Analisis Kadar Semaphorin-3B dan Cullin-1 serta Protein terkait Kaskade Hantaran Sinyalnya pada Patologi Preeklamsia Berdasarkan Perbedaan Usia Kehamilan saat Persalinan = Analysis of Semaphorin-3B, Cullin-1, and Protein Related to the Signal Transduction Cascade in Pathology of Preeclampsia Based on Diffrences in Gestational Ages at Delivery

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Abstrak

Latar belakang: Semaphorin-3B (SEMA3B) sebagai faktor antiangiogenik dan Cullin-1 (CUL1) sebagai faktor proangiogenik merupakan contoh dua protein yang bekerja secara antagonis dalam invasi trofoblas, yang bila terjadi ketidakseimbangan akan menyebabkan preeklamsia (PE). VEGF, MMP9, E-cadherin, p21, dan CASP3 merupakan kandidat protein terkait kaskade hantaran sinyal SEMA3B dan CUL1. Tujuan umum penelitian ini adalah untuk menganalisis kadar SEMA3B dan CUL1, serta kandidat protein terkait kaskade hantaran sinyalnya pada patologi PE berdasarkan perbedaan usia kehamilan saat persalinan.
Metode: Penelitian diadakan di RS Cipto Mangunkusumo dan RS Budi Kemuliaan dari April 2017-April 2018. Studi potong lintang dengan observasi analitik dilakukan untuk mengukur kadar SEMA3B dan CUL1 dan kandidat protein terkait kaskade hantaran sinyalnya dalam plasenta, serta kadar SEMA3B dan CUL1 dalam serum ibu pada 70 pasien PE berdasarkan dua kelompok usia kehamilan saat persalinan: <34 minggu dan 34 minggu. Pemeriksaan dilakukan di Laboratorium Terpadu Fakultas Kedokteran Universitas Indonesia.
Hasil: Kadar SEMA3B, CUL1, VEGF, dan E-cadherin secara bermakna lebih rendah pada kelompok usia kehamilan <34 minggu. Pada kelompok usia kehamilan <34 minggu: terdapat korelasi positif antara usia kehamilan dengan SEMA3B, CUL1, dan protein terkait kaskade hantaran sinyalnya; terdapat korelasi positif antara SEMA3B dengan VEGF dan p21; terdapat korelasi positif antara CUL1 dengan VEGF, MMP9, E-cadherin, p21, dan CASP3; dan korelasi negatif antara rasio p21/CUL1 dengan usia kehamilan. Pada kelompok usia kehamilan 34 minggu: terdapat korelasi positif antara SEMA3B dalam plasenta dengan SEMA3B dalam serum ibu; tidak ada korelasi SEMA3B dengan kandidat protein terkait kaskade hantaran sinyalnya; terdapat korelasi positif antara CUL1 dengan MMP9, E-cadherin, p21, dan CASP3. Kadar proangiogenik CUL1 dan VEGF yang rendah rendah dan ratio p21/CUL1 yang tinggi secara bermakna berhubungan dengan usia kehamilan <34 minggu saat persalinan. Analisis multivariat menunjukkan kadar CUL1 yang rendah meningkatkan risiko melahirkan sebesar empat kali lebih besar pada usia kehamilan <34 minggu dibandingkan usia kehamilan 34 minggu.
Kesimpulan: Pada PE usia kehamilan <34 minggu saat persalinan, gambaran patologi PE lebih berat, kadar SEMA3B yang lebih rendah, serta kadar CUL1 yang lebih rendah memiliki risiko empat kali lebih besar terjadi persalinan dibandingkan usia kehamilan 34 minggu saat persalinan.
.....Background: Semaphorin-3B (SEMA3B) as an antiangiogenic factor and Cullin-1 (CUL1) as a proangiogenic factor are examples of two proteins that work antagonistically in trophoblast invasion, which will cause preeclampsia (PE) if an imbalance occurs. VEGF, MMP9, E-cadherin, p21, and CASP3 are protein candidates related to the signal transduction cascade of SEMA3B and CUL1. The aim of this study

was to analyze SEMA3B and CUL1 levels, as well as protein candidates related to the signal transduction cascade in pathology of PE based on differences in gestational age at delivery.
Methods: The study was conducted at Cipto Mangunkusumo Hospital and Budi Kemuliaan Hospital during April 2017 until April 2018. In this cross-sectional study SEMA3B, CUL1, and protein candidates related to the signal transduction cascade (VEGF, MMP9, E-cadherin, p21, CASP3) were measured in the placenta, as well as SEMA3B and CUL1 levels in maternal serum in 70 PE patients in two gestational age at delivery groups: <34 weeks and 34 weeks. Measurements were conducted at Integrated Laboratory of Faculty of Medicine Universitas Indonesia.
Results: Levels of SEMA3B, CUL1, VEGF, and E-cadherin were significantly lower in the gestational age group of <34 weeks compared to 34 weeks. In the gestational age group of <34 weeks: there were positive correlation between age gestational age and SEMA3B, CUL1, protein candidates related to their signal transduction cascade; there were positive correlations between SEMA3B and VEGF, p21; there were positive correlations between CUL1 and MMP9, E-cadherin, p21, CASP3; there were negative correlation between p21/CUL1 ratio and gestational age. In the gestational age group of 34 weeks: there were positive correlation between SEMA3B in placenta and SEMA3B in maternal serum; there were positive correlations between CUL1 and MMP9, Ecadherin, p21, CASP3; there were no correlation between SEMA3B and candidate protein related to the signal transduction cascade. Significantly, low level of proangiogenic CUL1 and VEGF, and high ratio p21/CUL1 were associated with <34 weeks of gestational age at delivery. Multivariate analysis showed that at <34 weeks of gestational age, low levels of CUL1 increased the risk of giving birth by four times greater than at 34 weeks of gestational age.
Conclusions: In PE at <34 weeks of gestation age at delivery, pathology of PE was worse, level of SEMA3B was lower, and lower level of CUL1 had four times greater risk of labor than at 34 weeks of gestational age at delivery.