



# Renal injury by administration of proton pump inhibitors

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Proton pump inhibitors (PPIs) are widely applied for the acid-suppression treatment (1). Their efficacy in remedying acid-related disorder processes is unique and their safety profile would be great. Despite this, some observational examinations suggest that their administration is related to a higher risk of several side health effects (2). Especially, the consumption of PPIs has been correlated with an increased risk of *Clostridium difficile* infection (3), development of dementia (4), fractures of the hip and spine (5), hypomagnesemia (6) and the community-acquired pneumonia (7). Similarly, PPIs consumption is also related with a higher risk of acute renal injury, acute interstitial nephritis (AIN), chronic kidney disease (CKD), and end-stage renal disease (ESRD) (8,9). This paper will focus on PPIs' side effects on kidney.

In 1998, Donna and colleagues showed that AIN could be the cause of acute kidney injury (10). After that, in 1992, Stephen and colleagues described that PPIs might be a reason of acute interstitial nephritis (11), with many case articles (12,13). Moreover, acute interstitial nephritis induced by PPIs is often without usual allergic signs, making it challengeable for physicians to readily recognize the problem. Furthermore, a recent examination exhibited that only about one quarter of patients were suspected to have PPI-induced acute interstitial nephritis (14). PPI-induced AIN is usually detected in the late phases of disease, which might be manifested weeks to months after drug initiation, may lead to the development of chronic interstitial fibrosis (14). Thus, PPI-induced acute interstitial nephritis should be considered in cases with urinalysis abnormalities or unexplained serum creatinine increment, prompting to a nephrology consultation and perhaps, kidney biopsy to confirm acute interstitial nephritis (15).

In 2016, Benjamin and colleagues prospectively reported that PPIs consumers may also present a significantly greater risk of CKD than non-consumers; which it was discovered among 10,439 patients for a period of 13.9 years in the atherosclerosis risk in communities (ARIC) survey (8). Generally, PPIs may be responsible for a very low proportion of acute interstitial nephritis; however,

## ■ Implication for health policy/practice/research/ medical education

Proton pump inhibitors (PPIs) are extensively recommended to cure several gastrointestinal diseases due to excessive acid creation. PPIs are widely observed as safe and efficient, among the most usually consumed drugs worldwide today; however, a series of observational investigations have reported a relationship between administration of PPIs and some side effects. In this paper, some PPIs' side effects on kidney have been explained.

■ **Keywords:** Proton pump inhibitors, Acute renal injury, Acute interstitial nephritis, Chronic kidney disease, End-stage renal disease, Acute kidney injury

their association with CKD does not seem to be notable, while presence of higher proportion of other comorbid disorders and other medications may also be responsible of chronic renal failure in these patients (16).

PPIs are using by millions of people worldwide (15). Generally, they have an excellent overall care profile. In spite of this, many concerns have been enhanced about kidney side effects, consisted of hypomagnesemia, hyponatremia, acute interstitial nephritis, and specifically chronic kidney disease over time (17) (Table 1).

Hence, it is important that physicians who may recommend these medications, should be aware of both the short-term AIN risk as well as the long-term chronic renal failure risk. This article has briefly focused on the fact that PPIs may have some side effects on the kidney, and worldwide, physicians should be aware of their side effects, considering them in any person taking PPIs.

## Authors' contribution

MA is the single author of the manuscript.

## Conflicts of interest

The author declared no conflicts of interest.

## Ethical consideration

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

## Funding/Support

None.

Received: 6 January 2017, Accepted: 2 April 2017, ePublished: 9 April 2017

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**Table 1.** Brief comparison of potential side effects related with PPIs therapy on kidney (16,18)

Potential PPI side effect on kidney	Underlying biological procedure	Clinical implications
Hypomagnesaemia	Reserve of intestinal magnesium absorption through transient receptor potential melastin (TRPM) 6 and 7 channels.	Routine examination for hypomagnesaemia only suggested in individuals cured with diuretics or affected by chronic diarrhea, chronic kidney disease, and malabsorption. Evaluate PPI removal in case of cardiac arrhythmia or seizures.
CKD	Unclear	The association between CKD and PPIs does not show to be real may be due to selection bias and various other confounding parameters regarding these patients.
Hyponatremia	Etiology of hyponatremia is uncertain, but appears most likely associated to inappropriate antidiuretic hormone (ADH) making.	Serum sodium concentrations extended from 108–124 mmol/L and often, patients were symptomatic (head-ache, confusion).
AIN	Unclear	AIN that grows following methicillin display presents clinically as a hypersensitivity answer, which is described by the triad of rash, fever and eosinophilia.

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**Citation:** Amiri M. Renal injury by administration of proton pump inhibitors. *J Renal Endocrinol.* 2017;3:e06. DOI: 10.15171/jre.2017.06  
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