ORIGINAL ARTICLE

Determine the Relationship between Proton Pump Inhibitors and Iron Deficiency Anemia

MEHREEN KHAN[1], SIRAJ-UD-DIN[2], ARIF MUMTAZ[3], *MUHAMMAD ATIF TAUSEEF[4], MUHAMMAD AYAZ[5], UMAIR UL ISLAM[6]*
[1]Medical Officer, Medical A Ward, DHQ Teaching Hospital KDA Kohat
[2]Senior Registrar Medical A Ward, DHQ Teaching Hospital KDA Kohat
[3]Assistant Professor, KMU-IMS Kohat
[4]Assistant Professor Medicine, KMU institute of Medical Sciences (KIMS)Kohat
[5]Senior Registrar Medicine, Muhammad Teaching Hospital Peshawar
[6]Medical Specialist, Medical Officer, Department of Medicine DHQ Teaching Hospital Kohat
Correspondence to Dr. Mehreen Khan Email: mehreenfjmc@gmail.com Cell +923365699718

ABSTRACT

Aim: To examine the relationship between iron deficiency anemia and patients with proton pump inhibitors therapy.

Study design: Retrospective/observational

Place and Duration of Study: Medical OPD DHQ Kohat and Medical Unit from 1st January 2018 to 31st August 2018.

Methods: Total 100 patients of both genders with ages 20 to 65 years presented with gastrointestinal diseases and advised to use proton pump inhibitors therapy were enrolled in this study. Patients detailed demographic including age, sex and residence were recorded after taking informed written consent. Serum ferritin level and iron level were examined at start and at 8 months of PPI therapy.

Results: Fifty eight (58%) patients were males while 42 (42%) were females with mean age 40.25±11.66 years. Majority of patients 59 (59%) had urban residency. At start of treatment mean serum ferritin level was 67.85±32.52ng/ml and at 8 months it was 26.54±14.62ng/ml, a significant difference was observed with p-value <0.001. Mean iron level at start of treatment was 19.34±5.45umol/l and at 8 months it was 16.5±4.66 µmol/l. Iron deficiency anemia was found in 26 (26%) patients at 8 months follow-up

Conclusion: There was strong relationship between iron deficiency anemia and proton pump inhibitor therapy.

Keywords: Gastrointestinal disease, Serum ferritin level, Proton pump inhibitors, Anemia

INTRODUCTION

Proton pumpinhibitors (PPIs) speak to the most generally endorsed antisecretory operators.[1] Prolonged PPIs use isn't without results, anyway[1,2] Concerns have been raised about a potential relationship between delayed PPIs use and expanded hazard for nutrient and mineral inadequacies.[3] It has been recommended that their delayed use may impact iron status because of intense concealment of gastric corrosive emission by parietal cells, which could have significant ramifications for clinical practice[4].

Iron insufficiency is a typical nourishing lack and the main source of weakness in the United States, where the predominance in grown-up females is up to 9% in those matured 5069 years and 6% in those more established than 70 years. Iron insufficiency can bring about different side effects[5] including weariness, impeded effort, rest issue, and different entanglements[6].

Distinguishing modifiable elements that impact the hazard for iron lack or obstruct its treatment, for example, through weakened assimilation, can essentially impact general wellbeing. Corrosive inhibitors are among the most regularly utilized pharmaceuticals in the United States: in 2012 alone, 14.9 million patients got 157 million remedies for proton siphon inhibitors (PPIs).[7] Gastric corrosive encourages nonheme iron retention by discharging iron

from food particles and changing over it from its ferrous structure to the more absorbable ferric structure.[8,9] In this way, PPIs smother gastric corrosive creation, can prompt iron malabsorption. Corrosive concealment is of enthusiasm as a potential essential hazard factor for iron insufficiency, as a contributing danger factor and as an obstacle to press substitution treatment. The couple of prior investigations of corrosive concealment and iron insufficiency have been generally constrained to little case arrangement (the biggest discovered was 109 patients) or specialty populaces (e.g. patients with hemochromatosis); likewise, they have yielded conflicting outcomes[10-12].

The present study was conducted to examine the association between proton pump inhibitors and iron deficiency anemia in patients with gastrointestinal diseases.

MATERIALS AND METHODS

This retrospective/observational study was conducted Medical OPD DHQ Kohat and Medical Unit from 1stJanuary 2018 to 31stAugust 2018. Total 100 patients of both genders with ages 20 to 65 years presented with gastrointestinal diseases and advised to use proton pump inhibitors therapy were enrolled. Patients detailed demographic including age, sex and residence were recorded. Patients with previous medical diagnoses known to increase the risk of iron deficiency or bleeding, patients with parenteral and/or oral supplements of iron, vitamin B12 and folic acid, respectively, as well as any of the

----

antisecretory agents (including PPIs) during preceding at 8 months treatment were excluded. 5ml blood samples were taken at the beginning and at final follow-up at 8 months from all the patients and sent to laboratory to examine the serum ferritin level and serum iron level. Compare the findings pre and post treatment. Serum ferritin level <12ng/ml was considered as iron deficiency anemia. Frequency of iron deficiency anemia was examined at final follow-up. Follow-up was taken at 8 months. Data was analyzed by SPSS 24. Chi-square test was applied to compare pre and post treatment values of serum ferritin level and iron level. P-value <0.05 was taken as significant.

RESULTS

Fifty eight (58%) patients were males while 42 (42%) were females with mean age 40.25±11.66 years. Majority of patients 59 (59%) had urban residency while 41 (41%) patients had rural residency (Table 1). At start of treatment mean serum ferritin level was 67.85±32.52ng/ml and at 8 months it was 26.54±14.62ng/ml, a significant difference was observed with p-value <0.001. Mean iron level at start of treatment was 19.34±5.45umol/l and at 8 months it was 16.5±4.66 µmol/l (Table 2). Iron deficiency anemia was found in 26 (26%) patients at 8 months follow-up while 74 (74%) patients had not found iron deficiency anemia (Fig. 1).
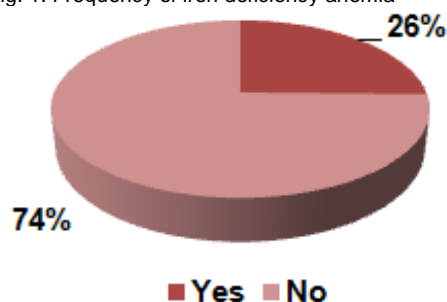
Table 1: Demographics of all the patients

Variable	No.	%
Gender		
Male	58	58.0
Female	42	42.0
Residence		
Urban	59	59.0
Rural	41	41.0

Table 2: Association of iron deficiency anemia with PPI user

Variable	Group A	Group B	P value
Serum Ferritin Level (ng/ml)	67.85±32.52	26.54±14.62	<0.0001
Serum Iron (umol/l)	19.34±5.45	16.5±4.66	0.001

Fig. 1: Frequency of iron deficiency anemia

DISCUSSION

Iron deficiency anemia is one of the most common clinical disorders found all over the world. It is considered one of the leading cause in developing severe life threatening complications.[13,14] Proton pump inhibitors are widely used for the treatment of gastrointestinal diseases. Many of studies demonstrated that chronic use of proton pump inhibitors increases the risk of minerals and vitamins inadequacy.[15]The present study was conducted to examine the association between iron deficiency anemia and proton pump inhibitors therapy in patients with gastrointestinal diseases. In this study mostly 58% were males while females were 42% and the mean age was 40.25±11.66 years. These results were similar to many of previous studies in which male patients were predominant 55% to 68% as compared to females and the majority of patients were ages above 40 years[16,17].

In present study at beginning of treatment mean serum ferritin level was 67.85±32.52ng/ml and at 8 months it was 26.54±14.62ng/ml, a significant difference was observed with p-value <0.001. Mean iron level at start of treatment was 19.34±5.45umol/l and at 8 months it was 16.5±4.66 µmol/l, significant difference was observed (p=0.001). A study conducted by Qorrajet al[18] reported that statistical analysis showed significant changes within PPIs group and specific PPIs subgroups between the two-time points in serum ferritin and vitamin B12 levels, respectively, while no significant changes in serum iron and homocysteine levels were shown. Another study conducted by Douwes[19] regarding use of PPIs and iron status in renal transplant patients and the reported chronic use of PPIs significantly decreases serum ferritin and iron level and excessive PPIs use significantlyncrease the prevalence of iron deficiency anemia.

Several previous studies demonstrated that patients with proton pump inhibitors therapy were on high risk for developing iron deficiency anemia[20-22+.]

In our study we found that 26 (26%) patients at 8 months follow-up while 74 (74%) patients had not found iron deficiency anemia. These results were comparable to many of previous studies[23,24].

CONCLUSION

There was strong relationship between iron deficiency anemia and proton pump inhibitor therapy. Frequency of iron deficiency was 26% in patients with PPI therapy.

REFERENCES

1. Ali T, Roberts DN, Tierney WM. Long-term safety concerns with proton pump inhibitors. Am J Med 2009; 122: 896–903.
2. Collaborators GBDRF, Forouzanfar MH, Alexander L, Anderson HR, Bachman VF, Biryukov S, et al. Global, regional, and national comparative risk assessment of 79 behavioural, environmental and occupational, and metabolic risks or clusters of risks in 188 countries, 1990–2013: a systematic analysis for the Global Burden of Disease Study 2013. Lancet. 2015; 386: 2287-2323.
3. Ito T. Jensen R.T. Association of long-term proton pump inhibitor therapy with bone fractures and effects on absorption of calcium, vitamin B12, iron, and magnesium. Curr. Gastroenterol. Rep. 2010; 12: 448-457
4. IMS Health Report. 2009 top therapeutic classes by US dispensed prescriptions. Available at: http://www.imshealth.com/deployed files/imshealth/Global/Content/StaticFile/Top_Line_Data/Top %20 Therapy%20Classes%20by%20U.S.RXs.pdf. Accessed 9 June 2010.

5. Ruscin JM, Page RL 2nd, Valuck RJ. Vitamin B(12) deficiency associated with histamine (2)-receptor antagonists and a proton-pump inhibitor. Ann Pharmacother 2002;36:812-6.
6. Tran-Duy A, Connell NJ, Vanmolkot FH, Souverein PC, de Wit NJ, Stehouwer CDA, Hoes AW, de Vries F, de Boer A Use of proton pump inhibitors and risk of iron deficiency: a population-based case–control study J Intern Med 2018;
7. Niu Q, Wang Z, Zhang Y, et al. Combination use of clopidogrel and proton pump inhibitors increases major adverse cardiovascular events in patients with coronary artery disease: a meta-analysis J CardiovascPharmacolTher 2016.
8. Ngamruengphong S, Leontiadis GI, Radhi S, et al. Proton pump inhibitors and risk of fracture: a systematic review and meta-analysis of observational studies. Am J Gastroenterol 2011;106:1209–18.
9. Khalili H, Huang ES, Jacobson BC, et al. Use of proton pump inhibitors and risk of hip fracture in relation to dietary and lifestyle factors: a prospective cohort study. BMJ. 2012;344:e372.
10. FDA Drug Safety Communication: Low magnesium levels can be associated with long-term use of proton pump inhibitor drugs (PPIs). FDA. March 14, 2011.
11. denElzen WP, Groeneveld Y, de Ruijter W, et al. Longterm use of proton pump inhibitors and vitamin B12 status in elderly individuals. Aliment PharmacolTher. 2008; 27(6):491-7.
12. Rozgony NR, Fang C, Kuczmarski MF, et al. Vitamin B(12) deficiency is linked with long-term use of proton pump inhibitors in institutionalized older adults: could a cyanocobalamin nasal spray be beneficial? J Nutr Elder. 2010; 29(1):87-99.
13. Damiao CP, Rodrigues AO, Pinheiro MF, et al. Prevalence of vitamin B12 deficiency in type 2 diabetic patients using metformin: a cross-sectional study. Sao Paulo Med J. 2016.
14. Mössner J. The Indications, Applications, and Risks of Proton Pump Inhibitors. DtschArzteblattInt. 2016; 113:477–83.
15. Schnoll-Sussman F, Katz PO. Clinical Implications of Emerging Data on the Safety of Proton Pump Inhibitors. Curr Treat OptionsGastroenterol. 2017; 15:1–9.
16. Sharma VR, Brannon MA, Carloss EA. Effect of omeprazole on oral iron replacement in patients with iron deficiency anemia. South Med J. 2004; 97:887–9.
17. Sarzynski E, Puttarajappa C, Xie Y, Grover M, Laird-Fick H. Association between proton pump inhibitor use and anemia: a retrospective cohort study. Dig Dis Sci. 2011; 56:2349–53.
18. Qorraj-Bytyqi H, Hoxha R, Sadiku S, Bajraktari IH, Sopjani M, Thaçi K, Thaçi S, Bahtiri E. Proton Pump Inhibitors Intake and Iron and Vitamin B12 Status: A Prospective Comparative Study with a Follow up of 12 Months. Open Access Maced J Med Sci 2018.
19. Rianne M. Douwes et al. Chronic Use of Proton-Pump Inhibitors and Iron Status in Renal Transplant Recipients. J. Clin. Med. 2019, 8, 1382.
20. Al-Nasser AN, Husain RS, Al-Marhabi AA. Proton pump inhibitors induce hemolytic anemia. J Family Med Prim Care 2019;8:1486-7.
21. Ratcliffe, L.E.K.; Thomas, W.; Glen, J.; Padhi, S.; Pordes, B.A.J.; Wonderling, D.; Connell, R.; Stephens, S.; Mikhail, A.I.; Fogarty, D.G.; et al. Diagnosis and Management of Iron Deficiency in CKD: A Summary of the NICE Guideline Recommendations and Their Rationale. Am. J. Kidney Dis. 2016, 67, 548–558.
22. Priyanka,Sofka, Sarah, Reynolds, Gorman. Effect of Long—Term Proton Pump Inhibitor Use on Iron Absorption: A Systematic Review. AJG. October 2018 - Volume 113 - Issue - p S702-S704
23. Imai R, Higuchi T, Morimoto M, Koyamada R, Okada S. Iron Deficiency Anemia Due to the Long-term Use of a Proton Pump Inhibitor. Intern Med. 2018;57(6):899–901.
24. Lopez A, Cacoub P, Macdougall IC, Peyrin-Biroulet L. Iron deficiency anemia. Lancet 387: 907-916, 2016.