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## **Comparative Efficacy of Treatment Options for Prevention of Post-TIPS Hepatic Encephalopathy: A Systematic Review and Network Meta-analysis**

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**Introduction:** Transjugular intrahepatic portosystemic shunt (TIPS) is commonly used to treat complications of portal hypertension including refractory ascites, as well as secondary prophylaxis of variceal bleeding in patients with liver cirrhosis. Unfortunately, 35-50% of patients develop overt hepatic encephalopathy (HE) after TIPS. However, data on the utility of lactulose and rifaximin to prevent post-TIPS HE are limited. Therefore, we conducted a network meta-analysis to investigate the efficacy of multiple pharmacological regimens in preventing post-TIPS HE.

**Methods:** A comprehensive search strategy to identify reports of studies of rifaximin use and post-TIPS hepatic encephalopathy was developed in Embase (Embase.com, Elsevier) by an experienced health sciences librarian [WL-S], using truncated keywords, phrases, and subject headings. This strategy was translated to MEDLINE (PubMed platform, NCBI), Cochrane Central Register of Controlled Trials (CochraneLibrary.com, Wiley), and the Web of Science Core Collection (Web of Science platform, Clarivate) with all searches performed on 10 February 2022 (see Supplementary Information for detailed search strategies). No publication date or language limits were used.

**Results:** The results of this meta-analysis demonstrate no benefit from prophylactic administration of either a non-absorbable disaccharide (lactulose/lactitol) alone or a non-absorbable antibiotic (rifaximin) alone compared to placebo/no prophylaxis for the prevention of post-TIPS HE. However, there is weak evidence supporting the combination of lactulose and rifaximin in preventing post-TIPS HE based on the P-score rankings in our network meta-analysis.

**Conclusion:** In conclusion, lactulose/lactitol or rifaximin alone did not prevent post-TIPS HE. Despite this, there is weak evidence that the combination of lactulose and rifaximin is superior at preventing post-TIPS HE. Further research is warranted to determine if there is an ideal time for therapy initiation and duration of treatment in order to appreciate significant benefit of administering pharmacological prophylaxis to prevent post-TIPS HE.