Peran prostaglandin E2, vascular endothelial growth factor immature platelet fraction dan efek pemberian ibuprofen oral pada duktus arteriosus paten neonatus cukup bulan = The Role of prostaglandin vascular endothelial growth factor immature platelet fraction and efficacy of oral ibuprofen in patent ductus arteriosus of full term neonates

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Abstrak

Latar belakang: Morbiditas akibat duktus arteriosus paten (DAP) pada neonatus cukup bulan (NCB) cukup tinggi. Peran prostaglandin E2 (PGE2), trombosit (immature platelet fraction, IPF), dan vascular endothelial growth factor (VEGF) pada penutupan DA secara fungsional dan anatomis pada NCB belum banyak diteliti. Patofisiologi terjadinya DAP dapat memengaruhi tata laksana farmakologi dini yang belum terstandardisasi pada NCB. Penggunaan obat antiinflamasi nonsteroid seperti ibuprofen dimungkinkan dapat menghambat jalur sintesis prostaglandin dengan efek samping minimal.

Tujuan: Mengkaji peran prostaglandin E2, VEGF, IPF, dan efek pemberian ibuprofen oral dalam proses penutupan DA pada NCB.

Metode: Penelitian dilakukan di rumah sakit (RS) Sanglah Denpasar, RS Prima Medika Denpasar, dan RS Umum Daerah Wangaya Denpasar, dalam periode Maret sampai Agustus 2015. Penelitian terdiri dari 2 desain, pertama desain potong lintang pada pasien dengan DAP dan tanpa DAP secara consecutive sampling dan desain kedua uji klinis acak terkontrol ganda pada pasien DAP usia ≥ 48 jam. Pasien dengan DAP kemudian dimasukkan dalam uji klinis, dilakukan randomisasi untuk diberikan perlakuan ibuprofen oral dosis hari pertama 10 mg/kg, hari kedua dan ketiga 5 mg/kg atau plasebo. Pemantauan hemodinamik dan efek samping obat dilakukan selama pemberian perlakuan. Pemeriksaan ekokardiografi, PGE2, VEGF, IPF, dan kreatinin dilakukan pada hari pertama dan keempat pascapemberian perlakuan.

Hasil: Terdapat 64 subjek yang diteliti pada desain pertama dan 32 subjek pada desain kedua. Rerata kadar PGE2 lebih tinggi pada kelompok dengan DAP dibanding tanpa DAP, sedangkan rerata kadar VEGF dan IPF tidak berbeda. Ibuprofen oral tidak terbukti menurunkan diameter DA pascaperlakuan, tidak terdapat perbedaan rerata diameter pada kedua kelompok. Terdapat hubungan positif sedang terhadap perubahan kadar PGE2 dengan perubahan diameter DAP pascaperlakuan. Tidak terdapat perubahan hemodinamik atau efek samping akibat pemberian ibuprofen oral atau plasebo pada NCB dengan DAP.

Simpulan: Tingginya kadar PGE2 terbukti berperan dalam patensi DA pada NCB. Ibuprofen oral dosis 10 - 5 - 5 mg/kgBB tidak mengecilkan diameter DAP.
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Background: Serious morbidity impact due to patent ductus arteriosus (PDA) in full-term neonates remains high. The functional role of prostaglandin E2 (PGE2), platelet (immature platelet fraction, IPF), and

vascular endothelial growth factor (VEGF) has not been studied in the closure mechanism of ductus arteriosus (DA). Understanding of pathophysiology of PDA may influence early pharmacological treatments, which have not been standardized in full-term neonates. The use of non-steroidal anti-inflammatory drugs such as ibuprofen can be beneficial as a pharmacological agent in enhancing the closure of PDA with minimal adverse effects.

Objectives: To evaluate the role of prostaglandin E2, VEGF, IPF, and the effect of oral ibuprofen in the process of DA closure in full-term neonates.

Methods: This study was conducted in Sanglah General Hospital, Prima Medika Hospital, and Wangaya Hospital Denpasar. The study consisted of two designs, the first was cross-sectional design in subjects with and without PDA using consecutive sampling and the second was double blind randomized controlled trial in full-term infant aged ≥ 48 hours. Subjects with PDA were randomized to oral ibuprofen and placebo administration, in which ibuprofen was given consecutively 10 - 5 - 5 mg/kg. All subjects underwent echocardiography, PGE2, VEGF, and IPF assays. Hemodynamics monitoring was evaluated during trial and adverse effect due to ibuprofen was recorded by measuring urine volume and plasma creatinine level.

Results: From March to August 2015, there were 64 subjects recruited for the first design and 32 subjects in the second design. The mean level of PGE2 was higher significantly in the group with PDA than non PDA group, while the mean levels of VEGF and IPF showed no difference. In the second design, oral ibuprofen showed no effect in reducing DA diameter after treatment. There were no differences in mean diameter of DA in both groups before and after treatments. There was moderate positive relationship between levels of PGE2 and the change of PDA diameter. There were neither hemodynamic changes nor adverse effect due to the administration of oral ibuprofen or placebo.

Conclusions: A high level of PGE2 appears to play a pivotal role in DA patency of full-term neonates. Administration of oral ibuprofen in 10 - 5 - 5 mg/kg schedule could not induce PDA closure in full-term neonates.