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PROTON PUMP INHIBITORS USE AND THE RISK OF CHRONIC KIDNEY DISEASE: EVIDENCE BASED SYSTEMATIC REVIEW AND META-ANALYSIS

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Objectives : Proton pump inhibitors (PPIs) are one of the widely used drugs available as over the counter for treatment of several acid-related gastrointestinal disorders. Concerns have been raised about the risk of developing chronic kidney disease (CKD) with the prolonged use of PPIs. This systematic review aims to determine the association between PPI use and the risk of developing CKD.

Methods : The methodology complies with our registered protocol at PROSPERO (registration number CRD42016040073). Databases including PubMed and Embase were searched from inception to January 2017. Two reviewers independently screened and selected the observational studies that compared CKD outcome in patients on PPI. The methodological quality of selected studies was assessed using the Newcastle-Ottawa Scale (NOS). The pooled risk ratio was calculated using a random-effects model. Subgroup analysis according to the disease status, duration of exposure and study design was performed. Sensitivity analysis was also done by excluding each study sequentially. All the analysis were performed using RevMan v5.3.

Results : The 5 studies comprised of 3 cohort studies and 2 case-control studies with 605,875 patients from cohort and 106,885 patients from case-control studies were included. Three (60%) of the studies were of the highest methodological quality score. All of the studies were conducted in the US except one in Taiwan. In the patients receiving the PPI pooled relative risk (RR) of developing CKD was 1.08 (95%CI = 0.71 to 1.63). In subgroup analysis based on the duration of exposure period, the RR of developing the CKD was found to be 0.97 (95%CI = 0.59 to 1.61) for long-term exposure vs. 1.19 (95%CI = 0.74 to 1.89) for short-term exposure. Based on study design, the pooled data from three cohort studies showed the RR of CKD to be 1.21 (95%CI = 0.83 to 1.78) whereas for the single case-control study included, it was found to be1.10 (95%CI = 1.05 to 1.16).

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We found deteriorative effect of PPI use in diabetic subjects with a pooled RR of 2.06 (95% CI1.39 to 3.05). It shows that diabetic PPI user group has 106% more chance of developing CKD as compared to non-diabetic PPI user. Exclusion of any of the specific studies did not demonstrate any alteration in the results as evident from the sensitivity analysis.

Conclusions : An association between the PPI use and risk of developing CKD was found in the study. However, owing to the inherent demerits of the observational studies, randomized controlled trials are warranted to confirm or counter the findings.

Keywords : Chronic Kidney Disease; Meta-analysis; Proton Pump Inhibitors; Systematic review