Peran Granulocyte-Colony Stimulating Factor (G-CSF) untuk Perbaikan Skor PELD dan Status Nutrisi Pretransplantasi Hati pada Sirosis Hati Anak Melalui Imunomodulasi Neutrofil, Sel CD34+, TNF-, HGF, dan IL-10. = The Role of Granulocyte-Colony Stimulating Factor (G-CSF) to Improve PELD Score and Nutritional Status in Pretransplant Pediatric Liver Cirrhosis Patients through Immunomodulation of Neutrophils, CD34+ Cells, TNF-âº, HGF, And IL-10.

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Abstrak

Sirosis dekompensata pada anak merupakan indikasi utama transplantasi hati. Mayoritas pasien yang menunggu transplantasi hati memiliki masalah malnutrisi dan infeksi yang berhubungan dengan prognosis buruk, sehingga dibutuhkan terapi antara untuk memperbaiki kondisi pasien sebelum transplantasi hati. Skor pediatric end-stage liver disease (PELD) adalah sistem penilaian yang digunakan untuk menentukan prioritas transplantasi hati. Semakin tinggi nilainya, semakin buruk kondisi pasien. Terapi granulocyte colony-stimulating factor (G-CSF) telah memberikan hasil yang menjanjikan pada pasien sirosis dewasa, namun penelitian pada sirosis dekompensata anak belum pernah dilakukan. Penelitian ini dilakukan dengan tujuan untuk mengetahui pengaruh G-CSF terhadap skor PELD dan status nutrisi. Juga dinilai pengaruh terapi G-CSF terhadap neutrofil, CD34+, sitokin pro-inflamasi dan anti-inflamasi, hepatocyte growth factor (HGF), biomarker fungsi hati, adverse event dan kesintasan.
Penelitian ini dilaksanakan pada bulan September 2019–Februari 2022 di Rumah Sakit dr. Cipto Mangunkusumo (RSCM), bersifat uji acak terkontrol open-label. Subjek adalah pasien anak dengan usia antara 3 bulan hingga 12 tahun dengan diagnosis sirosis dekompensata yang dibagi dalam kelompok intervensi (n = 26) dan kelompok kontrol (n = 24). Subjek pada kelompok intervensi diberikan 12 kali injeksi subkutan G-CSF (5 µg/kg/hari) serta terapi standar sirosis, dan pada kelompok kontrol hanya diberikan terapi standar sirosis.
Tidak terdapat penurunan skor PELD yang bermakna setelah pemberian G-CSF. Terdapat perubahan bermakna pada kadar neutrofil dan leukosit (uji ANOVA, p < 0,001, untuk kedua parameter). Terdapat tanda mobilisasi sel punca yang dilihat dari peningkatan kadar CD34+, namun hasilnya tidak bermakna. Pemberian G-CSF secara bermakna menurunkan kadar tumor necrosis factor (TNF)- (uji ANOVA, p = 0,001), dan meningkatkan interleukin (IL)-10 dan HGF (uji ANOVA, p = 0,003 untuk kedua parameter) yang menunjukkan bahwa imunitas bawaan dan regenerasi hati subjek dapat diperbaiki. Tidak ada perbedaan bermakna antara lingkar lengan atas (LILA) dan triceps skinfold thickness (TST) berdasarkan z-score setelah pemberian G-CSF. Kadar alanine aminotransferase (ALT) menurun secara bermakna pada kelompok intervensi (uji ANOVA, p = 0,038). Subjek yang mengalami kejadian infeksi lebih rendah pada kelompok intervensi dibanding kelompok kontrol (uji eksak Fisher, p = 0.04).
.....Decompensated cirrhosis in children is the main indication of liver transplantation. The majority of patients awaiting liver transplantation have malnutrition and infection problems that are associated with poor prognosis, thus requiring a bridging therapy to treat these conditions prior to liver transplantation. Pediatric end-stage liver disease (PELD) score is a scoring system used to determine liver transplantation priority,

higher scores indicates a worse prognosis. Granulocyte colony-stimulating factor (G-CSF) therapy has shown promising results in adult liver cirrhosis. Our study aimed to investigate the effect of G-CSF on pediatric end-stage liver disease (PELD) scores and nutritional status in pediatric liver cirrhosis. The study also investigated the effects of G-CSF on neutrophils, CD34+ cells, pro-inflammatory and anti-inflammatory cytokines, hepatocyte growth factor (HGF), liver function markers, adverse events, and survival.

This study was conducted on September 2019–February 2022 at dr. Cipto Mangunkusumo Hospital (RSCM). This was an open-label, randomized controlled trial (RCT) including subjects between 3 months and 12 years of age with decompensated cirrhosis. The subjects were divided into intervention group (n = 26) and control (n = 24). Subjects from the intervention group received 12 courses of subcutaneous injection of G-CSF (5 g/kg/day) plus standard medical treatment (SMT) for liver cirrhosis, while the control received SMT.

Our study did not identify a significant difference in PELD scores between the intervention and control groups after 3 months of G-CSF treatment. Leucocyte and neutrophil counts showed significant differences between the intervention and control groups (ANOVA test, $p > 0.001$, for both). There was evidence of stem cell mobilization based on increased CD34+ cells in the intervention group; however, the results were not significant. G-CSF administration significantly decreased TNF- (ANOVA test, $p = 0{,}001$), and significantly increased IL-10 and HGF (ANOVA test, $p = 0{,}0003$, respectively) indicating improvement in subjects' immunity. There was no significant difference in nutritional status according to mid-upper arm circumference (MUAC) and triceps skinfold thickness (TST) based on the z-scores. Alanine aminotransferase (ALT) levels significantly decreased in the intervention group (ANOVA test, $p = 0{,}038$). Subjects in the intervention group experienced fewer infection events, with a significant difference in the occurrence of sepsis in the intervention group compared to the control (Fisher's exact test, $p = 0.04$).