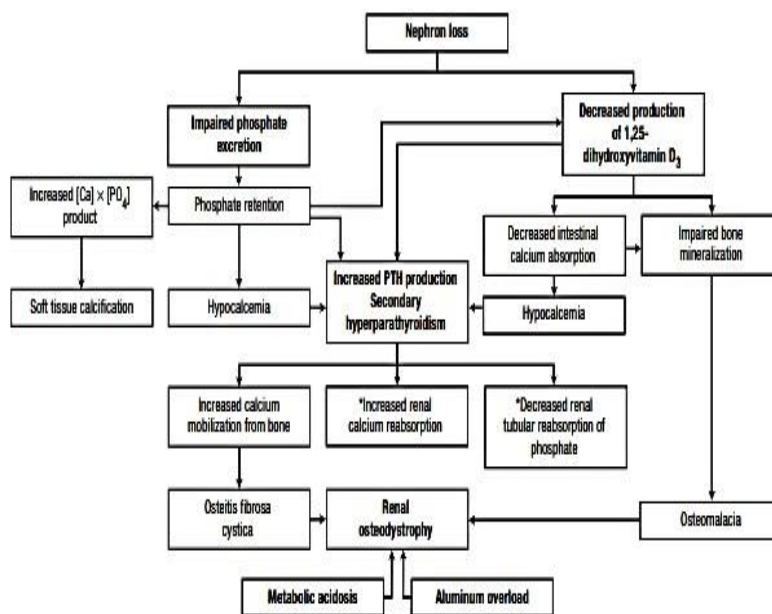
HYPERPHOSPHATEMIA:

Hyperphosphatemia can result from increased intestinal absorption, from cellular release or rapid shifts of phosphorous from the intracellular to the extracellular compartment, or from decreased kidney excretion. ^[14]

Serum phosphorous more than 4.5 mg/dl is hyperphosphatemia. In Hemodialysis patients serum phosphorous >5.5 mg/dl is required for treatment as per KDIGO guidelines. ^[14]

PATHOPHYSIOLOGY

- The most common cause of hyperphosphatemia is decreased phosphorous excretion, secondary to decreased glomerular filtration rate.



- Large amount of phosphorous can be released from intracellular stores in patients who have rhabdomyolysis and in patients who receive chemotherapy for acute leukemia and lymphoma.^[4]

TREATMENT:

- Preventive measures should be initiated in patients in early stages of CKD to improve outcomes by the time they reach stage 5 CKD or ESRD.
- The KDOQI guidelines provide desired ranges of calcium, phosphorus, calcium-phosphorus product, and intact PTH based on the stage of CKD
- Measurements should be repeated every 12 months for stage 3, every 3 months for stage 4, and more frequently for stage 5.
- Dietary phosphorus restriction (800 to 1,000 mg/day) should be first-line intervention for stage 3 or higher CKD.
- By the time ESRD develops, most patients require a combination of phosphate-binding agents, vitamin D, and calcimimetic therapy to achieve KDOQI goals
 - The most effective way to treat hyperphosphatemia is to decrease phosphate absorption from the GI tract with phosphate binders.
 - Severe symptomatic hyperphosphatemia manifesting as hypocalcemia and tetany is treated by the IV administration of calcium salts.^[1]

PHOSPHATE-BINDING AGENTS

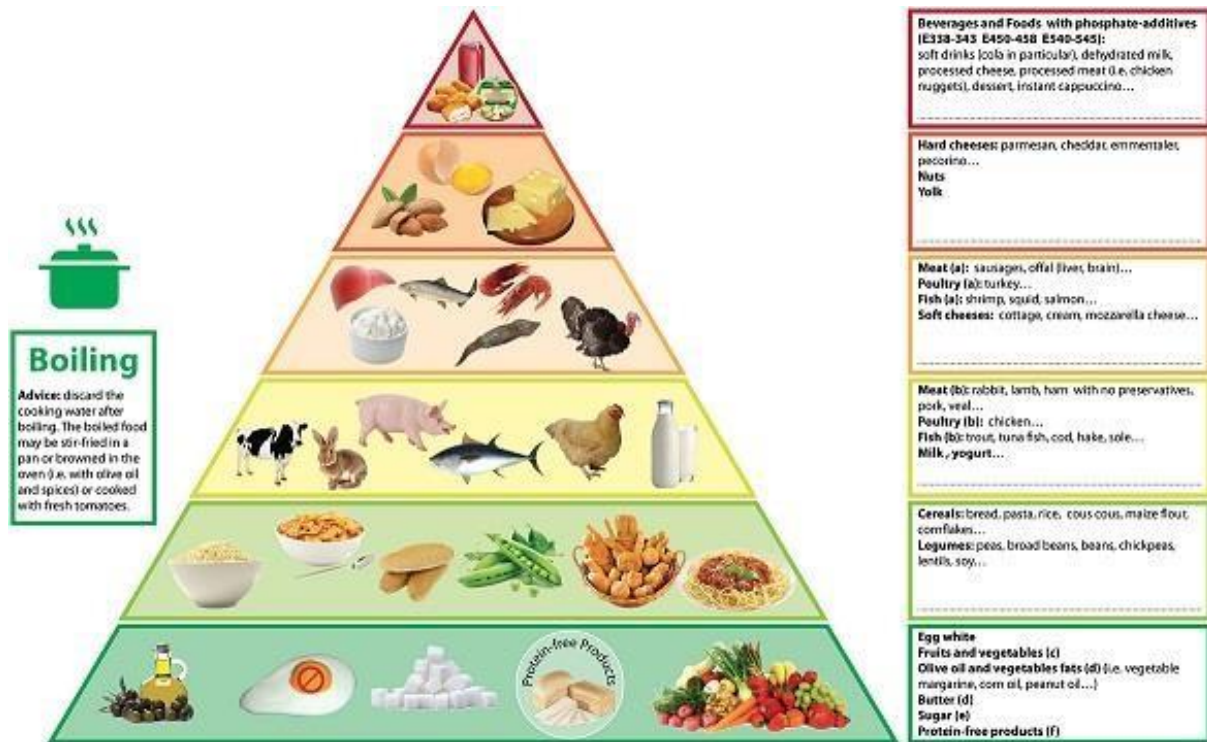
Patients with CKD, especially those with ESRD, typically require phosphate-binding agents in addition to dietary interventions to limit GI absorption and thereby control serum phosphorus.^[4]

TYPES OF PHOSPHATE BINDERS

- A variety of phosphate-binding agents are available including elemental calcium, iron, and lanthanum-containing compounds, and the nonelemental agent sevelamer.
- Binding affinity varies depending on the binding agent (e.g., calcium, iron, etc.).^[1]

CATEGORY	DRUG	DOSE
CALCIUM-BASED BINDERS	Calcium acetate (25% elemental calcium)	1,334 mg three times a day with meals.
	Calcium carbonate	0.5 to 1 g three times a day with meals.
IRON BASED BINDERS	Ferric citrate	420 mg three times a day with meals.
	Sucroferric oxy hydroxide	500mg three times a day with meals.
RESIN BINDERS	Sevelamer carbonate	800 to 1,600 mg three times a day with meals.
	Sevelamer hydrochloride	800 to 1,600 mg three times a day with meals.
OTHER ELEMENTAL BINDERS	Lanthanum carbonate	1,500 mg daily in divided doses with meals.
	Aluminium hydroxide	300 to 600 mg three times a day with meals.
	Magnesium carbonate	70 mg with meals.
	Magnesium hydroxide	300 to 400 with meals.

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DIET CHART:**AIM**

To Study on the effect of phosphate binders on serum levels of calcium & phosphorous among Chronic Kidney Disease patients undergoing maintenance haemodialysis.

OBJECTIVES

- To study the effect of phosphate binders on serum levels of calcium & phosphorous among Chronic Kidney Disease patients undergoing maintenance haemodialysis with hyperphosphatemia.
- To assess the patients adherence to the medicine and to investigate the knowledge attitude and practices about phosphate binders.
- To Enumerate the possible factors that leads to non-adherence to phosphate binders.
- To investigate the impact of pharmacist-led education and counselling to enhance the adherence of phosphate binders.

METHODOLOGY**STUDY POPULATION**

A pilot study is conducted and a total of 10 patients with Chronic Kidney Disease who undergo maintenance hemodialysis with hyperphosphatemia and phosphorous levels greater than 5.5mg/dl and are prescribed with phosphate binders were included in this prospective observational study in the Department of Nephrology at a Multispeciality Hospital in Thiruvananthapuram. Written informed consent was obtained from each subject following a detailed explanation of the objectives and protocol of the study.

DATA SOURCE :

All the relevant information regarding the study was collected from case records and direct interview with patients. Datas were collected by using pre designed data collection form or proforma. The study was

approved by Research and Ethical Committee of Cosmopolitan hospital ,Thiruvananthapuram, Kerala,India.

The patient's adherence to phosphate binders were assessed using **ADHERENCE TO REFILL AND MEDICATIONS SCALE (ARMS)**. There are 12 questions in the questionnaire. The range of possible scores is 12-48. Lower scores indicate better adherence. Adherence was calculated on the basis of total score of questionnaire as follows:

- <19 score - Good adherence**
- 19 – 30 score - Moderate adherence**
- >30 score - Poor adherence**

The patient's **KNOWLEDGE ATTITUDE PRACTICE (KAP)** was assessed using KAP questionnaire. It comprises a total of 15 questions. All the 3 categories contain 5 questions each. The possible scores range from -15 to 15. The KAP were calculated on the basis of total score of questionnaire as follows:

- Above 12 score (>80%) - Good**
- 6-12 score (40%-80%) - Moderate**
- Below 6 score (<40%) - Poor**

The scores were assessed before and after providing proper counselling and education through the Patient Information Leaflet (PIL)

STATISTICAL ANALYSIS

Statistical analysis was performed using Microsoft Excel. Paired t-test was used to analyse the effectiveness of the drug and to assess the adherence and Knowledge Attitude Practice (KAP) of the patients before and after providing proper counseling and education. The P value < 0.05 is considered as statistically significant.

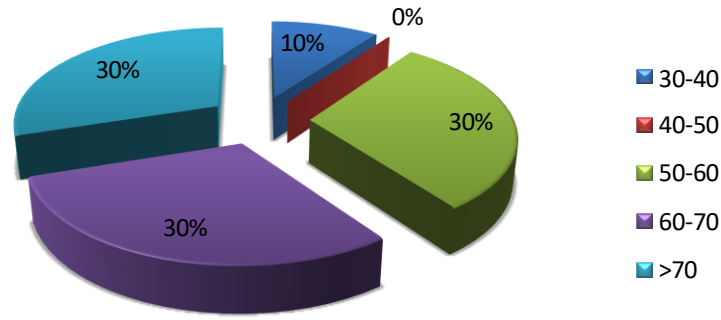
RESULT AND DISCUSSION:

In this pilot study, 10 patients were enrolled as per the inclusion exclusion criteria. The results are as follows

AGE WISE DISTRIBUTION OF PATIENTS

AGE IN YEARS	NUMBER (n=10)	PERCENTAGE (100%)
30-40	1	10
40-50	0	0
50-60	3	30
60-70	3	30
>70	3	30

AGEWISE DISTRIBUTION OF PATIENTS



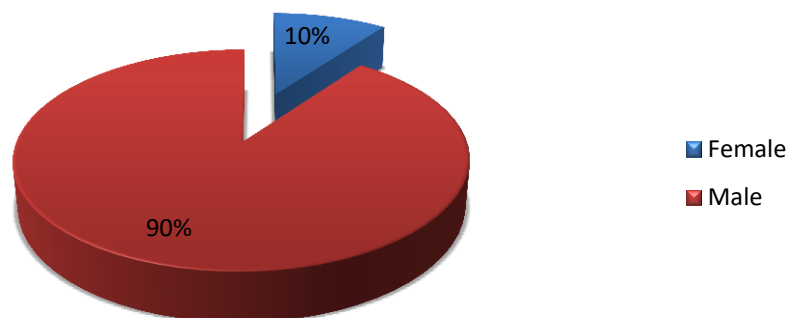
Out of 10 patients, 10% of the study population comes under the age group of 30-40, 30% comes under the age group of 50-60, 30% comes under the age group of 60-70 and again 30% population comes under the age above 70 years while no patients were found between the age group of 40-50 years. It shows that when the age increases, the probability of occurrence of the disease condition (CKD) also increases.

GENDER WISE DISTRIBUTION OF PATIENTS

GENDER	NUMBER (n=10)	PERCENTAGE (100%)
MALE	9	90%
FEMALE	1	10%

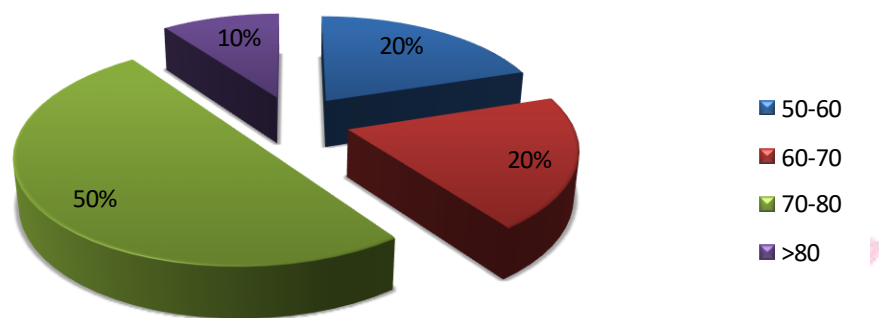
Out of 10 patients, 90% were males and 10% were females. It shows that CKD occurs more in males than females.

GENDER WISE DISTRIBUTION OF PATIENTS



DISTRIBUTION OF WEIGHT

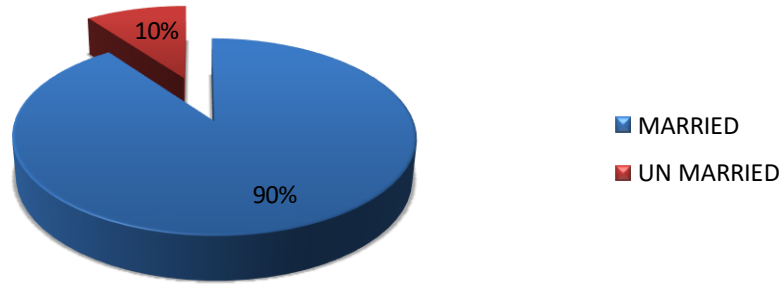
WEIGHT (Kg)	NUMBER (n=10)	PERCENTAGE (100%)
50-60	2	20
60-70	2	20
70-80	5	50
>80	1	10

DISTRIBUTION OF WEIGHT

Out of 10 patients, 50 % patients comes under the weight group 70-80, 20% patients were evenly distributed among two groups: 50-60 & 60-70.10 % patients comes under the weight group greater than 80 kg. It shows that when the weight increases the risk occurrence of CKD also increases.

DISTRIBUTION OF MARITAL STATUS

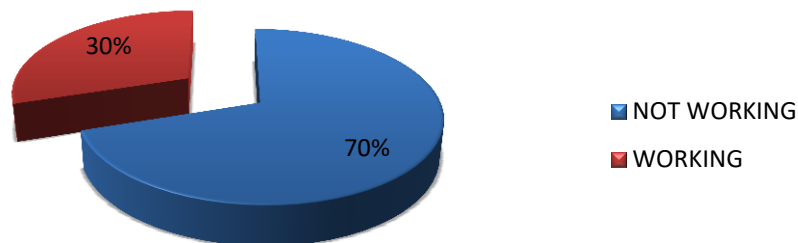
MARITAL STATUS	NUMBER (n=10)	PERCENTAGE (100%)
MARRIED	9	90
UNMARRIED	1	10

DISTRIBUTION OF MARITAL STATUS

Out of 10 patients, 90% were married and remaining 10% were unmarried. Here majority of the patients were married.

DISTRIBUTION OF OCCUPATION

OCCUPATION	NUMBER (n=10)	PERCENTAGE (100%)
NOT WORKING	7	70
WORKING	3	30

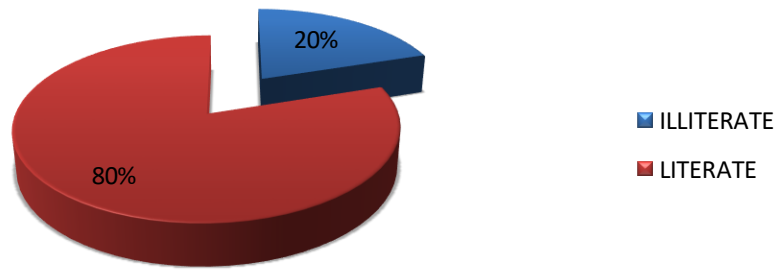
DISTRIBUTION OF OCCUPATION

Out of 10 patients, 70% were not working and 30% were working. Here majority of the patients were unemployed.

DISTRIBUTION OF LITERACY STATUS

LITERACY	NUMBER (n=10)	PERCENTAGE (100%)
ILLITERATE	2	20
LITERATE	8	80

DISTRIBUTION OF LITERACY STATUS

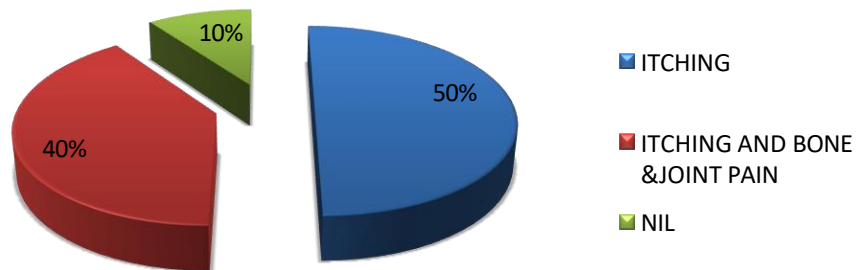


Out of 10 patients, 80% patients were literate and 20% patients were illiterate. It shows that the literate patients are higher than illiterate patients.

DISTRIBUTION OF SYMPTOMS

SYMPTOMS	NUMBER (n=10)	PERCENTAGE (100%)
ITCHING	5	50
ITCHING AND BONE & JOINT PAIN	4	40
NIL	1	10

DISTRIBUTION OF SYMPTOMS

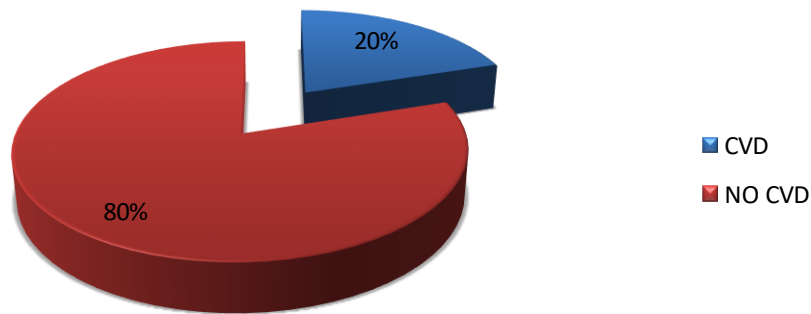


Out of 10 patients, 50% has itching, 40% has itching and bone & joint pain and 10% had none of the symptoms. These symptoms occur when the high levels of phosphorous may cause the calcium level to decline.

DISTRIBUTION OF COMORBIDITIES

COMORBIDITY	NUMBER (n=10)	PERCENTAGE (100%)
CVD	2	20
NIL	8	80

DISTRIBUTION OF COMORBIDITIES

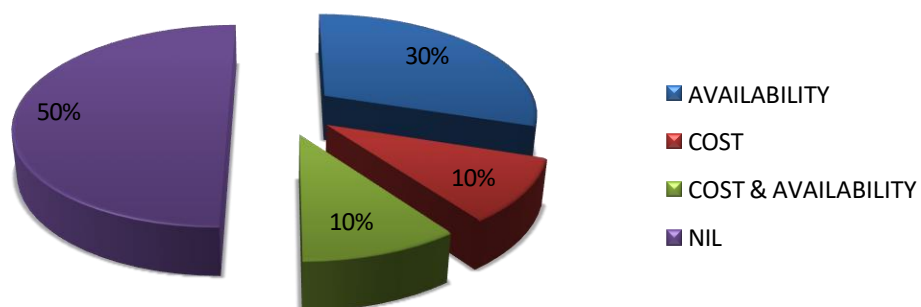


Out of 10 patients 20% of patients had coexisting cardiovascular disease and 80% of patients had no cardiovascular diseases.

POSSIBLE REASONS FOR NON-ADHERENCE

REASON	NUMBER (n=10)	PERCENTAGE (100%)
AVAILABILITY	3	30
COST	1	10
COST & AVAILABILITY	1	10
NIL	5	50

POSSIBLE REASONS FOR NON-ADHERENCE

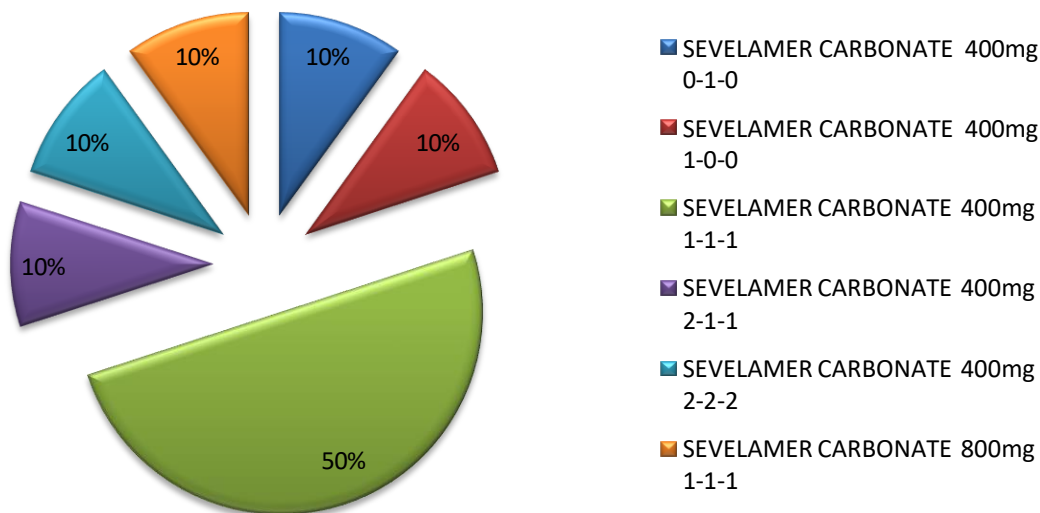


Out of 10 patients the possible reasons for the non-adherence are availability for 30% of patients, cost for 10% of patients, cost & availability for 10% of patients and have no reason for 50% of patients.

DRUG AND FREQUENCY

DRUG AND FREQUENCY	NUMBER (n=10)	PERCENTAGE (100%)
T.SEVELAMER CARBONATE 400mg 0-1-0	1	10
T. SEVELAMER CARBONATE 400mg 1-0-0	1	10
T. SEVELAMER CARBONATE 400mg 1-1-1	5	50
T. SEVELAMER CARBONATE 400mg 2-1-1	1	10
T. SEVELAMER CARBONATE 400mg 2-2-2	1	10
T. SEVELAMER CARBONATE 800mg 1-1-1	1	10

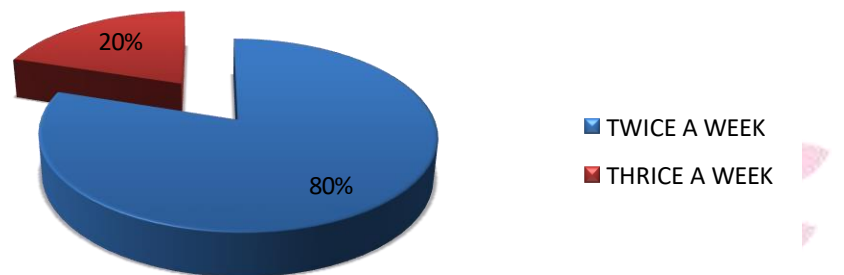
DRUGS USED BY THE PATIENTS AND ITS FREQUENCY



Out of 10 patients included in the study, 10% take T.REVELAMER 400mg once daily with afternoon meals, 10% take T.REVELAMER 400mg once daily with morning meals, 50% take T.REVELAMER 400mg thrice daily with meals, 10% take T.REVELAMER 400mg thrice daily but 2 tablets during morning time with meals, 10% take T.REVELAMER 400mg 2 tablets thrice daily with meals, 10% take T.REVELAMER 800mg thrice daily with meals.

FREQUENCY OF DIALYSIS

FREQUENCY	NUMBER (n=10)	PERCENTAGE (100%)
TWICE A WEEK	8	80
THRICE A WEEK	2	20

FREQUENCY OF DIALYSIS

Out of 10 patients, 80% patients undergoing dialysis twice a week and 20% patients undergoing dialysis thrice a week.

COMPARISON OF PHOSPHOROUS

	PRE COUNSELLING	POST COUNSELLING
Mean Score	7.00	5.47
SD	0.82	1.69
Significant value	0.001 (p<0.05)	

Comparing pre and post counselling score, a paired t-test is administered. The result is significant and we reject the null hypothesis that the scores are equal and conclude that the post counselling score is significant. Thus the phosphate binder have desirable effect on the hyperphosphatemic patients in CKD patients those who undergo maintenance hemodialysis.

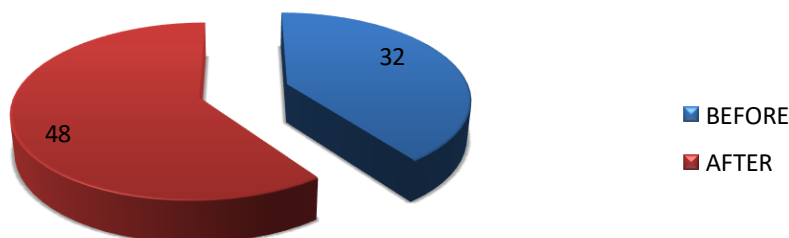
COMPARISON OF CALCIUM

	PRE COUNSELLING	POST COUNSELLING
Mean Score	7.51	8.624
SD	1.377	0.872
Significant value	0.044 (p<0.05)	

Comparing pre and post score, a paired t-test is administered. The result is significant and we reject the null hypothesis that the scores are equal and conclude that the post counselling score is significant. Thus the phosphate binders have desirable effect in the serum levels of calcium in hyperphosphatemic patient where the calcium levels are lower than the normal levels.

KNOWLEDGE OF PATIENTS BEFORE AND AFTER EDUCATION

PATIENT KNOWLEDGE	SCORES (50)	PERCENTAGE (100%)
BEFORE	32	64%
AFTER	48	96%

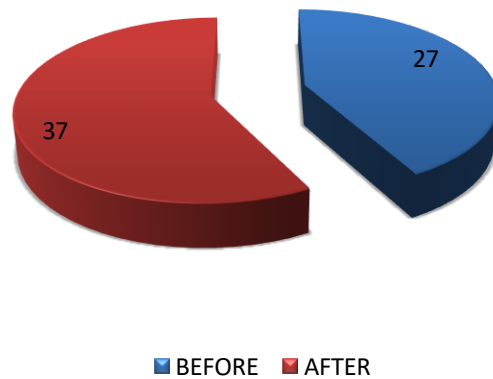
KNOWLEDGE OF PATIENTS BEFORE AND AFTER EDUCATION

Out of 10 patients, it was found that the patients knowledge on phosphate binders before(64%) and after (96%) education was statistically significant. (P Value = 0.001)

ATTITUDE LEVEL OF PATIENTS BEFORE AND AFTER EDUCATION

PATIENT ATTITUDE	SCORES (50)	PERCENTAGE (100%)
BEFORE	27	56.1%
AFTER	37	74%

ATTITUDE SCORES OF PATIENTS BEFORE AND AFTER EDUCATION

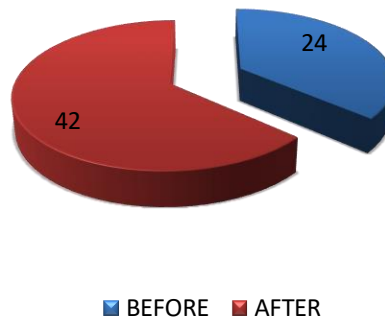


Out of 10 patients , it was found that the patients attitude towards phosphate binders before(56.1%) and after (74%) education was statistically significant. (P Value = 0.001)

PRACTICE LEVEL OF PATIENTS BEFORE AND AFTER EDUCATION

PATIENT PRACTICE	SCORES (50)	PERCENTAGE (100%)
BEFORE	24	48%
AFTER	42	84%

PRACTICE SCORES OF PATIENTS BEFORE AND AFTER EDUCATION



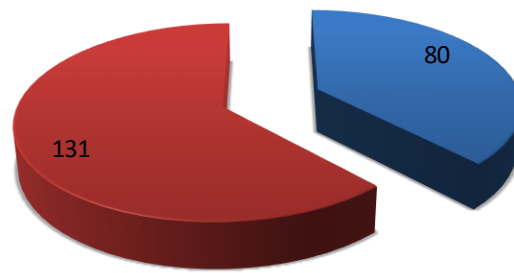
Out of 10 patients , it was found that the patients practice on phosphate binders before(48%) and after (84%) education was statistically significant. (P Value = 0.001)

TOTAL KAP SCORE

OVERALL KAP BEFORE AND AFTER EDUCATION

OVERALL KAP	SCORES (150)	PERCENTAGE (100%)
BEFORE	80	53.3%
AFTER	131	87.3%

OVERALL KAP SCORES OF PATIENTS BEFORE AND AFTER EDUCATION



■ BEFORE ■ AFTER

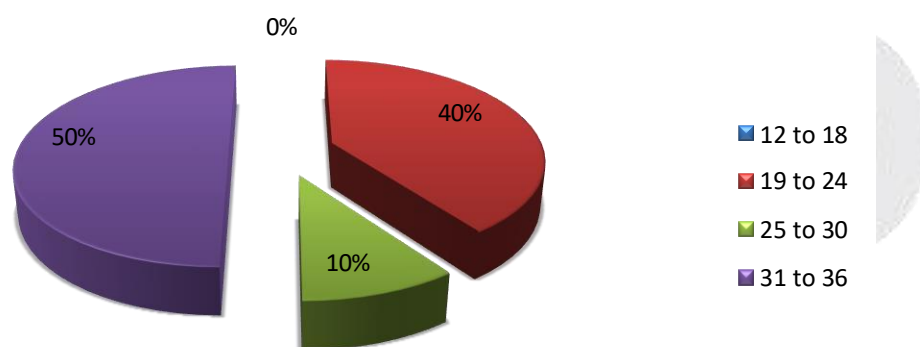
Out of 10 patients, it was found that the patients overall KAP on phosphate binders before(53.3%) and after (87.3%) since education was statistically significant. (P Value = 0.001)

ADHERENCE

ADHERENCE OF PATIENTS BEFORE COUNSELLING

SCORE	NUMBER (n=10)	PERCENTAGE (100%)
12-18	0	0
19-24	4	40
25-30	1	10
31-36	5	50

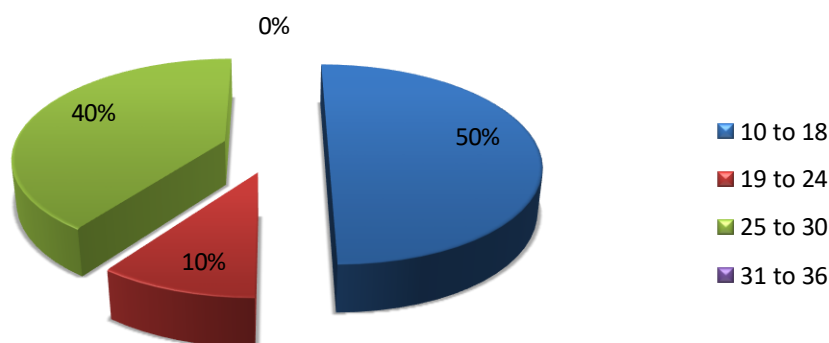
ADHERENCE OF PATIENTS BEFORE COUNSELLING



Out of 10 patients, 50% have moderate adherence to the drug and 50% have poor adherence to the drug before providing counselling to the patients.

ADHERENCE OF PATIENTS AFTER COUNSELLING:

SCORE	NUMBER (n=10)	PERCENTAGE (100%)
12-18	5	50
19-24	1	10
25-30	4	40
31-36	0	0

ADHERENCE OF PATIENTS AFTER COUNSELLING

Out of 10 patients, 50% have good adherence to the drug and 50% have moderate adherence to the drug after providing counselling to the patients.

COMPARISON OF ADHERENCE

	PRE COUNSELLING	POST COUNSELLING
Mean Score	29.80	22.20
SD	5.75	5.61
Significant value	.001* (p<0.05)	

Comparing pre and post score a paired t-test is administered. The result is significant and we reject the null hypothesis that the scores are equal and conclude that the post score is significant than the pre score

CONCLUSION

This pilot study shows that phosphate binders are effective in the treatment of hyperphosphatemia in chronic kidney disease patients undergoing maintenance hemodialysis. The drug has salient effect on the serum levels of phosphorous and calcium. All the patients show improvement in the levels of phosphorous and majority of the patients show desirable effect in the calcium level. This study also emphasizes the Knowledge Attitude & Practice and Medication Adherence of the patient towards phosphate binders which is improved by patient education and patient counselling respectively. Through the improved KAP and medication adherence it has directly contributed to the effectiveness of the drug in the hyperphosphatemic management. Also it enlists the possible factors for non-adherence in the patients. By the gradual decline in

the hyperphosphatemia, the patients have reduced chances of cardiovascular mortality and the progression of mineral bone disorders. The only limitation this pilot study had to confront is that the number of participants. The results will be more accurate and precise if the participant quantity is greater than the existing ones.

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