

Study of the frequency of Hypomagnesemia in Hemodialysis patients using Proton Pump Inhibitors (PPI)

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ABSTRACT

Objective: To study the frequency of Hypomagnesemia in Hemodialysis patients using Proton Pump Inhibitors (PPI)

Study Design: Observational Study

Place and Duration of Study: This study was conducted at the Idrees Teaching Hospital of Sialkot Medical College, Sialkot from January 2018 to January 2019.

Materials and Methods: A total of 135 patients were selected in Hemodialysis Unit, Idris teaching Hospital, Sialkot with proper written informed consent. Information was then collected using Performa. Participants were selected through non probability consecutive sampling technique. Samples for serum magnesium levels were taken immediately before dialysis. Serum magnesium levels were measured using photometric methods.

Results: A total of 135 patients fulfilling the inclusion/exclusion criteria were enrolled in the study to calculate the frequency of hypomagnesemia in End Stage Renal Disease patients using PPI.

Conclusion: We conclude that frequency of hypomagnesemia in hemodialysis patients using PPI is 79.3%.

Key Words: Hypomagnesemia, Hemodialysis, Proton pump inhibitors

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INTRODUCTION

Magnesium is the fourth most abundant cation in the body and the second most abundant intracellular cation. It is one of the most essential elements in the human body and is involved in majority of the metabolic processes. Magnesium plays pivotal role in mitochondrial function, inflammatory and immune processes and stress. It regulates neuromuscular transmission, cardiac excitability, vasomotor tone and blood pressure¹.

Average daily intake of magnesium in an adult is about 360 mg. Various factors modify intestinal magnesium absorption like serum magnesium and calcium levels, activity of aldosterone and atrial natriuretic peptide (ANP)².

Magnesium is excreted mainly through the kidneys and also to some extent through intestine.

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Normal daily magnesium elimination through the kidneys is 100mg³. Hypomagnesemia is a very important and usually under diagnosed electrolyte abnormality. Hypomagnesemia has been found to have detrimental effects in critically ill patients. It is associated with other electrolyte abnormalities like hypocalcemia, hypophosphatemia and hypokalemia, and leads to neuromuscular abnormalities including hyperexcitability and respiratory muscle weakness⁴. Hypomagnesemia can be caused by decreased magnesium intake, redistribution of magnesium into the cells, increased intestinal and renal losses. Drugs like proton pump inhibitors, aminoglycosides, amphotericin B and cyclosporine are notorious in causing hypomagnesemia⁵. Proton pump inhibitors (PPI) are one of the most commonly used drugs. They are used for the treatment of gastroduodenal ulcers, gastroesophageal reflux and H. pylori eradication. PPI are routinely used in hemodialysis patients for the relief of symptoms of uremic gastritis. PPI is a documented cause of hypomagnesemia⁶.

In the face of decreased oral magnesium intake, normally there is increased active intestinal absorption of magnesium, which is mediated by the transient receptor potential melastatin-6 (TRPM6) and -7 (TRPM7) transport system. This prevents the development of hypomagnesemia when dietary intake is low. PPIs impair intestinal magnesium

absorption by disrupting active transport by TRPM 6 and 7 channels. PPIs lower the gut pH, which in turns decrease the affinity of TRPM channels with magnesium⁷.

Hypomagnesemia has been associated with increased cardiovascular and all-cause mortality in hemodialysis patients.

MATERIALS AND METHODS

It was a cross sectional study. : Study was conducted in Hemodialysis Unit, Idris Teaching Hospital Sialkot
Sample size: The sample size was of 135 by using 95% confidence level, 7% margin of error with expected percentage of hypomagnesemia in ESRD patients using PPI to be 79%. It was non-probability consecutive sampling.

Inclusion criteria:

1. Patient having age ≥ 18 years and ≤ 80 years.
2. Patients who were on twice weekly maintenance hemodialysis for at least 1 year.
3. Patients who were using PPI for at least 3 months.

The minimum doses of PPI was:

- A)Omeprazole 20 mg daily(B)Esomeprazole 20 mg daily(C)Lansoprazole 15mg daily
(D)Pantoprazole 20mg daily

Exclusion criteria:

1. Patients who had history of chronic diarrhea in the preceding 3 months.
2. Patients with history of heavy alcohol consumption.
3. Patients with serum calcium levels ≥ 10.5 mg/dl
4. Patients using any loop or thiazide diuretics.
5. Patients with history of Parathyroidectomy in the preceding 3 months.

Data collection: Patients were selected in Hemodialysis Unit, Shaikh Zayed Hospital Lahore with proper written informed consent. Information was then be collected using Performa (as shown in Annexure I).Participants were selected through non probability consecutive sampling technique.

Samples for serum magnesium levels were taken immediately before dialysis. Serum magnesium levels were measured using photometric methods.

Data Analysis: Data was entered and analyzed in SPSS v23.0. Quantitative variables include age, duration of dialysis and duration of PPI use and were expressed as mean \pm standard deviation. Qualitative variables include gender and presence of hypomagnesemia and were expressed as frequencies and percentages. Data was stratified for age, gender, duration of dialysis, duration of PPI use and type of PPI used to deal with effect modifiers. Post-stratification, Chi-square test was used. $P \leq 0.05$ will be considered significant.

RESULTS

A total of 135 patients fulfilling the inclusion/exclusion criteria were enrolled in the study to calculate the

frequency of hypomagnesemia in End Stage Renal Disease patients using PPI. The mean age of the patients was 52.42 ± 13.63 years. 50.4 % (n=68) of the patients had age 18-49 years, while 49.6 % (n=67) of patients had age 50-80 years.(Table No. 1).

Gender distribution shows that 60% (n=81) were males while 40 % (n=54) were females. (Table No. 2). The mean duration of dialysis was 6.28 years. (Table No. 3) The mean duration of PPI use was 10.31 months. (Table No. 4). The frequency of use of different types of PPI was Omeprazole 20.7 %, Esomeprazole 50.4%, Lansoprazole 19.3% and pantoprazole 9.6%. (Table 5).

The frequency of hypomagnesemia in hemodialysis patients using PPI was 79.3% (n=107) (Table No. 6).

When stratified with respect to age 44.8% (n=48) of the patients with hypomagnesemia had age 18-49 while 55.2% (n=59) had age 50-80 years. (Table No. 7).

When stratified with respect to gender 63.5% (n=68) of the hypomagnesemic patients were males and 36.5% (n=39) were females. (Table 8). When data was stratified with respect to duration of dialysis, 42.9% (n=46) of patients had duration of dialysis 1-6 years while 57.1% (n=61) had duration of dialysis 7-12 years. (Table 9).

When data was stratified with respect to duration of PPI use, 54.2% (n=58) of patients had duration of dialysis 1-9 months while 45.8% (n=49) had duration of dialysis 10-18 months. (Table 10). When data was stratified with respect to the type of PPI used, it showed that 57.1% (n=16) of patients using omeprazole developed hypomagnesemia, 76% (n=52) of patients using esomeprazole developed hypomagnesemia, 100% (n=26) of patients using lansoprazole developed hypomagnesemia while 100% (n=13) of patients taking pantoprazole also developed hypomagnesemia. (Table 11).

Table No. 1: Age Distribution (n=135)

Age(in years)	No. of patients	%
18-49	68	50.4
50-80	67	49.6
Total	135	100
Mean \pm SD	52.42 \pm 13.63	

Table No. 2: Gender Distribution (n=135)

Gender	No. of patients	%
Male	81	60
Female	54	40
Total	135	100

Table No. 3: Mean Duration of Dialysis (n=135)

Duration of Dialysis (Years)	Mean	SD
	6.28	3.10

Table No. 4: Mean Duration of PPI use (n=135)

Duration of PPI use (Months)	Mean	SD
	10.31	4.36

Table No. 5: Frequency of use of different types of PPIs (n=135)

Type of PPI	Frequency	Percentage
Omeprazole	28	20.7%
Esomeprazole	68	50.4%
Lansoprazole	26	19.3%
Pantoprazole	13	9.6%
Total	135	100.0%

Table No. 6: Frequency of hypomagnesemia in hemodialysis patients using PPI (n=135)

Hypomagnesemia	Frequency	Percentage
Yes	107	79.3%
No	28	20.7%
Total	135	100.0%

Table No. 7: stratification frequency of hypomagnesemia in hemodialysis patients using PPI with respect to age (n=135)

Hypomagnesemia	Age		Total
	18-49	50-80	
Yes	48	59	107
No	20	8	28
Total	68	67	135

Table No. 8: Stratification frequency of hypomagnesemia in hemodialysis patients using ppi with respect to gender (n=135)

		Gender		Total
		Male	Female	
Hypomagnesemia	Yes	68	39	107
	No	13	15	28
Total		81	54	135

Table No. 9:Stratification frequency of hypomagnesemia in hemodialysis patients using ppi with respect to duration of dialysis (N=135)

		Duration of dialysis		Total
		1-6 years	7-12 years	
Hypomagnesemia	Yes	46	61	107
	No	22	6	28
Total		68	67	135

Table No. 10: Stratification frequency of hypomagnesemia in hemodialysis patients using ppi with respect to duration of PPI use (n=135)

		Duration of PPI use		Total
		1-9 months	10-18 months	
Hypomagnesemia	Yes	58	49	107
	No	22	6	28
Total		80	55	135

Table No. 11: Stratification frequency of hypomagnesemia in hemodialysis patients using PPI with respect to type of PPI used (n=135)

		PPI used				Total
		Omeprazole	Esomeprazole	Lansoprazole	Pantoprazole	
Hypomagnesemia	Yes	16	52	26	13	107
	No	12	16	0	0	28
Total		28	68	26	13	135

DISCUSSION

This cross sectional study was carried out to calculate the frequency of hypomagnesemia in hemodialysis patients using PPI. PPI are widely used in ESRD patients for the treatment of dyspepsia and uremic gastritis. They have been associated with the development of hypomagnesemia, which is associated with significant cardiovascular mortality in ESRD patients.

A total of 135 patients fulfilling the inclusion/exclusion criteria were enrolled in the study to calculate the frequency of hypomagnesemia in End Stage Renal Disease patients using PPI.

The mean age of the patients was 52.42 ± 13.63 years. 50.4 % (n=68) of the patients had age 18-49 years, while 49.6 % (n=67) of patients had age 50-80 years.

Gender distribution shows that 60 % (n=81) were males while 40 % (n=54) were females. The mean duration of dialysis was 6.28 years.

The mean duration of PPI use was 10.31 months. The frequency of use of different types of PPI was Omeprazole 20.7 %, Esomeprazole 50.4%, Lansoprazole 19.3% and pantoprazole 9.6%.

The frequency of hypomagnesemia in hemodialysis patients using PPI was 79.3% (n=107). This figure is in accordance with previous studies. When stratified with respect to age 44.8% (n=48) of the patients with hypomagnesemia had age 18-49 while 55.2% (n=59) had age 50-80 years. These figures show that frequency of hypomagnesemia is not dependent on age of the patient. When stratified with respect to gender 63.5% (n=68) of the hypomagnesemic patients were males and 36.5% (n=39) were females. Hypomagnesemia turned out to be more common in males than in females.

When data was stratified with respect to duration of dialysis, 42.9% (n=46) of patients had duration of dialysis 1-6 years while 57.1% (n=61) had duration of dialysis 7-12 years. Thus hypomagnesemia was more common in patients with long duration of dialysis. When data was stratified with respect to duration of PPI use, 54.2% (n=58) of patients had duration of dialysis 1-9 months while 45.8% (n=49) had duration of dialysis 10-18 months. Duration of duration of PPI use had no effect on frequency of hypomagnesemia.

When data was stratified with respect to the type of PPI used, it showed that 57.1% (n=16) of patients using omeprazole developed hypomagnesemia, 76% (n=52) of patients using esomeprazole developed hypomagnesemia, 100% (n=26) of patients using

lansoprazole developed hypomagnesemia while 100% (n=13) of patients taking pantoprazole also developed hypomagnesemia. Frequency of hypomagnesemia was more common in patients using lansoprazole and pantoprazole. In this observational study, our data suggest an overall trend toward hypomagnesemia and increased all-cause mortality and CV mortality in HD patients on PPIs. Our findings are consistent with those of previous studies that also found increased hazards of CV disease and death with PPI use in other populations. Maggio et al. investigated the relationship between PPI use and study outcomes in patients 65 years or older who were discharged from acute care medical wards.^{9,10,11,12,13} The authors concluded that high-dose PPI use was associated with increased 1-year mortality. Charlot et al. studied aspirin-treated patients with first-time myocardial infarction and found that treatment with PPIs was associated with an increased risk of adverse CV events.^(10,14-16) Bell et al. observed that baseline PPI use was associated with all-cause mortality in 2 cohorts of institutionalized older persons.^{11,17-20}

CONCLUSION

We conclude that frequency of hypomagnesemia is 79.3% in hemodialysis patients using PPI.

Author's Contribution:

Concept & Design of Study:	Salman Yaqoub Saleh Muhammad, Ahmed Ammar
Drafting:	
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Revisiting Critically:	Salman Yaqoub, Saleh Muhammad
Final Approval of version:	Salman Yaqoub

Conflict of Interest: The study has no conflict of interest to declare by any author.

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