THE EFFECTIVENESS OF PEG 3350 COMPARED TO LACTULOSE FOR THE TREATMENT OF ACUTE HEPATIC ENCEPHALOPATHY IN ADULT CIRRHOTIC PATIENTS: A SYSTEMATIC REVIEW AND META-ANALYSIS

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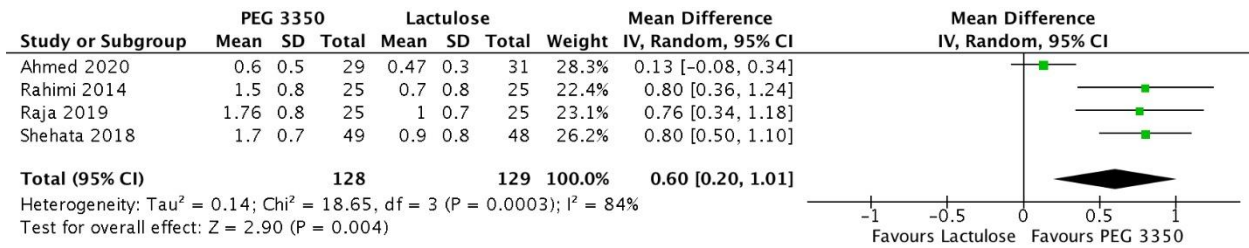
Background: Cirrhosis is the leading cause of liver-related death globally. Hepatic encephalopathy (HE) leads to significant morbidity and mortality. Lactulose is the current gold standard treatment for HE; it eliminates nitrogenous waste from the gut. Polyethylene glycol 3350–electrolyte solution (PEG) is a safe, common and effective purgative with recent studies suggesting its efficacy resulting in faster resolution of HE and shorter hospital length of stay.
Aims: To assess the efficacy and safety of PEG 3350 compared to lactulose in adult cirrhotic patients 18 years of age and older with overt hepatic encephalopathy on patient important outcomes including: improvement of hepatic encephalopathy, hospital length of stay and mortality.
Methods: We reviewed databases MEDLINE, EMBASE, OVID, CINAHL, Cochrane Database, PubMed, Trip database, the grey literature, and clinicaltrials.gov from inception to December 2020: PROSPERO CRD42021257641. Search strategy was developed in conjunction with medical librarian. Randomized controlled trials (RCTs), either published or non-published, were included in the review. Continuous data was analyzed using mean difference with random-effects model. Dichotomous data was analyzed using the Mantel-Haenszel method using random-effects model. Statistical effect-size heterogeneity was assessed using Chi^2 test and quantifying the relative proportion of variation using I^2 statistic. The overall certainty of evidence will be assessed using the Grading of Recommendations, Assessment, Development and Evaluations system (GRADE).
Results: From the 68 studies, 16 were assessed for full text review from which 5 studies were included in the meta-analysis representing a total of 351 patients. The primary outcome of mean change in Hepatic Encephalopathy Scoring Algorithm (HESA) at 24-hours from baseline demonstrated an improvement in the PEG group compared to lactulose group [Mean difference (MD)= 0.60, 95% CI (0.20, 1.01)]. In comparison to lactulose, PEG also demonstrated a shorter hospital length of stay [MD = -1.00, 95% CI (-1.99, -0.01)], shorter time to HE resolution [MD= -1.49, 95% CI (-1.81, -1.16)] and showed a mortality benefit [RR=0.35, 95% CI (0.13 to 0.92)]. There was no significant difference between change in ammonia levels at 24 hours [MD= -25.80, 95% CI (-95.39, 43.78)].
Conclusions: PEG leads to a faster improvement and resolution of HE when compared to the current standard of care, lactulose.

Study or Subgroup	PEG 3350 Mean	SD	Total	Lactulose Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI	Mean Difference IV, Random, 95% CI
Ahmed 2020	0.6	0.5	29	0.47	0.3	31	28.3%	0.13 [−0.08, 0.34]	
Rahimi 2014	1.5	0.8	25	0.7	0.8	25	22.4%	0.80 [0.36, 1.24]	
Raja 2019	1.76	0.8	25	1	0.7	25	23.1%	0.76 [0.34, 1.18]	
Shehata 2018	1.7	0.7	49	0.9	0.8	48	26.2%	0.80 [0.50, 1.10]	
Total (95% CI)			128			129	100.0%	0.60 [0.20, 1.01]	

Heterogeneity: Tau² = 0.14; Chi² = 18.65, df = 3 (P = 0.0003); I² = 84%

Test for overall effect: Z = 2.90 (P = 0.004)

Favours Lactulose   Favours PEG 3350