

Therapeutic Effect of Granulocyte Colony-Stimulating Factor Therapy In Cirrhosis: A Meta-Analysis of Randomized Controlled Trials

THE CAL CENTRES

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Background

- Decompensated cirrhosis is an advanced stage of cirrhosis in which liver scarring becomes so extensive that the liver is unable to function properly, leading to complications such as refractory ascites, recurrent infections, and hepatic encephalopathy.
- Currently, liver transplantation is the only definitive treatment, but it has a number of disadvantages, including high cost, restricted donor pool, and long-term immunosuppression.
- As a result, granulocyte colony stimulating factor (G-CSF) has emerged as an alternative therapy. However, its clinical efficacy is still debatable, so the aim of this meta-analysis was to determine the efficacy of G-CSF in patients with decompensated and compensated cirrhosis.

Figure 1: Survival rate in patients with compensated cirrhosis and decompensated cirrhosis

	Experim	ental	Contr	ol		Risk Ratio	Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% CI	M-H, Random, 95% Cl
De et al.2020	34	50	18	50	10.6%	1.89 [1.25, 2.86]	
Kedarisetty et al. 2015	20	29	7	26	6.0%	2.56 [1.30, 5.05]	
Newsome et al. 2018	27	27	25	27	18.4%	1.08 [0.95, 1.22]	•
Philips et al. 2019	12	48	13	24	6.9%	0.46 [0.25, 0.85]	
Prajapati et al. 2017	100	126	82	127	17.7%	1.23 [1.05, 1.44]	-
Venkitaraman et al. 2020	30	35	23	35	14.4%	1.30 [0.99, 1.72]	-
venkitaraman et al. 2022	29	33	22	33	14.5%	1.32 [1.00, 1.73]	-
Verma et al. 2018	20	21	12	21	11.4%	1.67 [1.14, 2.44]	-
Total (95% CI)		369		343	100.0%	1.29 [1.06, 1.58]	•
Total events	272		202				
Heterogeneity: Tau ² = 0.05	; Chi² = 28.	09, df=	7 (P = 0.0	0002);1	² = 75%		0.04 0.4 4 4.0 4.00
Test for overall effect: Z = 2	.55 (P = 0.0	01)					0.01 0.1 1 10 100 Favours [G-CSFI] Favours [control]

Methods

- MEDLINE and SCOPUS were queried from inception till June 2022 for randomized controlled trials (RCTs), without any restriction.
- RCTs evaluating effects of G-CSF on survival rates and occurrence of infection in patients with Cirrhosis were incorporated.
- The results were reported using a random-effects metaanalysis and the Mantel-Haenszel risk ratio (RR). The Subgroup analysis was done to investigate the influence of study-level factors such as study setting, population and etiology on the outcomes of interest.

Figure 2: Survival rate in patients with decompensated cirrhosis

	Experim	ental	Contr	ol		Risk Ratio	Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% CI	M-H, Random, 95% CI
De et al.2020	34	50	18	50	13.3%	1.89 [1.25, 2.86]	-
Kedarisetty et al. 2015	20	29	7	26	7.8%	2.56 [1.30, 5.05]	
Philips et al. 2019	12	48	13	24	8.9%	0.46 [0.25, 0.85]	
Prajapati et al. 2017	100	126	82	127	20.9%	1.23 [1.05, 1.44]	•
Venkitaraman et al. 2020	30	35	23	35	17.5%	1.30 [0.99, 1.72]	-
venkitaraman et al. 2022	29	33	22	33	17.5%	1.32 [1.00, 1.73]	-
Verma et al. 2018	20	21	12	21	14.2%	1.67 [1.14, 2.44]	
Total (95% CI)		342		316	100.0%	1.35 [1.07, 1.70]	•
Total events	245		177				
Heterogeneity: Tau ² = 0.06	; Chi² = 20.	07, df=	6 (P = 0.0	003); l²	= 70%	Ļ	04 04 4 40 4
Test for overall effect: $Z = 2$.53 (P = 0.0	01)				U	.01 0.1 1 10 1 Favours [G-CSF] Favours [control]

Results

- Eight studies (n = 8) were included in our metaanalysis. The total number of participants in our study was 712, and the median study duration was 12 months. Our pooled analysis demonstrates that G-CSF treatment did not improve survival rates (RR 1.29; 95% CI 1.06 to 1.58; p = 0.01; **Figure 1**) in patients with compensated cirrhosis and decompensated cirrhosis.
- In our subgroup analysis, G-CSF was also linked to lower survival rates among people with decompensated cirrhosis (RR 1.35; 95% CI 1.07 to 1.70; p = 0.01; Figure 2).

CONCLUSIONS

 Our findings indicate that G-CSF therapy is not beneficial in improving survival rates and does reducing the risk of infection in patients with Cirrhosis