

Journal of Clinical Gastroenterology

**Comparative Effectiveness and Safety of Polyethylene Glycol Electrolyte Solution Versus
Lactulose for Treatment of Hepatic Encephalopathy: A Systematic Review and Meta-
Analysis
(Supplementary File)**

Supplementary file 1. Search term

1. Pubmed

1# (((("Hepatic Encephalopathy"[Mesh]) OR (((((((((((((Encephalopathies, Hepatic) OR (Hepatic Encephalopathies)) OR (Encephalopathy, Hepatic) OR (Portal-Systemic Encephalopathy)) OR (Portal Systemic Encephalopathy)) OR (Encephalopathy, Portal-Systemic)) OR (Encephalopathies, Portal-Systemic)) OR (Encephalopathy, Portal Systemic)) OR (Portal-Systemic Encephalopathies)) OR (Encephalopathy, Portosystemic)) OR (Hepatocerebral Encephalopathy)) OR (Portosystemic Encephalopathy)) OR (Encephalopathies, Portosystemic)) OR (Portosystemic Encephalopathies)) OR (Encephalopathy, Hepatocerebral)) OR (Encephalopathies, Hepatocerebral)) OR (Hepatocerebral Encephalopathies)) OR (Hepatic Coma)) OR (Coma, Hepatic)) OR (Comas, Hepatic)) OR (Hepatic Comas)) OR (Hepatic Stupor)) OR (Hepatic Stupors)) OR (Stupor, Hepatic)) OR (Stupors, Hepatic)) OR (Fulminant Hepatic Failure with Cerebral Edema)))

2# ("Polyethylene Glycols"[Mesh]) OR ((((((((((polyethylene glycol electrolyte powder) OR (Macrogol)) OR (Macrogols)) OR (Polyethylene Oxide)) OR (Oxide, Polyethylene)) OR (Oxides, Polyethylene)) OR (Polyethylene Oxides)) OR (Polyethyleneoxide)) OR (Polyethyleneoxides)) OR (Polyoxyethylenes)) OR (Polyoxyethylene)) OR (Polyglycol)) OR (Polyglycols)) OR (Polyethylene Glycol)) OR (Glycol, Polyethylene)) OR (Glycols, Polyethylene)) OR (Carbowax)))

3# (randomized controlled trial[Publication Type] OR randomized[Title/Abstract] OR placebo[Title/Abstract])

2. Embase

1# 'Encephalopathies, Hepatic':ab,ti or 'Hepatic Encephalopathies':ab,ti or 'Encephalopathy, Hepatic':ab,ti or 'Portal-Systemic Encephalopathy':ab,ti or 'Portal Systemic Encephalopathy':ab,ti or 'Encephalopathy, Portal-Systemic':ab,ti or 'Encephalopathies, Portal-Systemic':ab,ti or 'Encephalopathy, Portal Systemic':ab,ti or 'Portal-Systemic Encephalopathies':ab,ti or 'Encephalopathy, Portosystemic':ab,ti or 'Hepatocerebral Encephalopathy':ab,ti or 'Portosystemic Encephalopathy':ab,ti or 'Encephalopathies, Portosystemic':ab,ti or 'Encephalopathy, Hepatocerebral':ab,ti or 'Encephalopathies, Hepatocerebral':ab,ti or 'Encephalopathy, Hepatocerebral':ab,ti or 'Hepatocerebral Encephalopathies':ab,ti or 'Hepatic Coma':ab,ti or 'Coma, Hepatic':ab,ti or 'Comas, Hepatic':ab,ti or 'Hepatic Comas':ab,ti or 'Hepatic Stupor':ab,ti or 'Hepatic Stupors':ab,ti or 'Stupor, Hepatic':ab,ti or 'Stupors, Hepatic':ab,ti or 'Fulminant Hepatic Failure with Cerebral Edema':ab,ti

2# 'polyethylene glycol electrolyte powder ':ab,ti or 'Macrogol':ab,ti or 'Macrogols':ab,ti or 'Polyethylene Oxide':ab,ti or 'Oxide, Polyethylene':ab,ti or 'Oxides, Polyethylene':ab,ti or 'Polyethylene Oxides':ab,ti or 'Polyethyleneoxide':ab,ti or 'Polyethyleneoxides':ab,ti or 'Polyoxyethylenes':ab,ti or 'Polyoxyethylene':ab,ti or 'Polyglycol':ab,ti or 'Polyglycols':ab,ti or 'Polyethylene Glycol':ab,ti or 'Glycol, Polyethylene':ab,ti or 'Glycols, Polyethylene':ab,ti or 'Carbowax':ab,ti

3# 'randomized controlled trial ':ab,ti or 'randomized ':ab,ti or 'placebo':ab,ti or 'RCT':ab,ti

3. Web of science

1# hepatic encephalopathy OR Encephalopathies, Hepatic OR Hepatic Encephalopathies OR Encephalopathy, Hepatic OR Portal-Systemic Encephalopathy OR Portal Systemic Encephalopathy OR Encephalopathy, Portal-Systemic OR Encephalopathies, Portal-Systemic OR Encephalopathy, Portal Systemic OR Portal-Systemic Encephalopathies OR Encephalopathy, Portosystemic OR Hepatocerebral Encephalopathy OR Portosystemic Encephalopathy OR Encephalopathies, Portosystemic OR Portosystemic Encephalopathies OR Encephalopathy, Hepatocerebral OR Encephalopathies, Hepatocerebral OR Hepatocerebral Encephalopathies OR Hepatic Coma OR Coma, Hepatic OR Comas, Hepatic OR Hepatic Comas OR Hepatic Stupor OR Hepatic Stupors OR Stupor, Hepatic OR Stupors, Hepatic OR Fulminant Hepatic Failure with Cerebral Edema

2# Polyethylene Glycol OR polyethylene glycol electrolyte powder OR Macrogol OR Macrogols OR Polyethylene Oxide OR Oxide, Polyethylene OR Oxides, Polyethylene OR Polyethylene Oxides OR Polyethyleneoxide OR Polyethyleneoxides OR Polyoxyethylenes OR Polyoxyethylene OR Polyglycol OR Polyglycols OR Polyethylene Glycol OR Glycol, Polyethylene OR Glycols, Polyethylene OR Carbowax

3# randomized controlled trial OR randomized OR placebo OR RCT

4. COCHRANE

1# (hepatic encephalopathy):ti,ab,kw OR (Encephalopathies, Hepatic):ti,ab,kw OR (Hepatic Encephalopathies):ti,ab,kw OR (Encephalopathy, Hepatic):ti,ab,kw OR (Portal-Systemic Encephalopathy):ti,ab,kw OR (Portal Systemic Encephalopathy):ti,ab,kw OR (Encephalopathy, Portal-Systemic):ti,ab,kw OR (Encephalopathies, Portal-Systemic):ti,ab,kw OR (Encephalopathy, Portal Systemic):ti,ab,kw OR (Portal-Systemic Encephalopathies):ti,ab,kw OR (Encephalopathy, Portosystemic):ti,ab,kw OR (Hepatocerebral Encephalopathy):ti,ab,kw OR (Portosystemic Encephalopathy):ti,ab,kw OR (Encephalopathies, Portosystemic):ti,ab,kw OR (Portosystemic Encephalopathies):ti,ab,kw OR (Encephalopathy, Hepatocerebral):ti,ab,kw OR (Encephalopathies, Hepatocerebral):ti,ab,kw OR (Hepatocerebral Encephalopathies):ti,ab,kw OR (Hepatic Coma):ti,ab,kw OR (Coma, Hepatic):ti,ab,kw OR (Comas, Hepatic):ti,ab,kw OR (Hepatic Comas):ti,ab,kw OR (Hepatic Stupor):ti,ab,kw OR (Hepatic Stupors):ti,ab,kw OR (Stupor, Hepatic):ti,ab,kw OR (Stupors, Hepatic):ti,ab,kw OR (Fulminant Hepatic Failure with Cerebral Edema):ti,ab,kw

2# (Polyethylene Glycol):ti,ab,kw OR (polyethylene glycol electrolyte powder):ti,ab,kw OR (Macrogol):ti,ab,kw OR (Macrogols):ti,ab,kw OR (Polyethylene Oxide):ti,ab,kw OR (Oxide, Polyethylene):ti,ab,kw OR (Oxides, Polyethylene):ti,ab,kw OR (Polyethylene Oxides):ti,ab,kw OR (Polyethyleneoxide):ti,ab,kw OR (Polyethyleneoxides):ti,ab,kw OR (Polyoxyethylenes):ti,ab,kw OR (Polyoxyethylene):ti,ab,kw OR (Polyglycol):ti,ab,kw OR (Polyglycols):ti,ab,kw OR (Polyethylene Glycol):ti,ab,kw OR (Glycol, Polyethylene):ti,ab,kw OR (Glycols, Polyethylene):ti,ab,kw OR (Carbowax):ti,ab,kw

3# (randomized controlled trial):ti,ab,kw OR (OR randomized):ti,ab,kw OR (Placebo):ti,ab,kw OR (RCT):ti,ab,kw

Supplementary file 2. Outcomes on improvement of polyethylene glycol vs lactulose on hepatic encephalopathy

Study	RR	[95% Conf. Interval]	% Weight
<hr/>			
Ahmed, S. (2020)	1.924	1.073 3.451	11.40
Ismail, K. B. (2020)	1.417	0.947 2.119	14.15
Naderian, M. (2017)	1.293	0.972 1.719	17.33
Rahimi, R. S. (2014)	1.756	1.180 2.612	14.69
Shehata, H. H. (2018)	1.306	1.083 1.573	42.44
<hr/>			
M-H pooled RR	1.456	1.260 1.682	100.00
<hr/>			

Heterogeneity chi-squared = **3.73** (d.f. = **4**) p = **0.444**

I-squared (variation in RR attributable to heterogeneity) = **0.0%**

Test of RR=1 : z= **5.09** p = **0.000**

Figure S2A Meta-analysis of the comparison of the clinical efficacy of PEG with lactulose at 24 hours.

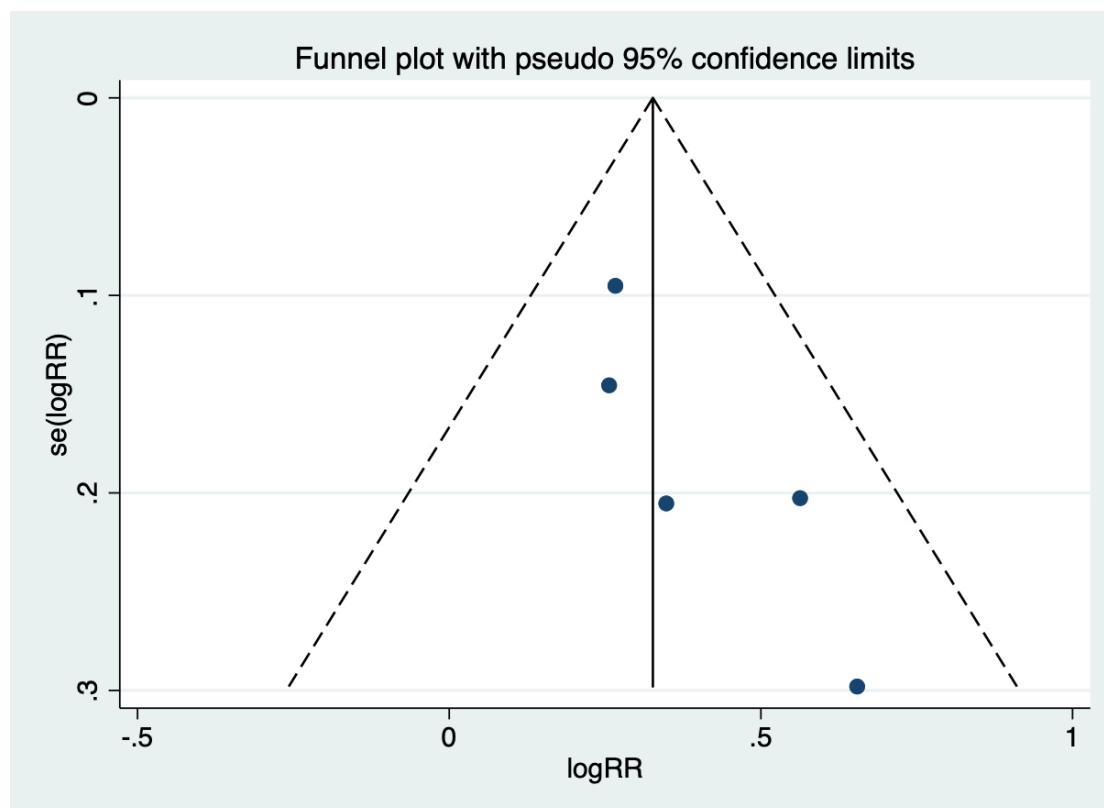


Figure S2B Funnel plot illustrating the comparison of the clinical efficacy of PEG with lactulose at 24 hours.

Begg's Test

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adj. Kendall's Score (P-Q) =      6
    Std. Dev. of Score =     4.08
    Number of Studies =      5
        z =     1.47
    Pr > |z| =   0.142
        z =     1.22 (continuity corrected)
    Pr > |z| =   0.221 (continuity corrected)

```

Egger's test

Std_Eff	Coef.	Std. Err.	t	P> t	[95% Conf. Interval]
slope	.0746425	.102553	0.73	0.519	-.251727 .401012
bias	1.791226	.6755987	2.65	0.077	-.3588306 3.941282

Figure S2C Publication bias of included studies on the comparison of the clinical efficacy of PEG with lactulose at 24 hours.

Supplementary file 3. Outcomes on adverse effects of polyethylene glycol vs lactulose on hepatic encephalopathy.

Study		RR	[95% Conf. Interval]	% Weight
Ahmed, S. (2020)		2.138	0.588 7.767	8.61
Bajwa, K. N. (2019)		0.714	0.244 2.091	20.78
Rahimi, R. S. (2014)		0.652	0.175 2.428	14.22
Shehata, H. H. (2018)		0.579	0.308 1.088	56.39
Ismail, K. B. (2020)		(Excluded)		
Naderian, M. (2017)		(Excluded)		
Raja W. (2019)		(Excluded)		
M-H pooled RR		0.752	0.475 1.189	100.00

Heterogeneity chi-squared = 3.23 (d.f. = 3) p = 0.357
I-squared (variation in RR attributable to heterogeneity) = 7.2%

Test of RR=1 : z= 1.22 p = 0.222

Figure S3A Meta-analysis of adverse events experienced by patients treated with PEG vs lactulose.

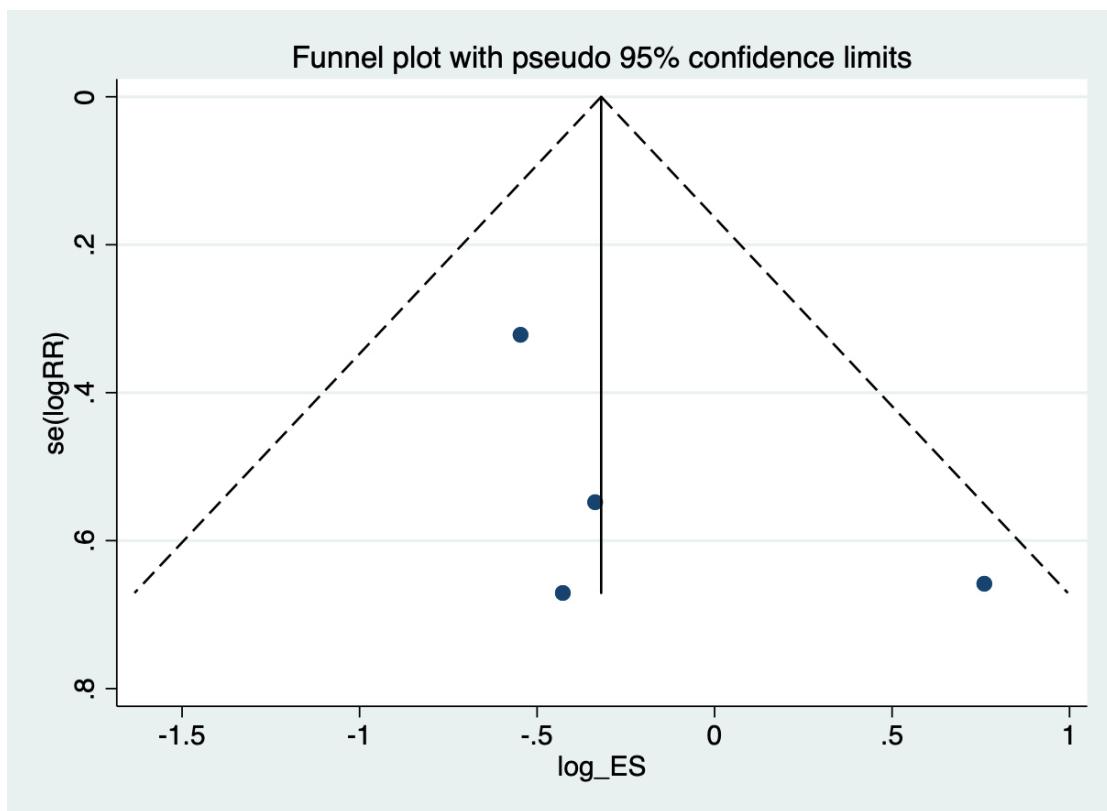


Figure S3B Funnel plot illustrating adverse events experienced by patients treated with PEG vs lactulose.

Begg's Test

```

adj. Kendall's Score (P-Q) =      2
Std. Dev. of Score =      2.94
Number of Studies =        4
z =      0.68
Pr > |z| =      0.497
z =      0.34 (continuity corrected)
Pr > |z| =      0.734 (continuity corrected)

```

Egger's test

Std_Eff	Coef.	Std. Err.	t	P> t	[95% Conf. Interval]
slope	-1.161969	.724799	-1.60	0.250	-4.280528 1.956589
bias	1.858448	1.51685	1.23	0.345	-4.66803 8.384926

Figure S3C Publication bias of included studies on the comparison of adverse events of PEG with lactulose

Supplementary file 4. Outcomes on hospitalization of polyethylene glycol vs lactulose on hepatic encephalopathy

Study		WMD	[95% Conf. Interval]	% Weight
Ahmed, S. (2020)		-3.874	-4.681 -3.068	18.62
Bajwa, K. N. (2019)		-0.810	-1.568 -0.052	18.93
Naderian, M. (2017)		-2.100	-2.481 -1.719	20.86
Rahimi, R. S. (2014)		-4.000	-8.861 0.861	3.16
Raja W, (2019)		0.040	-0.872 0.952	17.93
Shehata, H. H. (2018)		-1.700	-2.167 -1.233	20.51
D+L pooled WMD		-1.781	-2.716 -0.845	100.00

Heterogeneity chi-squared = **50.74** (d.f. = 5) p = **0.000**

I-squared (variation in WMD attributable to heterogeneity) = **90.1%**

Estimate of between-study variance Tau-squared = **1.0535**

Test of WMD=0 : z= **3.73** p = **0.000**

Figure S4A Meta-analysis of serum ammonia concentration before treating with PEG vs lactulose. (fixed effects analysis).

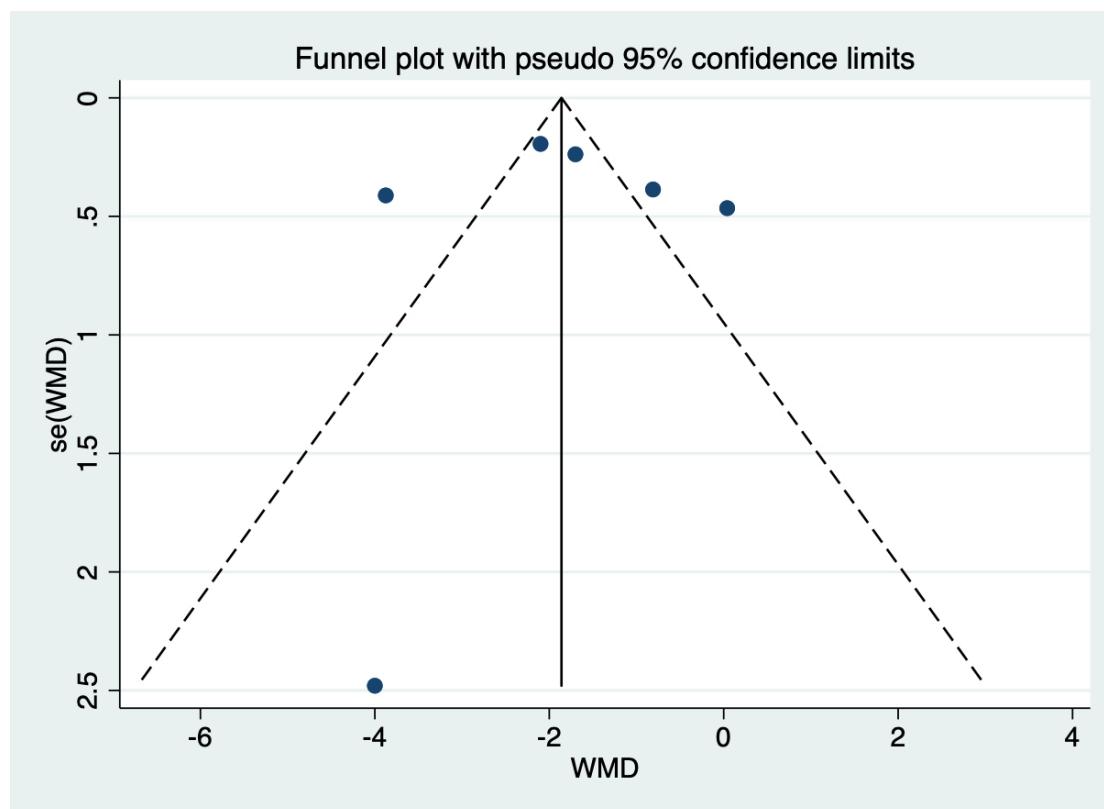


Figure S4B Funnel plot illustrating the comparison of hospital stays of PEG with lactulose

Begg's Test

```

adj. Kendall's Score (P-Q) =      3
    Std. Dev. of Score =      5.32
    Number of Studies =       6
        z =      0.56
    Pr > |z| =      0.573
        z =      0.38 (continuity corrected)
    Pr > |z| =      0.707 (continuity corrected)

```

Egger's test

Std_Eff	Coef.	Std. Err.	t	P> t	[95% Conf. Interval]
slope	-1.956431	.9560221	-2.05	0.110	-4.610774 .6979113
bias	.3514514	3.062102	0.11	0.914	-8.150306 8.853208

Figure S4C Publication bias of included studies on the comparison of hospital stays of PEG with lactulose

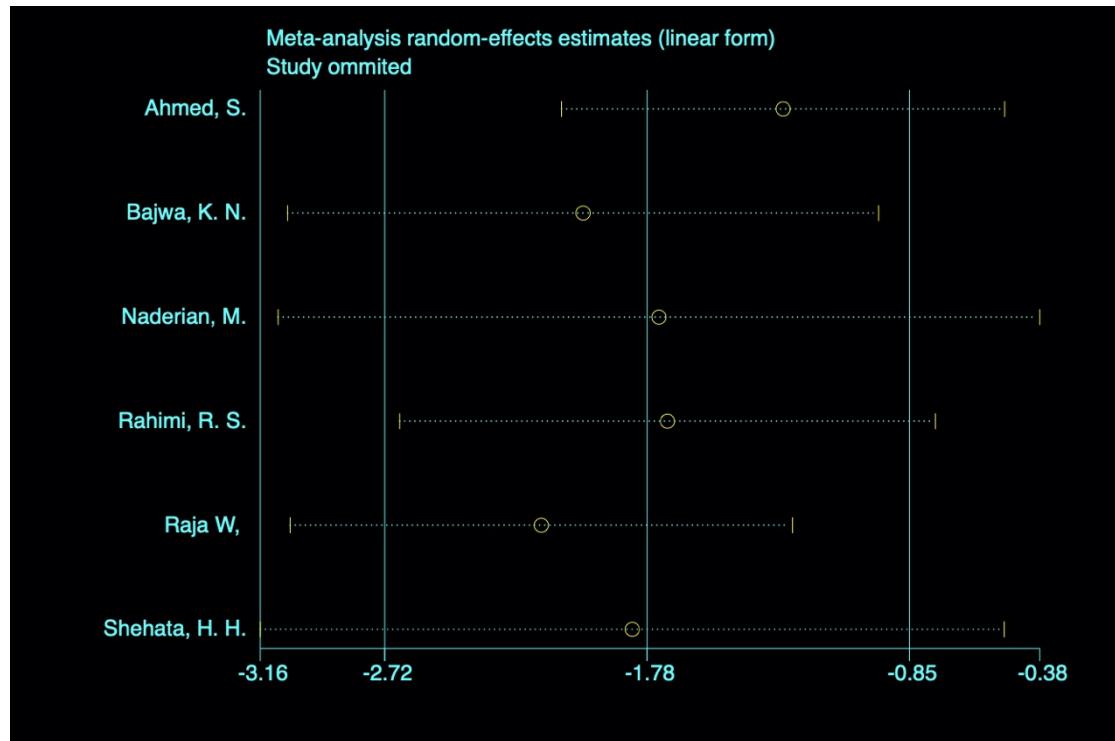


Figure S4D Sensitivity analysis of length of hospital stay comparing PEG with lactulose

Supplementary file 5. Outcomes on serum ammonia of polyethylene glycol vs lactulose on hepatic encephalopathy

Study		WMD	[95% Conf. Interval]	% Weight
Ahmed, S. (2020)		8.852	-1.351 19.055	88.02
Naderian, M. (2017)		9.600	-27.764 46.964	6.56
Rahimi, R. S. (2014)		-29.000	-70.139 12.139	5.41
I-V pooled WMD		6.851	-2.721 16.424	100.00

Heterogeneity chi-squared = 3.09 (d.f. = 2) p = 0.214

I-squared (variation in WMD attributable to heterogeneity) = 35.2%

Test of WMD=0 : z= 1.40 p = 0.161

Figure S5A Meta-analysis of serum ammonia concentration before treating with PEG vs lactulose. (fixed effects analysis).

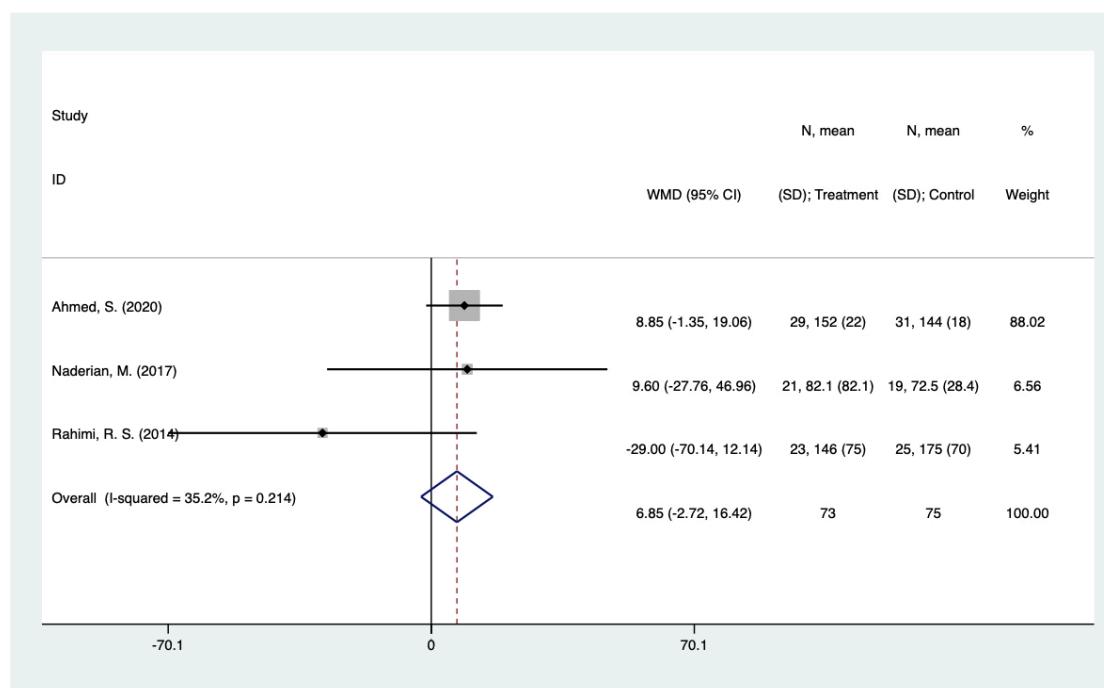


Figure S5B Forest plot illustrating serum ammonia concentration before treating with PEG vs lactulose. (fixed effects analysis).

Study		WMD	[95% Conf. Interval]	% Weight
Ahmed, S. (2020)		-9.996	-18.819 -1.173	38.73
Naderian, M. (2017)		8.100	-7.360 23.560	34.77
Rahimi, R. S. (2014)		38.000	10.972 65.028	26.50
D+L pooled WMD		9.017	-14.394 32.427	100.00

Heterogeneity chi-squared = **13.20** (d.f. = 2) p = **0.001**
I-squared (variation in WMD attributable to heterogeneity) = **84.9%**
Estimate of between-study variance Tau-squared = **348.1093**

Test of WMD=0 : z= **0.75** p = **0.450**

Figure S5C Meta-analysis of serum ammonia concentration after treating with PEG vs lactulose.
(random effects analysis).