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NIACIN THERAPY FOR THE TREATMENTOF HYPERPHOSPHATAEMIA IN END STAGE RENAL DISEASE PATIENTS

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ABSTRACT

Elevated serum phosphorus is a predictable accompaniment of end-stage renal disease (ESRD) in the absence of supplemental phosphate binders.. We have analyzed the distribution of serum phosphorus in samples of hemodialysis patients who have been receiving dialysis for at least 1 year. Recently, niacin, a traditional antilipemic agent, drew attention as an experimental treatment for Hyperphosphataemia.. Sodium-dependent phosphorus co-transport in the duodenum and jejunum appears to account for at least 50% of intestinal phosphorus absorption. Niacinamide reduces intestinal phosphate absorption by inhibiting the sodium-phosphate transporter in the gastrointestinal tract.The purpose of this study is to report on new findings regarding niacin's novel effects and to review the possibility of repurposing niacin for Hyperphosphataemia treatment in dialysis patients by elucidating its safety and efficacy profiles along with its synergistic clinical benefits. Niacinamide treatment decreased serum phosphorus from 6.26 to 5.47 mg/DL (*P* = .02), and no significant changes occurred in the placebo group. Among patients who demonstrated more than 80% adherence based on routine pill counts, the fall in serum phosphorus was more pronounced, decreasing from 6.45 to 5.28 mg/DL (*P* =. 002). . Thus, Niacin can be a patient-convenient and inexpensive alternative or adjunctive therapy for phosphorus management in dialysis patients.

KEYWORDS: niacin, nicotinic acid, niacinamide, hyperphosphatemia, C-peptide,dialysis.

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INTRODUCTION

Elevated serum phosphorus is a predictable accompaniment of end-stage renal disease (ESRD) in the absence/ with the use of supplemental phosphate binders.[1,2] Also the traditional phosphate binders have common drawbacks that may negatively influence patient adherence to the medication regimen.[3,4,5] .. Although vitamin D can enhance the absorption, especially under conditions of dietary phosphate depletion, intestinal phosphate absorption does not require the presence of active vitamin D.[6,7] Renal excretion of excess dietary phosphate intake ensures maintenance of phosphate homeostasis, maintaining serum phosphate at a level of approximately 3-4 mg/dL in the serum.[8,9,10]Phosphorus is the sixth most abundant element in the human body..Phosphorus (phosphate) is critical for bone mineralization, cellular structure, genetic coding, and energy metabolism...[11,] The most common cause of decreased renal phosphate excretion is kidney failure, acute or chronic of any cause (although marked hyperphosphatemia is usual in chronic renal insufficiency when the glomerular filtration rate (GFR) is less than 25 mL/min). (Normal -90 - 120 mL/min/1.73 m^2.).[18,19,20]Once renal insufficiency progresses to the loss of 40-50% of renal function, the decrease in the amount of functioning renal tissue does not allow excretion of the full amount of ingested phosphate required to maintain homeostasis and hyperphosphatemia develops.. The consequences of Hyperphosphataemia include the development and progression of secondary hyperparathyroidism and a predisposition to metastatic calcification when the product of serum calcium and phosphorus (Ca x PO4) is elevated.[21,22,23] Both of these conditions may contribute to the substantial morbidity and mortality seen in patients with ESRD. According to World Health Organization (WHO) Global Burden of Disease Project, disease of the kidney and urinary tract contribute to approximately 18,50,000 deaths every year of which Chronic Kidney Disease (CKD) is the 9th leading cause of death and 17th leading cause of disability in the world.[24,25,26,27.] The global increase in CKD is being driven by the global increase of diabetes mellitus, hypertension, obesity and aging. We have analyzed the distribution of serum phosphorus in samples of hemodialysis patients who have been receiving dialysis for at least 1 year or more. Most of the studied cases were from one hospital of Nephrology, some cases were picked from Govt Hospital, Because of Hyperphosphataemia these patients typically require oral phosphate binders for lifelong phosphorus management, in addition to dietary restrictions and maintenance dialysis. Recently, Niacin, a traditional antilipemic agent, drew attention as an experimental treatment for Hyperphosphataemia. Sodium-dependent phosphorus co- transport in the duodenum and jejunum appears to account for at least 50% of intestinal phosphorus absorption. Niacinamide reduces intestinal phosphate absorption by inhibiting the sodium-phosphate transporter in the gastrointestinal tract, although sodium-independent absorptive pathways remain intact. Previous studies have shown that Niacinamide prevents an increase in serum phosphate in animals with renal failure by reducing sodium-phosphate 2 b transporter expression in the jejunum and inhibiting intestinal phosphorus absorption. The magnitude of the risk is illustrated by the fact that Hyperphosphataemic compared with Normo-phosphataemic patients have a 52**%** higher risk of death from coronary artery disease, a 26**%** higher risk of sudden death, a 34% higher risk from other cardiac causes and a 39% higher risk of death from cerebro-vascular accidents .[28,29,30] In India approximate total burden of CKD is 800 per million population (pmp). It has been reported that Diabetes mellitus as the cause of CKD was found in 31.2-41% of ESRD patients in India. [31.32] *Indian Scenario* India has only 850 qualified nephrologists for a country of 1.2 billion people, two deaths every five minutes. That is how many kidney disease victims die in India - two lakh a year or roughly 547 everyday.India gets 1.5 lakh patients with kidney failures every year and a majority of them die within five years due to the acute shortage of dialysis units in the country, according to Dr D S Rana, secretary, Indian Society of Haemodialysis. “There are only 1,470 haemodialysis units in the whole country, whereas 40,000 of them are immediately required,”[33]Currently, about eight lakh patients with terminal renal disease in India require dialysis and transplantations. But only 4,000 patients are getting kidney transplantations and an equal number are on maintenance haemodialysis. Unfortunately, not a single dialysis unit is made in India and they have to be imported from Sweden and Germany, “Less than 10 per cent of the total patients requiring dialysis are able to avail the facility, while only half of them are able to afford it on a long term basis, due to cost, time and logistical factors. About 90 percent of these facilities are in the private sector for which patients, whether rich or poor, have to pay.”“Haemodialysis treatment is very expensive. A patient normally receives dialysis at least thrice a week, and monthly expenses amount to Rs 30,000. The medicines are also equally costly and a majority of the patients are not able to afford this treatment. Adding to the problem, health insurance policies do not cover the cost of dialysis owing to the high cost,”Chhattisgarh is a Stone Belt area and delayed-diagnosed renal stones are causes of kidney damage and CKD here. According to state health statistics every day 2-5 deaths are commonly due to renal failure, absence of dialysis because it is costly medical treatment. A survey done by us revealed that only 5 govt hospitals are having working dialysis machines presently including Govt Hospital in the state capital. Even inadequate dialysis (under-dialysis) affects cardiac death by mechanisms like Hyperphosphataemia , Hypervolaemia, poor control of blood pressure, malnutrition etc.Thus, all new therapies for the treatment of ESRD induced Hyperphosphataemia are important for the Indian community, as Chronic kidney disorders are like epidemic here because of absence / under dialysis.

The side effects of Phosphate Binders

Despite the introduction in the market of new P-binders, such as Ca Bicarbonate, Ca Acetate, sevelamer hydrochloride and lanthanum carbonate, the control of Hyperphosphataemia in haemodialysis (HD) patients remains difficult because of adverse

effects such as vomiting, nausea, constipation and faecal impaction, drug compliance and metal accumulation. Thus, the purpose of this study is to report on new findings regarding niacin's novel effects and to review the possibility of repurposing niacin for Hyperphosphataemia treatment in dialysis patients by elucidating its safety and efficacy profiles along with its synergistic clinical benefits. The following objectives are drawn To assess the initial serum Phosphorus level of the patients, because the aim of this study is to assess the condition of Hyperphosphataemia in renal dialysis patients, To assess the initial level of Calcium in serum of patients, because when the serum Phosphorus level gets high, simultaneously the serum Calcium level gets low, this induced hypocalcaemia has many adverse effects on body as CVD related problems. To assess the initial Total Lipid profile of the patients as Hyperphosphataemia and parallel hypocalcaemia has dislipidemia –precipitating effect. To assess the initial level of c- reactive protein, because higher serum Phosphorus level increases sensitivity and incidences of repeated infections. This causes higher levels of C- reactive proteins. To assess the serum level of Creatinine as this bio-indicator reflects the severity of CKD , because the excretion of Creatinine is hampered in Chronic renal disorder and co- related to the severity of the disease. Hemoglobin gm % values was assessed by using Hemoglobinometer , as in CKD absence of REF (Renal Erythropoietin Factor) precipitates severe anaemia. Also the other parameters were measured as they are also affected. To assess the total serum level of Parathyroid hormone, because elevated Phosphorus level changed the status of this very hormone or vice versa. To assess the serum gm % level of Albumin as in CKD, albuminurea is commonly seen symptom, related with the severity and blood's osmotic pressure changes related complications. To assess the serum status of enzyme -Creatine Kinase as the serum level of this enzyme indicates the condition of Cardiac Health, because chronic renal disease precipitates Ca precipitation on Cardiac soft tissues , thus Atherosclerosis and other Cardiac related ill effects are observed. To study Effect of supplementing Niacin in Nicinamide form on Serum Phosphorus and calcium Level of hemodialysis patients. To study the effect of supplementation on lipid profile and parathyroid hormone status of the hemodylitic patients, To study the effect of this supplementation on the prevalence of complications of Hyperphosphataemia. To study the side–effects of Niacin supplementation on patients. To study the effect of supplementation on C - reactive protein of the patients.To study the effect of supplementation on serum level Creatine Kinase of the patients.To study the placebo effect of supplementation on above mentionedbiochemicalparameters.

MATERIALS & METHODS

19 patients of ESRD were selected by contact in clinics and they were given intervention dose of Niacin for about 8 weeks after fulfilling all medical formalities and 19 patients of ESRD, having almost matched demographic profile were given Placebo dose. Their (Niacin given patients and Placebo Given patients) study-related biochemical parameters were assessed before and after intervention and results were compared for any significant changes. During the study period their dietary Phosphorus levels were tried to keep low and equal. Estimation of Serum Calcium was done by OCPC (Ortho-Cresolphthalein Complexone) method by using the kit of "Lab Care" in auto analyzer, model no-Star 21 Plus. 1 ml vial of reagent was mixed with 0.5 ml serum. The calcium in the patient serum/plasma reacts with OCPC to form a purple coloured complex. The intensity of the colour is directly proportional to the concentration of calcium in the sample. The concentration is measured calorimetrically at a wavelength of 578nm (550 – 590 nm) and compared with that of a standard. Estimation of serum Phosphorus was also done by using kit of Lab care and by using auto analyser, model no Star 21 Plus. In the reaction, inorganic phosphorus reacts with ammonium molybdate in an acidic solution to form a colored phosphomolybdate complex. The system monitors the change in absorbance at 365 nm at a fixed time interval. This change in absorbance is directly proportional to the concentration of phosphorus in the sample. C-reactive protein was assessed by using kit of Span Diagnostics, reagent kit, Surat [code 25934] used for in vitro detection of C - reactive protein (CRP) in human sera in auto-analyzer by agglutination method.50 micro ml serum was mixed with 1 ml reagent , clumping was indication of positive test . Hemoglobin gm % values was assessed by using Hemoglobinometer, also other parameters were assessed by using by using 5 Part Hematology Analyser, BC-5000 of Minray company. The HbA1c values were all were estimated, as higher Serum Glucose is strong etiological factor for diabetes and a correlation was observed among HbA1c values and serum creatinine level to assess the level of severity of CKD with status of diabetes. Also, a Library and Pub Med literature search was performed to capture prospective clinical trials on niacin's hypophosphatemic effects in dialysis patients. Serum Creatinine level was measured by using kit of MERCK company, in auto-analyser. Creatinine in a protein free solution reacts with Alkaline Picraete and produces a red colour complex, which is measured calorimetrically at 520 nm. The ECG was taken / collected reports from the patients to assess the effect of CKD on the cardiac health with the help of cardiologist. Those blood samples, which were found positive for C-reactive protein were sent to Ranbaxy Lab, Bombay via local sample collecting centre and were again quantitatively analysed. About 11 samples were sent outside, we analysed remaining samples ourselves and compare the results. We also got the same trend of serum values. The results were compared with the normal serum values. Qualitative and semi quantitative rapid latex slide test was used. We used kit of Span diagnostics, mixed 50 micro ml serum with 1 drop of reagent and within 6 seconds the result was read. As Serum Creatine Kinase is bio-indicator of cardiac damage-so quantitatively analysis of this enzyme is done to assess the severity of the cardiac damage. For analysis Kit of Tecko Diagnosis was used, for assessment kinetic method was adopted. Sample value of 50 micro ml serum was mixed with

reconstituted reagent with buffer, at 37 Ç, and the absorbance was read at 340nm,the time interval was 30 seconds. For serum Level of Niacin estimation with the help of Diagnostic centre five samples from each group were analysed . Sufficient blood was drawn in a lavender-top (EDTA) tube(s). Then the blood sample was spin down and transfer to a plastic Amber vial (T192) to protect from light within 30 minutes of collection. Then the sample was freeze Frozen and 4 mL of EDTA frozen sample was used for High Performance Liquid Chromatography. Serum Albumin gm % was assessed because in renal disorders albuninurea is common, and serum Albumin level gets low parallel to the severity of the disease. The level was assessed by using auto-analayser, model no 121 star , with the use of diagnostic kit for albumin analysis of Span company. Also total protein gm % level was assessed by using the Kit of the same company, because it is expected that total protein status is also significantly reduced in CKD. The intervention dosage for niacin ranged from 800 to 1,000 mg/day, with the average daily dose of approximately 500–800 mg in divided doses. In a randomized, double-blind, placebo-controlled crossover trial, 19 patients undergoing haemodialysis who had serum phosphorus levels > 5.0 mg/dL despite binder therapy were randomly assigned to placebo / Niacinamide for 8 weeks. Niacinamide and placebo were packaged in identical 250-mg capsules (taken as 1 capsule twice a day) to 750 mg/d (3 capsules thrice a day) over 8 weeks. The placebo group was supplied with the capsules, which were identical with the vitamin capsules in looks. They were regularly observed for any adverse effect of supplementation. The total lipid profile was estimated by Auto-analyzer star 21 Model-The following Kits were used- Chema Diagnostica Qualigens fine chemicals A division of Glaxo India Ltd.Span diagnostic limited, Surat, India.

  - Cholesterol Estimation Kit (one step method of Wybenga and Plleggi) (Catalog No. – 25924)
  - HDL Estimation Kit (One step method of Wybenga and Plleggi) (Catalog No.–25924)
  - Triglyceride Estimation Kit (Enzymatic colorimetric method GPO–PAP liquid stable single regent) (Catalog No. 77034 (6×250 ml)).
- Estimation of Parathyroid Hormone- Estimation was done by Mini Vidas (Biomarix company) Model XT-55, by using Kit of Merack Company.

The demographic profile of the subjects

The demographic profile of the patients- Mean age: 52.4 ± 10.8 years; 12 males, 7 females; 5 diabetes mellitus (DM), 5 non-DM; HD duration: 10.3 ± 7.0 years; serum albumin levels: 3.4 ± 1.3 g/dL; serum calcium (Ca) levels: 6.1 ± 0.6 mg/dL; serum P levels: 6.7 ± 0.8 mg/dL; serum intact parathyroid hormone (PTH) levels: 369 ± 321 pg/mL]. The demographic profile of the Placebo Group- 9 HD patients who did not receive Niacin capsules as a control group (age: 53.1 ± 12.6 years; 8 males, 11 females; 4 DM, 6 non-DM; HD duration: 10.1 ± 6.8 years; serum albumin levels: 3.3 ± 0.3 g/dL; serum Ca levels: 6.4 ± 0.9 mg/dL; serum P levels: 7.0 ± 0.8 mg/dL; serum intact PTH levels: 359 ± 324 pg/mL).

RESULTS

Before Intervention of Vitamin Supplementation-(Initial Values)

Normal serum calcium value is 9-10.5 mg/dL, the observed value is 6.71mg/dL average, thus a significant hypocalcaemia is observed among the studied group.Normal serum values for phosphorus is 2.4-4.5 mg/Dl, but the observed value is 9.9 mg/dL ,thus a significant Hyperphosphtaemia t value- 2.31 is observed in studied group. The normal serum creatinine level is 0.5-1.1mg/dL, but the estimated average level was >2.5 mg/dl, this was the basic criteria for the selection of patients included in this study. The normal Ca XP value is 55mg /dL , The average observed value was bit high -62mg/dl , but in 23% subjects the value was observed extremely elevated (average-83-106mg/dl.) The GFR was observed <15 ml/min/1.73m2 before starting therapy.(Collected data from hospitals)The Haemoglobin gm/100 ml value was observed lower than normal. 93 % of the studied subjects were having anemia. (Average-8.33gm%) The hematocrit value was almost normal (31%), also the size of RBCs was observed normal in hemogram-85 $mm^{2.}$.Thus the patients had normocytic –normochronic anaemia.The 23 % of the CRD had HbA1c values 8.11, 77% of these diabetic-CKD patients were females.The plasma level of Vitamin Niacin was 5.44 ug/ mL (Normal 0.50- 8.55 ug/ mL)Cardiovascular Events*:* We have collected the technical information from the cardiologists-the following cardiovascular events were observed in CKD patients-Ischemic Heart Disease (IHD)-11%, Arrhythmia-24% , Left ventricular hypertrophy (LVH)-9% , Congestive Heart Failure (CCF)-3% . We included clinical and ECG criteria to define cardiac events. Serum c-reactive protein initially was 3.6 mg/L, the normal value is 1.0 to 2.8 mg/L.The parathyroid hormones serum value is 113 $\pm$ 79 pgm/mL. (Normal level 55 pgm/mL)Serum Level of Creatine Kinase is 188 U/L , normal value is 145-171 U/L. Lipid Profile parameters before Vitamin intervention – Cholesterol 1.85 $\pm$ 0.17 mg/ ml, Triglyceride 1.49 $\pm$ 0.36 mg/ ml, HDL 0.29 $\pm$ 0.02 mg/ml, LDL (Calculated) -1.26 $\pm$ 0.16. Niacinamide treatment decreased serum phosphorus from 6.26 to 5.47 mg/dL (P = .02), and no significant changes occurred in the placebo group. Among patients who demonstrated more than 80% adherence based on routine pill counts, the fall in serum phosphorus was more pronounced, decreasing from 6.45 to 5.28 mg/dL (P = .002). Positive effects were observed on serum C-peptide level also. Serum P levels unexpectedly decreased significantly in the Third and fourth weeks due to oral administration of the Vitamin capsules. Serum P levels remained unchanged in the placebo and control group. Subsequently, serum P levels returned to original levels 4 weeks after the completion of oral treatment. After Intervention the Biochemical parameter changesThe serum Phosphorus level after Niacin

supplementation became- 5.47 mg /dl The serum Calcium level after intervention period became- 9.71mg /dl The Ca XP Value after intervention became -56 mg/ dl After the intervention period the analysed value of C – reactive protein was 2.9 mg /L. After supplementation in the study period the parathyroid hormonal level became 93 ± 7 p mg/m L. The plasma level of Niacin became 7.83 ug / m L, after supplementation. Serum C-reactive protein became 3.1mg / L The serum creatinine level became 1.5mg / dl after supplementation- The status of Parathyroid hormone became-79 ± 54 p gram/ m L The level of Creatine Kinase became-179 U/L Serum Albumin level remained unchanged. Also Hg gm % value , Hematocrit value was not changed , There was a marginal decrease in HbA1c values 8.09. The cardio vascular events were not corrected significantly, but the Electrical magnitude of T wave was 23 % increased, showing that the cardiac muscles were regaining strength perhaps due to corrected condition of hypocalcaemia. The Creatine Kinase level become 182 U/L, the change is not significant, but the intervention module showed downward trend in this parameter. There was a significant change in Lipid Profile –in all parameters- Cholesterol-1.25 ± 0.08 mg/ml, Triglyceride -0.98 ± 0.20 mg/ml, HDL 0.59 ± 0.18 mg/ml, LDL Calculated) - 0.54 ± 0.13.Thus there were significant positive changes in lipid total profile of Niacin users, but not in placebo group.

TABLE-1

Changes In values of Lipid Profile after Vitamin B $_3$ Intervention

Factors Of Lipid Profile	(mean ± SD)		difference in percent-age	t value
	After Intervention of Vitamin (n=09)	Initial Values (n=09)		
Cholesterol (mg/ml)	1.25 (±0.08)	1.85 (±0.17)	48%	17.63*,**
Triglyceride (mg/ml)	0.98 (±0.20)	1.49 (±0.36)	53%	18.68*,**
HDL (mg/ml)	0.59 (±0.18)	0.29 (±0.02)	+ 51%	24.29,*,**
LDL (mg/ml)	0.54 (±0.16)	1.26 (±0.17)	131%	49.00,*,**

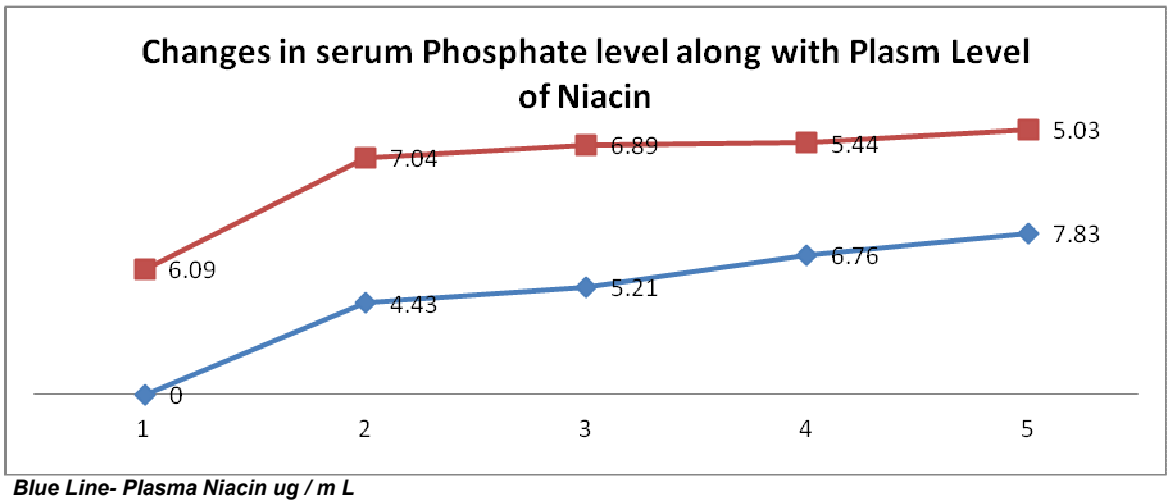
Mean, SD & 't' Values of lipid profile of victims in comparison with healthy controls
P<0.05 level, **P<0.01 level. SD Values showed in parenthesis

TABLE-2

Changes in Biochemical parameters after Niacin Intervention

Sr No	Biochemical Parameters	After Niacin intervention	Initial Values	Percentage change
1	Serum Ca- mg %	9.71	6.6	↑ 44.92 %
2	Serum P- mg %	5.47	9.9	↓ 44.74 %
3	Serum Creatinine mg / dl	1.5	2.5	↓ 40.00 %
4	Ca X P mg/ dl	56	62	↓ 9.67 %
5	Hb gm %	8.33	8.31	↑ 0.24 %
6	Hb A1c	8.09	8.11	↓ 0.25 %
7	c-reactive protein mg/ L	3.1	3.6	↓13.88 %
8	Parathyroid hormone p gm / ml	79	113	↓ 30.08 %
9	Creatine Kinase U/L	179	188	↓ 4.78 %
10	Niacin ug/ml	7.83	5.44	↑ 30.52 %

Graph -3
Changes in Serum P level along with Niacin supplementation



Blue Line- Plasma Niacin ug / m L
Red Line- Serum Phosphorus level mg / dl

DISCUSSION

After supplementing Niacin for about 8 weeks a significant correction was observed in serum values of Phosphate (44.74 % decreased) along with correction in condition of Hypocalcaemia (44.92 % increased), this indicates the Niacin has antilipemic capacity, also significant increase in serum Calcium level after intervention shows that Niacin has prominent impact on mineral absorption mechanism ,perhaps by changing the pH and also by changing the Ca absorptive mechanism , which previously was blocked by Sodium dependent Phosphorus absorptive process. This effect of Niacin was also reflected in the reduced serum level of Phosphorus. Also serum creatinine values (40 % decreased) and CA X P values were corrected (9.67 % decreased), but not much change was observed in plasma values of Haemoglobin and values of Glucosylated Hb .As Hyperphosphataemia interferes with the correcting trend of serum in terms of end products of protein metabolism, after supplementation with Niacin the status of serum Phosphorus corrects and serum Creatinine level also showed a declining pattern. But unaffected values of Haemoglobin and Glucosylated Hb showed that the supplementing with Niacin does not have effects on diseased kidneys, as after intervention,Renal Erythropoietin Factor (REF) did not show any improvement in the Hb status of the subject , the very supplement had no diabetes correcting impact , as there was no change in the status of Glucosylated Hb of the patients. The value of C- reactive protein was 13.88 % decreased, because of the correction in serum Phosphorus value. High serum Phosphate is always related with increased incidences of various infections, reduction of serum level of phosphorus also reduced the infection rate and hence the level of C - reactive protein was also reduced, which is indicator of repeated infections. The creatine Kinase showed some corrective trend (4.78 % decreased), the high serum Phosphorus is cardio-damaging , after correction in this aspect , the creatine Kinase , related to cardiac functioning showed an improved trend.The serum parathyroid value also showed a 30.08 % decrease after Niacin supplementation, because correction in serum values of Phosphorus. Parathyroid hormone is increased due to high serum level of phosphorus, this increases the excretion of Phosphorus via urinary tubules, as after Vitamin supplementation the level of Phosphate became almost normal, thus the hormone secretion also declined.The Plasma value of Niacin showed 30.52 % increase after vitamin intervention. A negative co-relation was observed between serum level of Niacin and level of P (- 0.958) as Niacin reduced the absorption of Phosphate in intestine, so after regular supplementing patients with this vitamin, the serum Phosphorus level declined. The findings suggest that niacin supplementation can be a patient-convenient and lesser expensive alternative or adjunctive therapy for phosphorus management in dialysis patients. It is found that a graded independent relation between higher levels of serum phosphate and the risk of cardiovascular events exists in people .Further well-designed, large-scale, long-term, comparative trials are needed to successfully repurpose this vitamin for the new indication. This can also be concluded that continuous supplementation of the vitamin is essential to maintain the serum Phosphorus level within the limits. Also the study suggests that kidney disease could potentially be seen as a useful prognostic marker for coronary heart disease. Nicotinamaide supplementation could be an effective therapeutic tool for the maintenance of serum Phosphorus level within limits; this treatment is cost effective as well as safe also.

CONCLUSION

Our study suggests niacin may emerge as a safe, low-cost therapy in combination with /without other phosphate binders for phosphate control. The modest increase in HDL values may be another beneficial effect of this treatment. However, larger and longer term controlled trials are needed to establish the optimal dosage and the clinical significance of niacin treatment.

REFERENCES

1. Kestenbaum B, Sampson JN, Rudser KD, Patterson DJ, Seliger SL, Young B, et al. Serum phosphate levels and mortality risk among people with chronic kidney disease. J Am Soc Nephrol. 2005 ;(16):520–8.
2. Six I, Maizel J, Barreto FC, Rangrez AY, Dupont S, Slama M, et al. Effects of phosphate on vascular function under normal conditions and influence of the uraemic state. Cardiovasc Res. 2012;(96):130–9.
3. Hruska KA, Mathew S, Lund R, Pratt R. Hyperphosphatemia of chronic kidney disease. Kidney Int.2008 ;(74):148–157.
4. Spasovski G, Massy Z, Vanholder R. Phosphate metabolism in chronic kidney disease: from pathophysiology to clinical management. Semin Dial. 2009;(22):357–36.
5. Giachelli CM. The emerging role of phosphate in vascular calcification. Kidney Int. 2009;(75):890–897.
6. Prie D, Urena Torrres P, Friedlander G. Latest findings in phosphate homeostasis. Kidney Int.2009 ;(75):882–889.
7. Hruska KA, Mathew S, Lund R, Memon I, Saab G. The pathogenesis of vascular calcification in the chronic kidney disease mineral bone disorder: The links between bone and vasculature. Semin Nephrol.2009 ;(29):156–165.
8. Feng JQ, Ye L, Schiavi S. Do osteocytes contribute to phosphate homeostasis? Curr Opin Nephrol Hypertens. 2009:(19)285–291. Stubbs J, Liu S, Quarles LD. Role of fibroblast growth factor 23 in phosphate homeostasis and pathogenesis of disordered mineral metabolism in chronic kidney disease. Semin Dial. 2007;(20):302–308.
9. kaore S.N, Yadav V.K. and Kaore N.M. Niacin and Niacin / Laropiprant combination: opening new Hopes for dyslipidemia and cardiovascular diseases With few novel actions, Int J Pharm Bio Sci 2013 July; 4(3): (P) 1053 – 1078.
10. 13.Wolf M. Fibroblast growth factor 23 and the future of phosphorus management. Curr Opin Nephrol Hypertens. 2009 ;(18):463–468.
11. Liu S, Quarles LD. How fibroblast growth factor 23 works? J Am Soc Nephrol. 2007;(18):1637–1647
12. Kuro-o M. Klotho in chronic kidney disease: what's new? Nephrol Dial Transplant. 2009;(24):1705–1708
13. Kestenbaum B, Sampson JN, Rudser KD, Patterson D J, Selinger SL, Young B, Serum phosphate levels and mortality risk among people with chronic kidney disease. J Am Soc Nephrol. 2005;(16):520–528
14. Chonchol M, Dale R, Schrier RW, Estacio R. Serum phosphorus and cardiovascular mortality in type 2 diabetes. Am J Med. 2009;(122):380–386.
15. Tonelli M, Sacks F, Pfeffer M, Gao Z, Curham G. Relation between serum phosphate level and cardiovascular event rate in people with coronary disease. Circulation. 2005;(112):2627–2633.
16. Mathew S, Tustison KS, Sugatani T, Chaudhary LR, Rifas L, Hruska KA. The mechanism of phosphorus as a cardiovascular risk factor in CKD. J Am Soc Nephrol. 2008 ;(19):1092–105.
17. Kidney Disease: Improving Global Outcomes (KDIGO) CKD-MBD Work Group. KDIGO clinical practice guideline for the diagnosis, evaluation, prevention, and treatment of chronic kidney disease-mineral and bone disorder (CKD-MBD). Kidney Int Suppl. 2009 ;(113):S1–130.
18. Lumlertgul D, Burke TJ, Gillum DM, Alfrey AC, Harris DC, Hammond WS, Phosphate depletion arrests progression of chronic renal failure independent of protein intake. Kidney Int. 1986;(29):658–66.
19. Haut LL, Alfrey AC, Guggenheim S, Buddington B, Schrier N. Renal toxicity of phosphate in rats. Kidney Int. 1980;(17): 722–31.
20. Hsu CH. Are we mismanaging calcium and phosphate metabolism in renal failure? Am J Kidney Dis. 1997 ;(29):641–9.
21. Ramirez JA, Emmett M, White MG, Fathi N, Santa Ana CA, Morawski SG, The absorption of dietary phosphorus and calcium in hemodialysis patients. Kidney Int. 1986;(30):753–9.
22. Tonelli M, Pannu N, Manns B. Oral phosphate binders in patients with kidney failure. N Engl J Med. 2010;(362):1312–24.
23. Coladonato JA. Control of hyperphosphatemia among patients with ESRD. J Am Soc Nephrol. 2005;(16)(Suppl 2):S107–14.
24. Hutchison AJ, Smith CP, Brenchley PEC. Pharmacology, efficacy and safety of oral phosphate binders. Nat Rev Nephrol. 2011;(7):578–89.
25. Bellasi A, Kooienga L, Block GA. Phosphate binders: new products and challenges. Hemodial Int. 2006;(10):225–34.
26. Block GA, Wheeler DC, Persky MS, Kestenbaum B, Ketteler M, Spiegel DM, Effects of phosphate binders in moderate CKD. J Am Soc Nephrol. 2012 ;(23):1407–15.
27. Di Iorio B, Bellasi A, Russo D, INDEPENDENT Study Investigators. Mortality in kidney disease patients treated with phosphate binders: a randomized study. Clin J Am Soc Nephrol. 2012;(7):487–93.
28. Chase P, Dupre J, Mahon J, Ehrlich R, Gale E, Kolb H, Nicotinamide and prevention of diabetes. Lancet. 1992;(339): 1051–2.
29. Gale EAM, Bingley PJ, Emmett CL, Collier T. European Nicotinamide Diabetes Intervention Trial (ENDIT): a randomized controlled trial of intervention before the onset of type 1 diabetes. Lancet. 2004 ;(363):925–31.