Risk and Severity of Hospital-Acquired Clostridium difficile Infection in Patients Taking Proton Pump Inhibitors

Background:

- In recent years Proton Pump Inhibitors (PPIs) have been linked to increased risk of opportunistic gastrointestinal infections, including *Clostridium Difficile* because of increased gastric pH. *C. Difficile* is the leading cause of hospital-acquired infections at the Johnson City Medical Center.

Objective:

- To evaluate overall rates of CDI among patients taking PPIs versus those not taking PPIs. In addition, investigators evaluated rates of hospital-acquired CDI vs community-acquired CDI, levels of severity of CDI, and appropriateness of PPI prescribing.

Methods:

- **Design:** Retrospective, cohort study, of all patients admitted to the Johnson City Medical Center from Jan 2013-May 2014
- **Inclusion criteria:** 2 patient cohorts – defined as either having received at least 1 dose of PPI (PPI group) or never having received a dose (control). 41,663 patients hospitalized. 17,471 (41.9%) in the PPI group and 24,192 (58.1%) in the control group.
- **Primary outcome measures**: Occurrence of patients with HA-CDI in the PPI group vs. control group.
- **Secondary outcome measures:** Number and % of patients taking a PPI, overall rates of CDI, rates of CDI present of admission, and severity of CDI in the PPI group versus control group.
- Confidence Intervals were set at 95%. Results were considered statistically significant if lower limit of CI was > than 1 or the upper limit was <1.

Results:

- 41,663 patients hospitalized. 17,471 PPI group (41.9%), 24,192 (58.1%) control group.
- **Primary outcome measure:** 65 patients (0.38%) developed HA-CDI in the PPI group compared with only 14 patients (0.058%) who developed HA-CDI in the control group.
- **Secondary outcome measures:** 234 patients (1.34%) in PPI group had CDI. 114 patients (0.47%) in control had CDI. Of the 65 patients who developed HA-CDI while taking a PPI, 29 had mild-moderate infections, 14 had severe infections, and 22 had severe-complicated infections. Of the 22 patients with severe-complicated infections, 3 patients also met IDSA criteria for surgical consultation for possible colectomy. Of the 14 patients who developed HA-CDI in the control group, 6 had mild-moderate infections, 6 had severe infections, and 2 had severe-complicated infections; no patient met the criteria for surgical consultation in the control group. For the 65 patients with HA-CDI in the PPI group, 35 patients (54%) were continued on their home doses of PPIs compared with 30 patients (46%) who were initiated on PPI therapy during hospitalization. Of the 35 patients who continued their PPI therapy from home, 12 continued without a documented indication for PPI therapy. Of the 30 patients newly started on PPI therapy in the hospital, one did not have a documented indication, and 8 had a PPI started for stress ulcer prophylaxis without meeting the specified criteria. A total of 20 (31%) of the 65 patients with

HA-CDI were prescribed a PPI without an indication. There was a higher rate of complicated CDI in patients taking a PPI without an indication than in those taking a PPI with an indication, although the difference was not statistically significant, 45% versus 29% (p=0.26), respectively.

- **Authors' conclusion**: Use of PPIs was associated with an increase in the rate and severity of HA-CDI. Patients who were prescribed a PPI without an indication developed higher rates of complicated CDI than patients not taking a PPI.

Strengths:

- Large study population
- Appropriate statistical tests used for data
- Evaluated some pertinent patient baseline demographic and clinical characteristics

Limitations:

- Retrospective study dependent on accuracy and completeness of patient medical charts
- Important baseline characteristics that could significantly influence results such as patient comorbidities, duration of PPI use, dose and duration of previous antibiotics, indication for home PPI use, length of hospitalization, and length of ICU stay were not evaluated
- Criteria for "appropriate PPI indication" was reportedly generous in this institution
- Potential for Type II error exists as the incidence of complicated C. diff was higher in patients taking a PPI without an indication than in those taking a PPI with an indication, but this was not statistically significant.
- Results were unadjusted and are susceptible to potential bias between groups as confounding variables were not accounted for.

Conclusion:

- Although this study reported use of proton pump inhibitors was associated with an increase in both the rate and severity of hospital-acquired *C. diff* infections, further research is needed to fully evaluate this correlation. This study had several major weaknesses which limits is usefulness in clinical practice and its ability to be generalized to other institutions. A prospective study including more baseline characteristics, especially number of PPI doses received, would be beneficial to further determine true significance between PPIs and the risk of *C.diff.*

Reference: Lewis PO, Litchfield JM, Tharp JL, Garcia RM, Pourmorteza M, Reddy CM. Risk and Severity of Hospital-Acquired Clostridium difficile Infection in Patients Taking Proton Pump Inhibitors. Pharmacotherapy. 2016 Sep;36(9):986-93.

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