Perbandingan efektivitas Allopurinol dan Metilprednisolon dalam mengurangi cedera reperfusi pada bedah pintas arteri koroner : kajian terhadap kadar Malondialdehyde, skor inotropik dan vasoaktif, dan kejadian atrial fibrilasi pascabedah = Comparison of the effectiveness of Allopurinol and Methylprednisolone in reducing reperfusion injury in coronary artery bypass surgery: study of Malondialdehyde levels, Vasoactive-Inotropic Score, and the occurrence of postoperative atrial fibrilation

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Abstrak

Latar Belakang: Cedera reperfusi akibat dilepaskannya reactive oxygen species(ROS) saat penggunaan Cardiopulmonary bypass(CPB) dan kembalinya mengalir darah yang kaya oksigen pada miokard yang iskemia, dapat menyebabkan kerusakan miokard. Allopurinol sebagai penghambat xanthine oksidase, telah diteliti sebelumnya mengenai efektivitas dalam mengurangi cedera reperfusi pada bedah jantung terbuka yang belum menunjukkan hasil yang konklusif, meskipun pada beberapa penelitian memberikan hasil yang cukup baik pada pemulihan dari stunningmiokard, biomarker cedera reperfusi maupun kejadian atrial fibrilasi pascabedah (AFPB). Metilprednisolon juga dipakai untuk mengurangi efek inflamasi dan cedera reperfusi pada pasien bedah jantung terbuka karena perannya dalam menghambat secara indirek pengaktifan enzim NADPH oksidase.Tujuan penelitianini adalah untuk membandingkan efektifitas pemberian allopurinol peroral 600 mg pada malam hari dan 1 jam sebelum pembedahan dengan metilprednisolon intravena 15 mg/kgbb saat induksi anestesi dalam mengurangi cedera reperfusi pada bedah pintas arteri koroner.

Metode: Telah dilakukan penelitian uji klinis acak tersamar ganda pada 42 pasien yang menjalani bedah pintas arteri koroner menggunakan CPB antara bulan Oktober 2019 hingga Maret 2020, yang dialokasikan ke dalam kelompok allopurinol atau kelompok metilprednisolon.Pemeriksaan biomarker cedera reperfusi dilakukan dengan pemeriksaan sampel darah malondialdehyde(MDA) yang dilakukan sesaat setelah pemasangan kateter vena sentral (basal) dan 5 menit setelah klem jepit aorta dilepas (pascareperfusi). Pemeriksaan MDA dilakukan dengan metode ELISA. Penilaian skor inotropik dan vasoaktif (SIV) dilakukan pada 24 jam pertama perawatan pascabedah. Sedangkan penilaian kejadian atrial fibrilasi pascabedah dilakukan selama 48 jam pertama pascabedah. Data yang diperoleh dianalisis dengan uji statistik yang sesuai dengan piranti lunak program SPSS 21. Uji hipotesis pada variabel kadar MDA akan menggunakan uji T tes tidak berpasangan bila sebaran data normal. Pada variabel skor inotropik dan vasoaktif akan menggunakan uji T test tidak berpasangan (bila sebaran data normal) atau dengan uji mann whitney(bila sebaran data tidak normal). Dan uji hipotesis untuk variabel kejadian AFPB menggunakan uji chi-squared(bila syarat x2terpenuhi) atau dengan uji fisher(bila syarat x2tidak terpenuhi).

Hasil : 42 pasien yang menjalani bedah pintas arteri koroner yang memenuhi kriteria penerimaan, 40 pasien dianalisis karena 2 pasien meninggal sebelum 48 jam pertama pascabedah. Karakteristik demografi dan kadar MDA basal seimbang pada kedua kelompok. Peningkatan kadar MDA pascareperfusi lebih rendah pada pemberian allopurinol, namun secara statistik tidak berbeda bermakna (p=0,379). Nilai SIV

pascabedah pada pemberian allopurinol secara statistik lebih rendah bermakna (median 6 vs 22, p=0,009). Kejadian AFPB pada kedua kelompok menunjukkan perbedaan yang tidak bermakna secara statistik (p=0,231).
Simpulan : Allopurinol tidak lebih efektif daripada metilprednisolon dalam upaya mengurangi cedera reperfusi pada bedah pintas arteri koroner.
.....Background: Reperfusion injury due to the release of reactive oxygen species (ROS) when using cardiopulmonary bypass (CPB) and the return of oxygen-rich blood flow to ischemic myocardium after the release of aortic clamps, can cause myocardial damage. Allopurinol as an inhibitor of xanthine oxidase, has been studied previously about its effectiveness in reducing reperfusion injury in open heart surgery which shows inconclusive results, although in some studies it has given quite good results in recovery from myocardial stunning, biomarkers of reperfusion injuries and postoperative atrial fibrilation (POAF). Methylprednisolone is also used to reduce the effects of inflammation and reperfusion injury in open heart surgery patients because of its role in indirectly inhibiting the activation of the enzyme NADPH oxidase. The aim of this study was to compare the effectiveness of oral administration of allopurinol 600 mg at night and 1 hour before surgery with 15 mg/kg intravenous methylprednisolone during anesthesia induction in reducing reperfusion injury in coronary artery bypass surgery.

Methods: A double-blind randomized clinical trial study was conducted on 42 patients undergoing coronary artery bypass surgery using CPB between October 2019 and March 2020, which was allocated to the allopurinol group or the methylprednisolone group. Examination of biomarkers of reperfusion injury is carried out by examination of a blood sample of malondialdehyde (MDA) which is performed shortly after the installation of a central venous catheter (basal) and 5 minutes after the aortic clamp are removed (post-reperfusion). MDA examination is done by the ELISA method. Assessment of vasoactive-inotropic scores (VIS) was carried out in the first 24 hours of post-surgical treatment. While the assessment of the incidence of POAF was performed during the first 48 hours after surgery. The data obtained were analyzed by the appropriate statistical tests using SPSS 21 software program. Hypothesis testing on MDA variables will use the T test unpaired if the data distribution is normal. In the VIS variables will use the T test unpaired (if the data distribution is normal) or with the Mann Whitney test (if the data distribution is not normal). And hypothesis testing for POAF variables will use the chi-square test (if the x2 requirement are met) or with the fisher test (if the x2requirements are not met).
Results:42 patients who underwent coronary artery bypass surgery who met the admission criteria, 40 patients were analyzed because 2 patients died before the first 48 hours after surgery. Demographic characteristics and basal MDA levels were balanced in both groups. The increased levels of MDA post-reperfusion were lower in allopurinol administration, but the statistics were not significantly different (p = 0.379). The postoperative VIS value in the administration of allopurinol was significantly lower than in the administration of methylprednisolone (median 6 vs 22, p = 0.009). The incidence of AFPB in the two groups showed no differences were statistically significant (p = 0.231).
Conclusion:Allopurinol is not more effective than methylprednisolone in an effort to reduce reperfusion injury in coronary artery bypass surgery.