

Low Dose Nicotinamide as an Adjunctive Therapy to Calcium Carbonate for Control of Hyperphosphatemia in Hemodialysis Patients



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Introduction & OBJECTIVES

Hyperphosphatemia
 Hyperphosphatemia remains a common problem in dialysis patients. Current therapies for the treatment of hyperphosphatemia are frequently insufficient to achieve the currently recommended target level of maintaining a serum phosphorus level between 3.5 and 5.5 mg/dL. Approximately 60% of HD patients have phosphorus levels above the upper recommended limit.

Nicotinamide use in hyperphosphatemia in hemodialysis patients:
 Phosphate binders need to be taken with each dialysis session. Hyperphosphatemia, which may cause cardiovascular, and the large oral doses can be both inconvenient and cause symptoms.

Phosphate binders
 Effective phosphate binders are available; however, aluminum-based binders cause bone and brain damage in hypophosphatemic patients, and calcium phosphate binders may have cardiovascular calcification progression when administered in high doses.

Nicotinamide
 Nicotinamide is water-soluble, a member of the B complex, which together with niacin and helps in various functions. However, the term of efficacy in the open literature often refers to both substances.

Pharmacology:
 Nicotinamide functions in the body as a component of two coenzymes, NAD (nicotinamide adenine dinucleotide, coenzyme I) and NADP (nicotinamide adenine dinucleotide phosphate, coenzyme II). These coenzymes participate in glycolysis, fat metabolism, and tissue respiration.

Aim of the study
 To evaluate the outcome (efficacy and safety) of using nicotinamide as adjunctive therapy to calcium based phosphate binder on phosphorus level in hemodialysis patients.

Study design
 This study is a prospective, interventional, case control open label study.

Setting:
 Regular hemodialysis patients in Ain Shams University Specialized Hospital, Hemodialysis Center, Cairo, Egypt.

METHODS

Patients:
 60 hemodialysis patients with a serum phosphorus level equal to or more than 5.0 mg/dl were enrolled in the study during the period from August 2020 to December 2020.

Patients:
 Patients were categorized into two groups:
Group I (Control group):
 Thirty patients received calcium carbonate tablets in dose of 500 to 1000 mg three times daily.
Group II (Study group):
 Thirty patients received calcium carbonate tablets in dose of 500 to 1000 mg three times daily and nicotinamide tablets in dose titrated up to 1000 mg/day for eight weeks.

Inclusion criteria:
 1. Patients on regular hemodialysis for more than three months.
 2. Stable dosage of calcium carbonate during the previous two months period.
 3. Age above 23 years.
 4. Serum inorganic phosphorus level equal to or greater than 5.0 mg/dl.

Exclusion criteria:
 1. Pregnancy
 2. History of liver disease
 3. Active peptic ulcer disease
 4. Patients on niacin therapy
 5. Non compliant patients.

Nicotinamide dosage titration:
 Nicotinamide was administered at a starting dosage of one tablet (500 mg) daily for one week. Then the dosage was increased to 1000 mg (two tablets) once daily at week two and continued till the end of the study.

RESULTS

Baseline characteristics of group I and group II

Parameter	Group I (n=30)	Group II (n=30)	P	SD
Age (years)	61.5 ± 9.81	61.65 ± 8.11	0.51	NS
Mean ± SD				
Dry wt. (kg)	74.28	70.81 ± 8.80	0.81	NS
Mean ± SD				
Duration of dialysis (years)	4.83 ± 1.82	2.08 ± 2.02	0.21	NS
Mean ± SD				
Male: Female ratio	22:8	11:6	0.51	NS

Serum level of inorganic phosphorus, calcium, calcium-phosphorus product, and intact parathyroid hormone of group I and II using student test at baseline.

Parameter	Group I (n=30)	Group II (n=30)	P	SD
Serum Ph. Level (mg/dl)	6.46 ± 0.81	6.72 ± 1.02	0.27	NS
Mean ± SD				
Serum Ca. Level (mg/dl)	8.87 ± 1.17	8.58 ± 0.72	0.78	NS
Mean ± SD				
Serum Ph-Ca product (mg ² /dl ²)	57.8 ± 12.94	58.72 ± 30.93	0.71	NS
Mean ± SD				
PTH level (pg/ml)	676.24	783.56	0.82	NS
Mean ± SD				

Lipid profile of the two studied groups

Parameter	Group I (n=30)	Group II (n=30)	P	SD
Total Cholesterol (mg/dl)	213.1 ± 32.12	202.1 ± 31.1	0.71	NS
Mean ± SD				
LDL Cholesterol (mg/dl)	126.8 ± 17.8	122.7 ± 18.1	0.71	NS
Mean ± SD				
HDL Cholesterol (mg/dl)	52.5 ± 12.1	51.2 ± 11.8	0.71	NS
Mean ± SD				
Triglyceride (mg/dl)	132.0 ± 12.0	131.0 ± 12.0	0.71	NS
Mean ± SD				

mean serum Ph. Level (mg/dl)

mean serum level Ca-Ph product (mg²/dl²)

mean serum Ph. Level (mg/dl) at the end of study

Comparison of serum level of Ph. Level, Ca. level, Ph-Ca product, and PTH between group I and group II at the end of study.

secondary end point
 evaluating the safety of using nicotinamide:
 During 8 weeks of study, possible side effects were observed to assess the safety of nicotinamide.

Side effects of nicotinamide in group II

Side effects	N (%)	Mean
Pruritus	1 (3.3%)	1.0
Tiredness	1 (3.3%)	1.0
GI disturbance	2 (6.6%)	2.0
Diarrhea	1 (3.3%)	1.0
Blurred vision	0 (0%)	0.0

CONCLUSIONS

Conclusion

The use of low dose nicotinamide (1000 mg/d) is effective in controlling serum phosphorus when co-administered with calcium carbonate as a phosphate binder in hemodialysis patients. It is cheap, and it has beneficial effect on lipid profile with mild potential side effects.

