International Journal of Medical and Health Research
ISSN: 2454-9142
Received: 29-12-2018; Accepted: 31-01-2019
www.medicalsciencejournal.com
Volume 5; Issue 2; February 2019; Page No. 98-100

Chronic use of anatcid-proton pump inhibitor precipitates renal damage

Dr. Kamlesh[1], Dr. Seema Mishra[2]
[1] Additional Director & Principal, Govt E Raghvendra Rao PG Science College, Bilaspur, Chhattisgarh, India
[2] Department of Clinical Nutrition, Bilasa P G Girls College, Bilaspur, Chhattisgarh, India

Abstract
Chronic kidney disease (CKD) affects approximately 13.6% of adults in India, is associated with a substantially increased risk of death and cardiovascular events and accounts for a disproportionately large burden on Medicare's financial resources. The increasing prevalence of CKD in the community cannot be fully explained by trends in known risk factors such as diabetes mellitus and hypertension, suggesting that other factors may contribute to the disease process. Medications may be a potential factor, particularly given trends towards polypharmacy. Identifying iatrogenic risk factors for CKD may help to promote the rational use of medications and reduce the burden of CKD worldwide. Proton Pimp Inhibitors are one of the most prescribed medicine even in India. Chronic use of PPI precipitates Hyponetremia, Hyperkalaemia, reduced Glomerular Filtration Rate and finally renal damage to some extent. In this present study a positive correlation is observed between chronic use of PPI and occurrence of AKD, as proved by estimations of relevant biochemical parameters.

Keywords: approximately, estimations, medicine, chronic kidney

Introduction

Proton pump inhibitors (PPI) are one of the most commonly prescribed medications and it has been estimated that between 25% and 70% of prescriptions have no appropriate indication. The duration of use frequently extends beyond recommended guidelines. There is also a trend towards PPI use in infants and children. Since the introduction of PPIs to the market in 1990, several observational studies have linked PPI use to uncommon but serious adverse health outcomes, including hip fractures, community acquired pneumonia, Clostridium difficile infections, acute interstitial nephritis (AIN) and acute kidney injury (AKI). It is plausible that PPI use may also be a risk factor for CKD, potentially mediated by recurrent AKI or hypomagnesemia, which has been associated with both PPI use and incident CKD. Proton pump inhibitors (PPIs) are taken by millions of people around the world, often for many months or even years, and some take PPIs on a permanent basis. PPIs, which are available both by prescription and over the counter, generally have an excellent overall safety profile. However, over time, a number of concerns have been raised about adverse renal events, including hyponatremia, hypomagnesemia, calcineurin inhibitor–related drug interactions, and specifically, acute interstitial nephritis (AIN). Although only a small proportion of patients develop AIN from PPIs, the widespread and prolonged use of these drugs has made them one of the most common causes of drug-induced AIN in the developed world. Although most clinicians accept that early AIN recognition with drug withdrawal and possibly, steroid therapy may lead to improved renal recovery, the potential burden of CKD is often forgotten. Long–standing unrecognized subclinical AIN may actually transition to chronic interstitial nephritis, leading to CKD and potentially, ESRD. This was suggested by a case series that showed development of CKD in patients after an episode of AIN. Moreover, given the absence of a reliable noninvasive test, it is possible that a substantial proportion of PPI-induced AIN in the general population may be missed and may contribute to the burden of CKD. The existence of PPI-associated CKD has remained purely hypothetical, however, because CKD has not been definitely shown to be a complication of PPI therapy. Chronic kidney disease (CKD) is more likely to develop in people who take proton pump inhibitors (PPIs), even if they do not first experience acute kidney injury (AKI), according to a new study. Proton pump inhibitors (PPIs) bind to enzyme H^+/K^+-ATPase and inhibit its activity in the stomach, thus decreasing the secretion of gastric acid. PPIs may trigger acute interstitial nephritis, a potentially severe adverse event commonly associated with acute kidney injury. Studies have found that prolonged use of PPIs may increase the risk of chronic kidney disease (CKD). The increase in prescription and inadequate use of this class of medication calls for studies on the effects of prolonged PPI therapy on renal function

Previously, researchers had suggested that unrecovered AKI is the sole mediator of chronic renal damage among PPI users. The acid-suppressing drugs are known to increase AKI and acute interstitial nephritis. New findings published in Kidney International hint that PPIs may harm the kidneys gradually, independent of AKI.

Based on these previous studies a research is designed to assess the effect of chronic use of antacids specially Beta Blockers on renal capacity.

Study Area: Raipur & Bilaspur city
Study duration: March 15-Feb 19
Study Population: Subjects are picked from contacts in various clinics, medical shops and randomly picked from society who are chronic users of antacids (above 1 year at least). Controls are demographically matched healthy persons with subjects, but not using antacids.
Subjects: 45, age range 43-64 years, 29 male & 16 females.The selection criteria is chronic use of Proton Pump

Inhibitors- Omeprazole, Esomeprazole, Lansoprazole, Pantoprazole, Dexalantoprazole.{Mainly H binders}

Controls

45, age range 43 -65 years, 34 males, 11 females. (Non users). The subjects & controls suffering from Hypertension, Diabetes, Cardiac Disorders & any other metabolic diseases are excluded from this study. Exposure to antihypertensive, anticoagulant, aspirin, statin, diuretic, and non-steroidal anti-inflammatory medications users were excluded in the same way.

Objectives

The objective of this study was to quantify the association between PPI use and incident kidney disease in the general population. We hypothesized that PPI use is an independent risk factor for CKD,

The following objectives are drawn for the conduction of study

1. Estimation of blood /urine pH, it expected to be disturbed due to chronic use of antacids. It was estimated by using Jellas Test Paper strips.
2. Estimation of serum Creatinin, this is indicator of renal functional capacity. It was estimated by using Biochemistry Auto analyzer star 100 by using kit of Span Diagnostics.
3. Estimation of serum Urea, this is indicator of renal functional capacity, It was estimated by using Biochemistry Auto analyzer star 100 by using kit of Merrak Diagnostics.
4. Estimation of GFR/min, this is indicator of renal functional capacity, this estimation values are done at Dubey's Hospital, Raipur, and the values were collected. Innulin was used to assess GFR.
5. Estimation of Serum Cholesterol, it is expected to be disturbed due to ARD. It was estimated by using Biochemistry Autoanalyzer star 100 by using kit of Span Diagnostics, by using method of Wybenga & Pelligi.
6. Estimation of serum Triglyceride, it is expected to be disturbed due to ARD, It was estimated by using Biochemistry Autoanalyzer star 100 by using kit of Span Diagnostics.
7. Estimation of Urinary and serum Albumin level it is expected to be disturbed due to ARD, It was estimated by using Biochemistry Autoanalyzer star 100 by using kit of Span Diagnostics.
8. Estimation of Blood Pressure, it is expected to be disturbed due to ARD, Auscultator was used for estimation.
9. Estimation of serum Sodium and Potassium level, it is expected to be disturbed due to ARD,digital electrolyte analyzer was used for estimation.
10. Estimation of BMI, it is expected to be disturbed due to ARD.
11. Estimation of acid content in gastric juice –by using Test Strips, Jellas Professional Acid Alkaline pH Test Paper Strips for Urine Saliva, pH Measure of 4.5-9.0.
12. Estimation of serum Phosphorus was also done by using kit of Lab care and by using auto analyser, model no Star 21 Plus. In the reaction, inorganic phosphorus reacts with ammonium molybdate in an acidic solution to form a colored phosphomolybdate complex. The system monitors the change in absorbance at 365 nm at a fixed time interval. This change in absorbance is directly proportional to the concentration of phosphorus in the sample. The serum Phosphorus level is indicator of renal functional capacity.
13. C-reactive protein was assessed by using kit of Span Diagnostics, reagent kit, Surat [code 25934] used for in vitro detection of C - reactive protein (CRP) in human sera in auto-analyser by agglutination method.50 micro ml serum was mixed with 1 ml reagent, clumping was indication of positive test. This parameter is indicator of organ/tissue damage due to any reason.
14. Estimation of Hg/gm% value, as it is strong indicator of renal capacity via REF. It was estimated by Acid Hematin method by using Hemocytometer.

Observations

Table 1

Sr no	Parameters	Normal Values	Subjects n-45	Controls n-45	t value n-88
			Observed Values	Observed Values	
1.	Urine pH	7.2 – 7.6	9.03± 6.22	7.3 ± 043	0.00206
2.	Serum Creatinine	0.6 to 1.2 mg/dl	3.45± 2.67	0.61± 0.23	2.616
3.	Serum Urea	7 to 20 mg/dl	11.33 ± 2.17	7.43 ± 0.56	4.638
4.	eGFR	90 to 120 mL/min/1.73 m^2	59.16 ± 2.83	112.3 ± 0.67	1.626
5.	Serum Cholesterol	200 and 239 mg/dl	248 ± 8.92	213.28 ± 2.56	0.00017
6.	Serum Triglyceride	150 to 199 mg/dl	239.52 ± 5.9	179.67 ± 3.11	9.071
7.	Serum Albumin	3.5 to 5.5 g/dl	2.91± 1.33	3.67 ± 0.41	0.0125
8.	Urinary Albumin	Trace	2.7 ± 3.2	0.02 Traceable	3.096
9.	Serum Sodium	135 and 145 mEq/L	121 ± 7.61 mEq/L	136.18 ± 1.22	8.465
10.	Urinary Sodium	39 -60 mEq/L	140.2 ± 10.56	45 ± 2.51	2.082
11.	Serum Potassium	3.5-5.0 mEq/L	6.9 ± 7.34	5.23 ± 1.02	0.00025
12.	BP	80/120 mm of Hg	93/136	96/132	0.004
13.	BMI	18-22	15.7	23.3	0.00135
14.	Acid content of Gastric Juice	1.5 to 3.5 pH	0.59 ± 0.37	1.23 ± 2.70	0.00122
15.	Renal stones	-----	12 persons affected	5 persons affected	--
16.	Serum Phosphorus	2.4-4.5 mg/Dl,	8.12 ± 0.67 mg/dl	4.9 ± 0.23 mg/dL	0.00297
17.	Serum C- Reactive protein	2.4-4.5 mg/Dl,	8.3 mg/dl	4.9 mg/dL	5.881
18.	Hg gm%	11-15 gm%	9.53 ± 1.22	10.83 ± 2.25	0.0338

Conclusion

Baseline characteristics of PPI-users and non-PPI users were compared using t-tests for continuous variables and correlation tests for categorical variables. Exposure to PPI was modeled as a binary variable at baseline and in secondary analyses, as a time-varying ever-use variable, in which a participant was considered an ever-user at the first instance of PPI use and at all time points thereafter. In study, adjustment was performed for demographic variables (age, sex, race and study center), socioeconomic status (health insurance status and highest level of education), clinical measurements (baseline eGFR, cigarette smoking, mean systolic blood pressure, BMI), prevalent comorbidities (diabetes, cardiovascular disease) and concomitant use of medications (antihypertensive medications and anticoagulant medications). Household income and concomitant use of non-steroidal anti-inflammatory drugs (NSAIDs), aspirin, diuretic, or statin medications were considered to be possible confounders; however, they did not affect the results of adjusted analyses and thus were not included in the final model. In the case of less comorbidity factors, analyses were adjusted for age, sex, race, eGFR, smoking status, BMI, systolic blood pressure, diabetes, history of cardiovascular disease, antihypertensive medication use, anticoagulant medication use and statin, aspirin, and NSAID use. It was appreciated from the above data that the blood and urinary pH was estimated significantly towards alkaline side than controls. Also the PPI users had biochemical parameters showing sluggishness of kidneys as evidenced by higher serum Phosphorus, Urea and Creatinine level. The net GFR was also profoundly lower than non-users. As renal damage precipitates dyslipidemias proved by many previous studies, the PPI users having parameters of renal damage in this study showed serum levels indicating strong dyslipedemia. Hyponatremia and Hyperkalemia are also prominent features observed in PPI users with renal damage. The stomach acid content was lower in subjects as expected due to lesser acid secretion in chronic PPI users. A large community-based study is required for further proves of data.

References

1. United States Renal Data System. 2014 USRDS Annual Data Report: An overview of the epidemiology of kidney disease in the United States, 2014.
2. Go AS, Chertow GM, Fan D, McCulloch CE, Hsu CY. Chronic kidney disease and the risks of death, cardiovascular events, and hospitalization. N Engl J Med. 2004; 351(13):1296-1305.
3. Coresh J, Selvin E, Stevens LA, *et al*. Prevalence of chronic kidney disease in the United States. JAMA. 2007; 298(17):2038–2047.
4. Grams ME, Juraschek SP, Selvin E, *et al*. Trends in
5. the prevalence of reduced GFR in the United States: a comparison of creatinine- and cystatin C-based estimates. Am J Kidney Dis. 2013; 62(2):253-260.
6. Maher RL, Hanlon J, Hajjar ER. Clinical consequences of polypharmacy in elderly. Expert Opin Drug Saf. 2014; 13(1):57-65.
7. Forgacs I, Loganayagam A. Overprescribing proton pump inhibitors. BMJ. 2008; 336(7634):2-3.
8. Grant K, Adhami N Al, Tordoff J, Livesey J, Barbezat G, Reith D. Continuation of proton pump inhibitors from hospital to community. Pharm World Sci. 2006; 28(4):189-193.
9. Wilhelm SM, Rjater RG, Kale Pradhan PB. Perils and pitfalls of long-term effects of proton pump inhibitors. Expert Rev Clin Pharmacol. 2013; 6(4):443-451.
10. Barron JJ, Tan H, Spalding J, Bakst AW, Singer J. Proton pump inhibitor utilization patterns in infants. J Pediatr Gastroenterol Nutr. 2007; 45(4):421-427.
11. De Bruyne P, Christiaens T, Vander Stichele R, Van Winckel M. Changes in prescription patterns of acid-suppressant medications by Belgian pediatricians: analysis of the national database, [1997–2009] J Pediatr Gastroenterol Nutr. 2014; 58(2):220-225..
12. Yang YX, Lewis JD, Epstein S, Metz DC. Long-term proton pump inhibitor therapy and risk of hip fracture. JAMA. 2006; 296(24):2947-2953.
13. Lambert AA, Lam JO, Paik JJ, Ugarte-Gil C, Drummond MB, Crowell TA. Risk of community-acquired pneumonia with outpatient proton-pump inhibitor therapy: a systematic review and meta-analysis. PLoS ONE. 2015; 10(6):e0128004.
14. Dial S, Alrasadi K, Manoukian C, Huang A, Menzies D. Risk of Clostridium difficile diarrhea among hospital inpatients prescribed proton pump inhibitors: cohort and case-control studies. Cmaj. 2004; 171(1):33-38.
15. Blank ML, Parkin L, Paul C, Herbison P. A nationwide nested case-control study indicates an increased risk of acute interstitial nephritis with proton pump inhibitor use. Kidney Int. 2014; 86(4):837-844.
16. Sierra F, Suarez M, Rey M, Vela MF. Systematic review: Proton pump inhibitor-associated acute interstitial nephritis. Aliment Pharmacol Ther. 2007; 26(4):545-553.