Dose Dependent Impact of Proton Pump Inhibitors on the Clinical Course of Spontaneous Bacterial Peritonitis

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Background:
- Spontaneous bacterial peritonitis (SBP) is a common complication in patients with decompensated liver cirrhosis associated with a high mortality.
- Proton pump inhibitors (PPI) are widely used in cirrhotic patients. PPI lower gastric acid production and can act as enteric antibiotics.
- The effect of PPI on the incidence of SBP has been investigated in a variety of studies using different study designs. As a consequence, conflicting results have been published.
- Currently, the impact of PPI on the incidence and severity of SBP is highly controversial.

Aim:
- We aimed to investigate the influence of PPI on the incidence and the clinical course of SBP in a large cohort of patients with decompensated liver cirrhosis and ascites.

Patients and Methods:
- A number of 1011 consecutive patients with decompensated liver cirrhosis and ascites who underwent at least one paracentesis between January 2012 and June 2016 at Hannover Medical School were considered for this study.
- Patients with evidence of a secondary intraabdominal infection, presence of a malignancy (except for hepatocellular carcinoma within the MILAN criteria), history of solid organ transplantation (except for liver transplantation), stem cell transplantation, congenital immune dysfunction, or presence of HIV infection were excluded.
- All remaining patients were carefully evaluated for PPI intake at hospitalization, within 7 days prior to the first paracentesis and to the diagnosis of SBP. Patients with insufficient data concerning PPI intake at the different time points were withdrawn from the respective analysis.
- Presence of SBP was considered with a leukocyte cell count ≥500/mm³ or a polymorphonuclear cell count ≥250/mm³.
- The far majority of patients used pantoprazole. In a few patients the prescribed PPI was omeprazole or rabeprazole. In patients taking omeprazole 20mg or rabeprazole 20mg were considered to be equivalent to 40mg pantoprazole.

Results:
- Impact of PPI on the incidence of SBP

Figure 2: Incidence of SBP according to PPI intake. Overall SBP incidence at the time of the first paracentesis in patients with (n=506) and without (n=107) PPI intake (a). Cumulative SBP incidence after the first paracentesis (b).
- There was no impact of PPI on the SBP incidence at the time of the first paracentesis.
- There was a trend towards a higher in hospital SBP incidence among patients who took a PPI at the time of their first paracentesis (Figure 2a).

Impact of PPI on the course of SBP

Figure 3: 28 day mortality and incidence of severe HE in patients with SBP adjusted for PPI intake

Figure 4: 28 day mortality and incidence of severe HE in patients without SBP adjusted for PPI intake

Figure 5: In SBP patients a high PPI dosage is associated with a higher risk of dying and developing severe encephalopathy within 28 days after the diagnosis of SBP compared with patients with SBP and low dose PPI therapy.

Conclusions:
- PPI intake is not associated with a significantly higher SBP incidence.
- Use of high PPI doses are associated with a higher risk for 28 day mortality and incidence of severe HE.
- Of note, this association is limited to cirrhotic patients with SBP.
- In patients at risk for SBP high PPI dosages should be avoided.