Proton Pump Inhibitors are Associated with a Higher Risk of Spontaneous Bacterial Peritonitis Independently of Gastrointestinal Bleeding: A Population-Based Study

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Abstract

Aim: The aim of this study is to identify whether PPI use is independently associated with a higher risk of SBP among cirrhotic patients.

Methods: Explorys Inc is a validated multicenter database that was used for this study. A subgroup of patients with "SBP" was identified from a cohort of patients with a SNOMED-CT diagnosis of "cirrhosis". We excluded all patients with age <18 years. Multivariate analysis was performed to adjust for multiple factor.

Results: 69,969,210 individuals were screened in the database and 12,850 were included in the final analysis. SBP was more common among cirrhotic patients using PPI (OR= 1.81) independently of GIB.

Conclusion: Cirrhotic patients using PPI were at higher risk of developing SBP independently of GIB.

Introduction

- Spontaneous Bacterial Peritonitis (SBP) is a common complication among patients with cirrhosis and is associated with increased **mortality**.
- Recent studies have suggested a possible increase in the risk of **SBP** among patients on Proton Pump Inhibitors (**PPIs**).
- The aim of this study is to identify whether PPI use is independently associated with a **higher risk** of **SBP** among cirrhotic patients.

Methods and Materials

- **Explorys** Inc is a validated **multicenter** database of more than 360 hospitals from 26 different healthcare systems and ~70 million patients across the United States, and was used for this study. A cohort of patients with a SNOMED-CT diagnosis of "**cirrhosis**" between 1999-2022 was selected. A subgroup of patients with "SBP" was later identified and used for the analysis. We **excluded** all patients with **age < 18** years.
- **SPSS** was used for statistical analysis, and for all analyses, a 2-sided p-value of **< 0.05** was considered statistically significant. **Multivariate analysis** was performed to adjust for multiple factors including age, gender, race, type 2 diabetes mellitus, benign hypertension, hyperlipidemia, obesity, smoking history, **GI bleeding** (GIB), and PPI use.

Results

- 69,969,210 individuals were screened in the database and 12,850 were included.
- The prevalence rate of SBP in cirrhotic patients was 18.36%. The baseline characteristics of cirrhotic patients are shown in **Table 1**.
- SBP was more common among cirrhotic patients using PPI (**OR= 1.81**) independently of GIB. The diagnosis of GI bleeding (**OR= 1.51**) and hepatic encephalopathy (**OR= 4.54**) offered a higher risk for SBP as well (**Figure 1, Table 2**).

		Cirrhotic with SBP (%)	Control (%)
Age	18-65	8103 (62.96)	177690 (48.73)
	>65	4760 (36.99)	185600 (50.90)
Gender	Male	8040 (62.47)	204120 (55.98)
	Female	4820 (37.45)	159860 (43.84)
Race	Caucasian	9280 (72.11)	258030 (70.77)
	African-American	1560 (12.12)	43260 (11.86)
	Asian	190 (1.48)	6170 (1.69)
Comorbidities	Type 2 Diabetes	5230 (40.64)	136730 (37.50)
	Benign Hypertension	2170 (16.86)	60450 (16.58)
	Hyperlipidemia	4840 (37.60)	163140 (44.74)
	Obesity	3490 (27.12)	90820 (24.91)
	Smoker	3240 (25.17)	76010 (20.85)
	GI bleeding	5980 (46.42)	106510 (29.16)
Medication	PPI use	10020 (77.86)	204190 (56)

Table 1. Baseline characteristics of cirrhotic patients with SBP and control

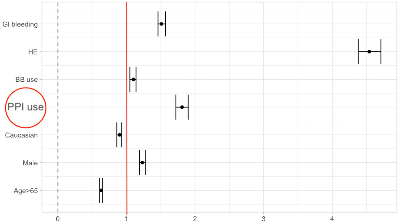

Figure 1. Forest Plot representing the different odds ratios of the independent variables of interest

		Odd Ratio (95% CI)	P-value
Demographics	Age> 65	0.63 (0.61-0.65)	0.00
	Male	1.23 (1.19-1.28)	0.00
	Caucasians	0.90 (0.86-0.93)	0.00
Medication	PPI use	1.81 (1.72-1.90)	0.00
Associated Medical Condition	Hepatic encephalopathy	4.54 (4.38-4.71)	0.00
	GI bleeding	1.51 (1.46-1.57)	0.00

Table 2. Multivariate analysis for cirrhotic with SBP in the Study Population

Discussion

- Evidence suggests that cirrhotic patients are predisposed to GI bacterial **overgrowth** resulting from **increased intestinal permeability**, **altered intestinal motility**, and **PPI use**.
- The risk of SBP in cirrhotic patients using PPI was already established in smaller scale studies but was **never** studied on a larger scale.

Conclusion

- This is the **largest** study for the prevalence of **SBP** in **cirrhotic** patients in the United States.
- Cirrhotic patients using **PPI** were at **higher risk** of developing SBP independently of **GI bleeding**.
- Results of this study are in line with those of other smaller ones done previously.

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