Pengaruh penambahan asam ursodeoksikolat terhadap durasi fototerapi pada Neonatus Kurang Bulan dengan Hiperbilirubinemia = The effect of adding ursodeoxycholic acid on duration of phototherapy in Preterm Neonates with Hyperbilirubinemia

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Abstrak

Latar Belakang: Neonatus kurang bulan berisiko mengalami hiperbilirubinemia 12,5 kali lipat lebih besar dibandingkan neonatus cukup bulan, 54% membutuhkan fototerapi. Hiperbilirubinemia dapat menyebabkan neurotoksisitas hingga kematian, sedangkan fototerapi dapat menyebabkan beberapa komplikasi. Terapi ajuvan seperti asam ursodeoksikolat diperlukan untuk meningkatkan klirens bilirubin sehingga mengurangi durasi fototerapi. Saat ini belum ada data yang tersedia mengenai pengaruh penambahan asam ursodeoksikolat terhadap durasi fototerapi pada neonatus kurang bulan dengan hiperbilirubinemia.
Tujuan: Penelitian ini bertujuan untuk menentukan durasi fototerapi dan penurunan kadar bilirubin pada neonatus kurang bulan yang mendapat fototerapi dan tambahan asam ursodeoksikolat.
Metode: Penelitian ini merupakan uji klinis, terandomisasi, tersamar ganda, dengan kontrol plasebo, mencakup neonatus usia gestasi <37 minggu, mengalami hiperbilirubinemia yang terindikasi fototerapi, dirawat di unit perinatologi Rumah Sakit Dr. Cipto Mangunkusumo sejak bulan Februari-Mei 2024, sudah mendapat minum per oral sebanyak 10 mL/kgBB/hari. Grafik American Academy of Pediatrics (AAP) tahun 2022 dan The Royal Women’s Hospital (RWH) tahun 2020 digunakan untuk menentukan batas fototerapi. Total 40 subjek yang dibagi menjadi 2 kelompok. Kelompok intervensi (n=20) mendapat asam ursodeoksikolat 10 mg/kgBB/hari (puyer) dibagi 2 dosis sebagai terapi tambahan fototerapi, sedangkan kelompok kontrol (n=20) hanya mendapat fototerapi. Kadar bilirubin total diukur setiap 24 jam dengan serum dan/atau Bilistick. Hasil: Rerata durasi fototerapi adalah 24 jam pada kelompok intervensi, 36 jam pada kelompok kontrol (p=0,289). Di kelompok intervensi, penurunan kadar bilirubin setelah 24 jam fototerapi 4,15 ± 5,50 mg/dL (p=0,758), setelah 48 jam fototerapi 4,99 ± 7,66 mg/dL (p=0,664). Kadar bilirubin setelah 48 jam fototerapi lebih rendah bermakna pada neonatus yang mendapat asam ursodeoksikolat (p=0,020).
Kesimpulan: Penambahan asam ursodeoksikolat tidak mengurangi durasi fototerapi maupun mempercepat penurunan kadar bilirubin pada neonatus kurang bulan dengan hiperbilirubinemia yang mendapat fototerapi setelah 24 jam dan 48 jam. Penelitian lanjutan perlu dilakukan sampai jumlah sampel terpenuhi.
.....Background: Preterm neonates have a 12.5 times higher risk of developing hyperbilirubinemia compared to full-term neonates, with 54% requiring phototherapy. Hyperbilirubinemia can lead to neurotoxicity and even death, while phototherapy can cause several complications. Adjuvant therapy, such as ursodeoxycholic acid, is needed to increase bilirubin clearance and reduce the duration of phototherapy. Currently, there is no available data on the effect of adding ursodeoxycholic acid on the duration of phototherapy in preterm neonates with hyperbilirubinemia.
Objective: This study aims to determine the duration of phototherapy and the reduction of bilirubin levels in preterm neonates who receive phototherapy and additional ursodeoxycholic acid.
Method: This study is a randomized, double-blind, placebo-controlled clinical trial, involving neonates with

a gestational age of less than 37 weeks who have hyperbilirubinemia requiring phototherapy, treated in the perinatology unit of Dr. Cipto Mangunkusumo Hospital from February to May 2024, and who have been fed orally at least 10 mL/kgBW/day. The 2022 American Academy of Pediatrics (AAP) and 2020 The Royal Women's Hospital (RWH) charts were used to determine the phototherapy threshold. A total of 40 subjects were divided into 2 groups. The intervention group (n=20) received 10 mg/kgBW/day of ursodeoxycholic acid (powder) divided into 2 doses as an additional phototherapy treatment, while the control group (n=20) received only phototherapy. Total bilirubin levels were measured every 24 hours using serum and/or Bilistick.

Results: The average duration of phototherapy was 24 hours in the intervention group and 36 hours in the control group (p=0.289). In the intervention group, the reduction in bilirubin levels after 24 hours of phototherapy was 4.15 ± 5.50 mg/dL (p=0.758), and after 48 hours of phototherapy was 4.99 ± 7.66 mg/dL (p=0.664). Bilirubin levels were significantly lower after 48 hours of phototherapy in neonates who received ursodeoxycholic acid (p=0.020).

Conclusion: The addition of ursodeoxycholic acid did not reduce the duration of phototherapy nor accelerate the decrease of bilirubin levels in preterm neonates with hyperbilirubinemia who received phototherapy after 24 and 48 hours. Further research needs to be conducted until the sample size is sufficient.