J Renal Inj Prev. 2024; x(x): e32260.

http://journalrip.com doi: 10.34172/jrip.2024.32260

Journal of Renal Injury Prevention

Renal failure following the administration of proton pump inhibitors; a mini-review article on recent findings

Parisa Tajdini[1,2], Majid Foroutan[3,4*]

[1]Department of Pediatrics, School of Medicine, Semnan University of Medical Sciences, Semnan, Iran
[2]Clinical Research Development Unit, Amir-Al-Momenin Educational, Research and Therapeutic Hospital, Semnan University of Medical Sciences, Semnan, Iran
[3]Department of Internal Medicine, Semnan University of Medical Sciences, Semnan, Iran
[4]Clinical Research Development Unit, Kowsar Educational, Research and Therapeutic Hospital, Semnan University of Medical Sciences, Semnan, Iran

ARTICLE INFO

Article Type:
Mini-Review

Article History:
Received: 22 Oct. 2023
Accepted: 1 Jan. 2024
ePublished: 29 Jan. 2024

Keywords:
Chronic kidney disease
Acute kidney injury
Proton pump inhibitors
Gastroesophageal reflux disease
Acute interstitial nephritis

ABSTRACT

Proton pump inhibitors (PPIs) are frequently administered for the treatment of acid-related disorders such as gastroesophageal reflux disease (GERD). However, there is growing concern about their capability of adverse effects, including renal failure. Several studies have described a relationship between PPI administration and an increased risk of acute kidney injury (AKI) and chronic kidney disease (CKD). The mechanism behind this association is not fully understood, but it may involve changes in renal blood flow and tubular function. The risk of renal failure appears to be higher in patients who use PPIs for extended periods of time or at high doses. It is also higher in patients with pre-existing kidney disease or other risk factors for renal impairment. Clinicians should be aware of the potential risks of PPI use and consider alternative treatment options in patients with renal impairment or other risk factors for AKI or CKD. Regular monitoring of kidney function may also be warranted in patients on long-term PPI therapy.

Mini-Review

Implication for health policy/practice/research/medical education:
The administration of PPIs is connected with an increased risk of renal disease, including AIN and AKI. Prolonged use of PPIs has been associated with an increased risk of CKD.

Please cite this paper as: Tajdini P, Foroutan M. Renal failure following the administration of proton pump inhibitors; a mini-review article on recent findings. J Renal Inj Prev. 2024; x(x): e32260. doi: 10.34172/jrip.2024.32260.

Introduction

Proton pump inhibitors (PPIs) are ordinarily administered medications for the treatment of acid-related diseases such as gastroesophageal reflux disease (GERD) (1). However, there is rising concern about their potential adverse effects, including renal failure. The risk of renal failure appears to be higher in patients who use PPIs for extended periods of time or at high doses. It is also higher in patients with pre-existing kidney disease or other risk factors for renal impairment (2). This study discusses the nephrotoxicity of PPIs across the treatment strategies.

Search strategy

For this review, we searched PubMed, Web of Science, EBSCO, Scopus, Google Scholar, Directory of Open Access Journals (DOAJ), and Embase, using different keywords including Proton pump inhibitors, Acute interstitial nephritis, chronic kidney disease, acute kidney injury, and gastroesophageal reflux disease.

Mechanistic impact of nephrotoxicity of PPIs

Several potential mechanisms have been proposed. One possible mechanism is related to changes in renal blood flow. PPIs may decrease nitric oxide production, a molecule that helps regulate blood flow in the kidneys. This could lead to decreased renal blood flow and impaired kidney function. Another possible mechanism involves changes in tubular function (3). PPIs may interfere with the transport of electrolytes and other molecules across renal tubules, leading to electrolyte imbalances and impaired

***Corresponding author**: Majid Foroutan, Email: dr_forotan@yahoo.com

kidney function. Additionally, PPIs may increase the levels of certain inflammatory markers in the kidneys, which could contribute to kidney damage. Prolonged use of PPIs has also been linked to an increased risk of hypomagnesemia in patients with CKD (2,4).

Risk factors for AIN from proton pump inhibitors

Acute interstitial nephritis (AIN) is a type of kidney inflammation that affects the interstitial tissue surrounding the kidney tubules. It is characterized by the infiltration of inflammatory cells into the interstitium, which can cause kidney damage if left untreated (5). AIN can be caused by various factors, including infections, autoimmune disorders, and medications such as PPIs. Several studies have suggested a link between PPI use and the development of AIN. PPI-induced AIN is an iatrogenic cause of renal damage that can be entirely or partly reversed in most cases (6,7).

The risk factors of AIN from PPIs are greater in patients over 60 years old. Moreover, AIN has been reported in patients taking PPIs in combination with other medications, such as nonsteroidal anti-inflammatory drugs. Meanwhile, patients with autoimmune disorders, infections, or other medical conditions may be at an increased risk of developing AIN from PPI use. Finally, certain genetic polymorphisms may increase the risk of developing AIN from PPI use (6,8).

Some studies regarded, prolonged administration of PPIs is a risk factor; however, PPI-induced AIN does not appear to be dose-dependent or related to the duration of treatment (9,10).

Treatment for PPI-induced acute interstitial nephritis

The inflammatory infiltrates in the renal interstitium caused by PPI-induced AIN can lead to irreversible inflammation, but early intervention can help prevent long-standing damage. Overall, the prognosis for PPI-induced AIN is generally favorable with appropriate management and discontinuation of PPI use (6,11).

The treatment for PPI-induced AIN involves prompt identification and discontinuation of the use of PPIs. Early intervention can help prevent long-standing damage and maximize the chances of reversal. In some cases, corticosteroids may be used to reduce inflammation and hasten the AIN. In most cases, AIN can be wholly or partially reversed, which helps avoid the occurrence of chronic renal failure and its complications (6,11).

Individuals with kidney disease or kidney failure may consider alternative medications or therapies for acid reflux or other gastrointestinal conditions. Individuals with kidney disease or kidney failure need to consult with their healthcare provider before taking any antacids or PPIs. They should discuss these medications' potential risks and limitations, especially if they are on dialysis (4,12).

Conclusion

Several studies have described a relationship between PPI administration and an increased risk of acute kidney injury (AKI) and chronic kidney disease (CKD). The mechanism behind this association is not fully understood, but it may involve changes in renal blood flow and tubular function. Clinicians should be aware of the potential risks of PPI use and consider alternative treatment options in patients with renal impairment or other risk factors for AKI or CKD. Regular monitoring of kidney function may also be warranted in patients on long-term PPI therapy.

Authors' contribution

Conceptualization: Majid Foroutan.
Data curation: Parisa Tajdini.
Funding acquisition: Parisa Tajdini, Majid Foroutan.
Investigation: Parisa Tajdini.
Resources: Parisa Tajdini.
Supervision: Majid Foroutan.
Validation: Parisa Tajdini, Majid Foroutan.
Visualization: Parisa Tajdini.
Writing–original draft: Majid Foroutan.
Writing–review and editing: Majid Foroutan.

Conflicts of interest

The authors declare that they have no competing interests.

Ethical Issues

Ethical issues (including plagiarism, data fabrication, double publication) have been completely observed by the authors.

Funding/Support

None.

References

1. Shin JM, Sachs G. Pharmacology of proton pump inhibitors. Curr Gastroenterol Rep. 2008;10:528-34. doi: 10.1007/s11894-008-0098-4.
2. Hart E, Dunn TE, Feuerstein S, Jacobs DM. Proton pump inhibitors and risk of acute and chronic kidney disease: a retrospective cohort study. Pharmacotherapy. 2019;39:443-453. doi: 10.1002/phar.2235.
3. Ghebremariam YT, LePendu P, Lee JC, Erlanson DA, Slaviero A, Shah NH, et al. Unexpected effect of proton pump inhibitors: elevation of the cardiovascular risk factor asymmetric dimethylarginine. Circulation. 2013;128:845-53. doi: 10.1161/CIRCULATIONAHA.113.003602.
4. Morschel CF, Mafra D, Eduardo JCC. The relationship between proton pump inhibitors and renal disease. J Bras Nefrol. 2018;40:301-306. doi: 10.1590/2175-8239-jbn-2018-0021.
5. Raghavan R, Eknoyan G. Acute interstitial nephritis - a reappraisal and update. Clin Nephrol. 2014;82:149-

62. doi: 10.5414/cn108386.
6. Sampathkumar K, Ramalingam R, Prabakar A, Abraham A. Acute interstitial nephritis due to proton pump inhibitors. Indian J Nephrol. 2013;23:304-7. doi: 10.4103/0971-4065.114487.
7. Naik RH, Annamaraju P. Interstitial Nephritis. [Updated 2023 Jan 15]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2023 Jan-. Available from: https://www.ncbi.nlm.nih.gov/books/NBK564349/
8. Antoniou T, Macdonald EM, Hollands S, Gomes T, Mamdani MM, Garg AX, et al. Proton pump inhibitors and the risk of acute kidney injury in older patients: a population-based cohort study. CMAJ Open. 2015;3:E166-71. doi: 10.9778/cmajo.20140074.
9. Fossmark R, Martinsen TC, Waldum HL. Adverse Effects of Proton Pump Inhibitors-Evidence and Plausibility. Int J Mol Sci. 2019;20:5203. doi: 10.3390/ijms20205203.
10. Lanas-Gimeno A, Hijos G, Lanas Á. Proton pump inhibitors, adverse events and increased risk of mortality. Expert Opin Drug Saf. 2019;18:1043-1053. doi: 10.1080/14740338.2019.1664470. Härmark L, van der Wiel HE, de Groot MC, van Grootheest AC. Proton pump inhibitor-induced acute interstitial nephritis. Br J Clin Pharmacol. 2007;64:819-23. doi: 10.1111/j.1365-2125.2007.02927.x.
11. Guedes JVM, Aquino JA, Castro TLB, Augusto de Morais F, Baldoni AO, Belo VS, et al. Omeprazole use and risk of chronic kidney disease evolution. PLoS One. 2020;15:e0229344. doi: 10.1371/journal.pone.0229344.