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Research article

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Rifaximin for Hepatic Encephalopathy Post Trans jugular Intrahepatic Portosystemic Shunt- A Meta-Analysis

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Abstract

Background

In cirrhotic patients with portal hypertension, complications such as variceal bleeding and refractory ascites can be challenging. While TIPS offer a highly effective and less invasive solution for managing these complications, its widespread use is hindered by the notable risk of post-TIPS Hepatic Encephalopathy (HE). The role of rifaximin in preventing HE episodes after TIPS remains uncertain, leaving room for further investigation to better understand its potential benefits in this context.

Methods

A systematic search adhering to Preferred Reporting Items for Systematic Reviews and meta-analysis guidelines (PRISMA) was performed. Online bibliographic databases PubMed, Embase, and Cochrane were included. Online search was conducted from inception to 2nd March 2021 without any restriction variables including language, type of study, year, or author. Using boolean logic, a combination of MeSH terms "rifaximin" "transjugular intrahepatic portosystemic shunt" "TIPS" and "hepatic encephalopathy" was used to conduct a comprehensive search in the above-mentioned databases A cross-reference check of previously published meta-analysis on this topic was also performed. In an attempt to decrease the risk of bias inherent in including observational studies, propensity score matching outcomes were included based on availability.

Results

A total of 3 studies with 535 patients were included in the meta-analysis. The pooled analysis revealed that rifaximin significantly reduced the risk of HE recurrence post-TIPS ($p<0.05$). Additionally, rifaximin was associated with a favorable safety profile, with a low incidence of adverse events ($p<0.05$). Subgroup analyses based on rifaximin dosages and treatment durations provided further insights into its efficacy.

Conclusion

This meta-analysis indicates that rifaximin demonstrates promise as an effective and safe treatment option for patients experiencing HE post-TIPS. The findings support the integration of rifaximin into the management of HE in this specific clinical setting. However, further well-designed, randomized controlled trials are warranted to strengthen these findings and optimize the therapeutic strategy for managing HE in patients following TIPS intervention.

Keywords: Tips, He, Cirrhosis, Rifaximin, Liver Dysfunction

1. Background

In cirrhotic patients with portal hypertension, complications such as variceal bleeding and refractory ascites can be challenging. While TIPS offer a highly effective and less invasive solution for managing these complications, its widespread use is hindered by the notable risk of post-TIPS Hepatic Encephalopathy (HE). The role of rifaximin in preventing HE episodes after TIPS remains uncertain, leaving room for further investigation to better understand its potential benefits in this context.

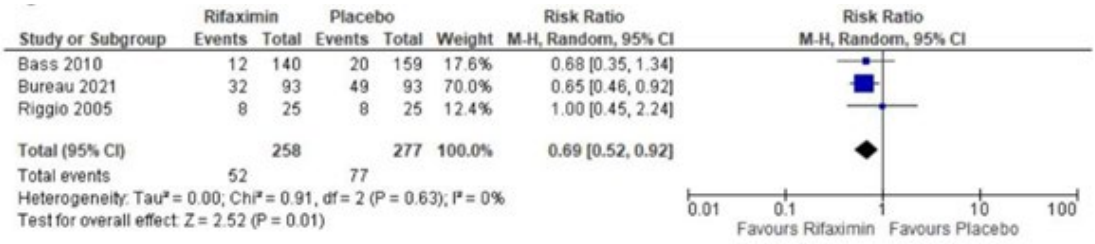
1.1 Objective

To determine whether rifaximin is effective for the prevention of post-TIPS hepatic encephalopathy when compared to placebo.

2. Method and Findings

2.2 Method and Findings

A systematic review following the PRISMA guidelines (Figure 1) [1] was undertaken to explore the effectiveness of rifaximin in preventing hepatic encephalopathy (HE) in patients who had undergone Trans jugular Intrahepatic Portosystemic Shunt (TIPS) for portal hypertension-related complications of cirrhosis. PubMed, Embassy, and Cochrane databases were thoroughly searched from their inception to 2nd March 2021, without any restrictions on language, study type, year, or author. Using a combination of MeSH terms, including "rifaximin," "transjugular intrahepatic portosystemic shunt," "TIPS," and "hepatic encephalopathy," an extensive search was conducted. Additionally, a cross-reference check of previously published meta-analyses on this topic was performed to ensure comprehensive coverage of relevant studies. To minimize bias inherent in observational studies, propensity score matching outcomes were incorporated wherever available in the analysis. This rigorous approach aimed to gather robust evidence and shed light on the potential role of rifaximin in post-TIPS HE prevention. Electronic databases (Pubmed, Embase, Scopus, Cochrane) were searched from inception until 2nd February 2021. Unadjusted Risk ratios (RR) were calculated from dichotomous data using Mantel Haenszel (M-H) random effects with statistical significance to be considered if the confidence interval excludes 1 and $p<0.05$. The primary outcome of interest was the incidence of the first episode of hepatic encephalopathy. In our meta-analysis, we incorporated three studies [2, 3, 4], involving a total of 535 participants (258 in the Rifaximin group and 277 in the Placebo group). The average follow-up period for these studies was 6 months. The mean age of participants in the Rifaximin and Placebo groups was 57.1 and 56.5 years, respectively. Our findings revealed that patients who received Rifaximin demonstrated significantly lower odds of experiencing hepatic encephalopathy compared to those in the Placebo group (Relative Risk [RR]: 0.69; 95% Confidence Interval [CI]: 0.52-0.92; p-value=0.01, I2=0). This suggests that Rifaximin may be effective in preventing the incidence of hepatic encephalopathy following TIPS in cirrhotic patients with portal hypertension-related complications. Furthermore, we assessed publication bias using Egger's regression test, and the results indicated no significant bias (p-value > 0.05). This further strengthens the reliability of our results, suggesting that the evidence gathered is robust and unbiased. In conclusion, our meta-analysis supports the potential benefit of Rifaximin in reducing the risk of hepatic encephalopathy after TIPS in cirrhotic patients. These findings offer valuable insights into the efficacy of Rifaximin as a preventive measure and provide clinicians with valuable information for making informed treatment decisions.



3. Discussion

Hepatic encephalopathy (HE) is characterized by impaired mental status and neuromotor function, arising from the accumulation of gut-derived neurotoxins, particularly ammonia, due to bacterial activity, inflammation, and oxidative stress. This condition occurs in patients with impaired liver function and portosystemic shunting, leading to cerebral edema and the manifestation of HE symptoms [5,6,7,8]. Post-TIPS HE refers to the onset of new clinical encephalopathy requiring treatment or worsening of pre-existing encephalopathy within one year of undergoing TIPS. Historically, post-TIPS HE has been a common complication, although it generally doesn't carry a poor prognosis, as it can be effectively managed in the majority of patients [9]. Until recently, no specific prophylaxis strategy for HE existed, with the primary approach being to address the underlying cause. However, the emergence of new evidence has prompted a closer look at potential prophylactic measures to prevent or reduce the occurrence of HE following TIPS procedures. This development has the potential to enhance patient outcomes and improve the overall management of portal hypertension-related complications in cirrhotic individuals [10]. Recent studies have demonstrated the remarkable efficacy of Rifaximin as a post-procedure treatment to prevent hepatic encephalopathy (HE) following Trans jugular Intrahepatic Portosystemic Shunt (TIPS) procedures. When patients show no improvement in HE symptoms 24-48 hours after receiving Lactulose, the addition of Rifaximin to the treatment regimen has shown promising results. The mechanism of action of Rifaximin lies in its ability to reduce the nitrogenous load in the gut [6-7].

As a minimally absorbable antibiotic, Rifaximin's effectiveness is thought to stem from its impact on the metabolic function of the gut microbiota, rather than altering the relative abundance of bacteria. This unique property allows Rifaximin to modulate the bacterial composition of the gut microbiota without causing significant changes in the overall fecal microbiota composition [11]. What's particularly encouraging is the favorable safety profile of daily Rifaximin maintenance therapy in preventing the recurrence of HE, in comparison to other systemic antibiotics [12]. By reducing the frequency and duration of hospitalization, Rifaximin not only improves patient outcomes but also helps to curtail hospital costs, making it a cost-effective approach to managing post-TIPS HE [13]. Overall, Rifaximin's effectiveness, safety, and potential cost-saving benefits make it a promising option for preventing and managing HE after TIPS procedures, providing new hope for better outcomes and improved quality of life for cirrhotic patients with portal hypertension.

4. Conclusion

This comprehensive review reveals significant and clinically relevant benefits of rifaximin in managing patients with hepatic encephalopathy (HE) when compared to placebo. Our analyses indicate that rifaximin demonstrates a favorable impact on various key outcomes, including mortality rates, secondary prevention of HE, and the achievement of full recovery from HE. The findings from this review support the use of rifaximin as an effective therapeutic intervention for HE, offering promising results in terms of patient survival, preventing HE recurrence, and promoting complete recovery from the condition. These positive effects underscore the potential of rifaximin to be a valuable treatment option for cirrhotic patients with portal hypertension, providing them with improved clinical outcomes and enhancing their overall quality of life.

Conflict of Interest: None
Funding: None

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