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Noradrenaline vs Terlipresson for hepatorenal syndrome (No To Hepatorenal Syndrome): A meta - analysis

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Research Question: Among patients with hepatorenal syndrome (HRS), how safe and effective is noradrenaline as compared to terlipressin in reducing mortality, its reversal and occurrence of adverse effects?

Background: Hepatorenal syndrome is functional renal impairment associated with advanced cirrhosis. The best treatment for HRS is liver transplantation, however many patients die before this can be done due to organ shortage and the short survival associated with HRS. Several randomized controlled trials and meta-analyses have proven that terlipressin, a vasopressin analogue, improves renal function in hepatorenal syndrome.

Objective: To determine the safety and effectiveness of noradrenaline in the management of hepatorenal syndrome in terms of 1) reducing mortality, 2) its reversal and 3) occurrence of adverse events.

Inclusion criteria: The review included randomized trials comparing noradrenaline to terlipressin for patients with type 1 HRS, without restrictions in control of bias, publication status or language. The population consisted of adults diagnosed with hepatorenal syndrome according to the criteria set by the International Ascites Club.

Search Strategy: A systematic review of English and Non-English articles using the following databases: PubMed, the Cochrane Library, GoogleScholar and Clinicaltrials.gov. was done. Manual searches were performed by scanning reference lists of articles, registers of ongoing trials, and correspondence with authors. Search terms included vasoconstrictor, noradrenalin, terlipressin, hepatorenal syndrome, randomized controlled trial, meta-analysis, and clinical trials.

Study Maneuvers: Eligibility assessment was performed independently in a standardized manner using predefined data fields (including study quality indicators) set by three reviewers. Disagreements among the reviewers were resolved by consensus.

Statistical Analysis: Results were presented as the odds ratio (OR) with 95% confidence intervals (CIs). I² values were calculated as measures of inter-trial heterogeneity. The analyses were done with the aid of Review Manager 5.0.23.

Results: A total of 36 articles were found after electronic and manual searching. Three eligible articles were assessed for validity and included in the final analysis. The total number of patients across all trials is 95. Noradrenaline was found to be not significantly different from terlipressin in terms of 15-day survival rate (OR 0.17; 95% CI: 0.01-2.66), reversal of HRS (OR 1.07; 95% CI: 0.47-2.44). Sensitivity analysis still revealed a slight advantage of terlipressin over noradrenaline, albeit not significant (survival at 15 days: OR=1.21 95% confidence interval = 0.52, 2.83; HRS reversal: OR= 1.33, confidence interval = 0.56, 3.13; disease-free survival at 15 days: 1.35, confidence interval = 0.56-3.25).

Conclusions: Overall, the present review suggests that there's no sufficient evidence that noradrenaline and terlipressin are significantly different in terms of reducing mortality and reversal of HRS. The main limitation of this study is its small sample size, which is mainly due to the rarity of this condition. Also, a next logical step in the field of HRS management is to do further analysis, using the Bayesian approach in order to prove the non inferiority of noradrenaline as compared to terlipressin.

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