Peran polimorfisme toll like receptor 2 dan toll interacting protein terhadap kejadian sepsis dan respons imun pada anak di bawah 1 tahun yang menjalani operasi jantung terbuka = Role of toll like receptor 2 and toll interacting protein polymorphism in the development of sepsis and immunology response in children less than 1 year old undergoing open heart surgery

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Abstrak

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Latar Belakang: Pada anak dengan penyakit jantung bawaan (PJB) yang menjalani operasi jantung terbuka, sepsis merupakan salah satu komplikasi pascaoperasi. Lama prosedur pintas jantung paru, usia, status gizi, timektomi, dan variasi genetik, seperti polimorfisme toll-like receptor (TLR) 2 dan tollinteracting protein (TOLLIP) dapat memengaruhi respons imun. Informasi mengenai peran faktor tersebut terhadap kejadian sepsis dan respons imun pascaoperasi jantung terbuka masih terbatas.
Tujuan: Mengetahui peran polimorfisme TLR2, TOLLIP, dan faktor lainnya terhadap kejadian sepsis dan respons imun pascaoperasi jantung terbuka untuk memperoleh strategi paling tepat dalam penanganan kasus bedah jantung pada anak.
Metodologi: Studi longitudinal dengan non-probability consecutive sampling dilakukan pada anak <1 tahun yang menjalani operasi jantung terbuka. Pemeriksaan polimorfisme TLR2 Arg677Trp, TLR2 N199N, TOLLIP rs5743867, sel CD4 dan CD8 yang menyekresikan IFN-γ intraselular, sel Dendritik yang mengekspresikan TLR2, dan sel NK. Pasien menjalani operasi jantung terbuka. Setelah operasi, pasien dimonitor untuk menilai sepsis dan respons imun pascaoperasi.
Hasil: Dari 108 subjek yang terlibat, 21,3% diantaranya mengalami sepsis. Seluruh subjek adalah mutan TLR2 Arg677Trp, 92,6% pasien adalah mutan TLR2 N199N, dan 52,8% pasien adalah mutan TOLLIP rs5743867. Polimorfisme TLR2 N199N dan timektomi total tidak diikutkan dalam model analisis multivariat. Polimorfisme TOLLIP rs5743867 (p = 0,358) menurunkan resiko sepsis, lama prosedur pintas jantung paru ≥90 menit (p = 0,002), usia neonatus (p = 0,032), dan gizi buruk (p = 0,558) meningkatkan risiko sepsis pascaoperasi. Jumlah respons imun bervariasi antara kategori, namun secara umum komponen respons imun lebih rendah pada pasien yang mengalami sepsis dibanding pada pasien yang tidak mengalami sepsis.
Simpulan: Lama prosedur pintas jantung paru dan usia neonatus secara signifikan memengaruhi risiko dan kecepatan sepsis pascaoperasi. Peran polimorfisme TLR2

N199N dan TOLLIP rs5743867 terhadap kejadian sepsis dan respons imun pascaoperasi memerlukan studi komprehensif lebih lanjut.
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ABSTRACT
Background: Sepsis is one of the complications in children with congenital heart defect who underwent open heart surgery. Cardiopulmonary bypass (CPB) time, age, nutritional status, thymectomy, and genetic variants, such as toll-like receptor (TLR) 2 and toll-interacting protein (TOLLIP) polymorphism affect immune response. Information regarding those factors in the development of sepsis and immune response after open heart surgery is still limited.
Objectives: To understand the role of TLR 2 and TOLLIP polymorphism, as well as other risk factors, in the development of sepsis and immune response following open heart surgery to develop the best strategy in open heart surgery in children.
Methods: Longitudinal study with consecutive sampling were done in children <1 year old who underwent open heart surgery. Blood sample was obtained to check for TLR2 Arg677Trp polymorphism, TLR2 N199N polymorphism, TOLLIP rs5743867 polymorphism, the numbers of intracellular interferon γ CD4 and CD8, TLR2 expression in Dendritic cells, and NK cells. Patient then underwent open heart surgery. Thymectomy was done as indicated and CPB time was recorded. After surgery, patient was monitored for signs of sepsis and immune response was checked.
Results: Out of 108 patients involved in this study, 21.3% developed postoperative sepsis. TLR2 Arg677Trp polymorphism was found in all patients, TLR2 N199N polymorphism was found in 92.6% of the patients, and TOLLIP rs5743867 polymorphism was found in 52.8% of the patients. TLR2 N199N polymorphism and thymectomy were not included in multivariate analysis. TOLLIP rs5743867 polymorphism (p = 0.358) reduced the risk of sepsis, CPB time ≥90 menit (p = 0.002), neonates (p = 0.032), and severe malnutrition (p = 0.558) increased the risk of postoperative sepsis. Immune response?s counts vary in each category, but were generally lower in patients who developed postoperative sepsis.
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