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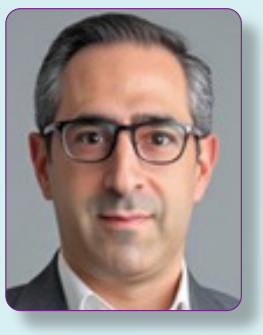
Yunha Noh, PharmD, PhD

Former postdoctoral fellow in Epidemiology, Biostatistics, and Occupational Health, McGill University

Current position: Assistant Professor, Chonnam National University, Gwangju, South Korea



Laurent Azoulay, PhD

Senior Investigator, Lady Davis Institute for Medical Research

Professor and William Dawson Scholar, Department of Epidemiology, Biostatistics & Occupational Health and Department of Oncology, McGill University

Gut

Proton pump inhibitors use and risk of inflammatory bowel disease in children

Yunha Noh, Ahhyung Choi, Hyesung Lee, Dong Keon Yon, Hyun-Soo Kim, Suyeon Kim, Ju-Young Shin, and Laurent Azoulay.

Proton pump inhibitors (PPIs) have been shown to induce gut microbiome alterations and increased oral-to-gut microbial transmission, mechanisms potentially implicated in inflammatory bowel disease (IBD). While adult studies have suggested an association between PPIs and IBD, evidence in children remains limited.

We conducted an active-comparator, new-user cohort study using Korea's nationwide claims database (2002–2020). Children aged 6–17 years newly initiating PPIs or histamine-2 receptor antagonists (H2RAs) between 2003 and 2014 were included, excluding those with prior exposure to either drug, previous IBD, other colitis-related conditions, or rare PPI indications. Incident IBD was defined using a validated algorithm requiring both an ICD-10 diagnosis code and an IBD-specific prescription on the same date. Patients were followed until IBD diagnosis, death, or end of study (31 December 2020), with a 2-year lag period to address protopathic bias. Calendar time–specific propensity scores and standardised morbidity ratio weighting were applied, and weighted hazard ratios (HRs) were estimated using Cox regression.

The cohort included 33,710 PPI initiators (mean age 11.8 years; 49.8% male) and 2,751,592 H2RA initiators. Over a mean follow-up of approximately 8 years, 77 IBD events occurred among PPI users and 6,708 among H2RA users (weighted incidence rate 2.9 vs 2.2 per 10,000 person-years). Compared with H2RA use, PPI initiation was associated with an increased risk of incident IBD (weighted HR 1.37; 95% CI 1.09–1.72). Risk estimates were higher for ulcerative colitis (HR 1.54; 95% CI 1.15–2.05) than for Crohn's disease (HR 1.16; 95% CI 0.79–1.70). Findings were consistent across sensitivity analyses.

In this large paediatric cohort, PPIs were associated with a modestly increased risk of IBD compared with H2RAs, particularly ulcerative colitis. Although absolute risk was low, these findings support cautious prescribing of PPIs in children and avoidance of overuse when indications are unclear.

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