Efek doksisiklin terhadap struktur dan fungsi Ventrikel Kiri pada Pasien Infark Miokard Akut dengan Elevasi Segmen ST Pasca Revaskularisasi = Effects of Doxycycline on Left Ventricle Structure and Function in Patients with ST-Elevation Acute Myocardial Infarction After Primary Percutaneous Coronary Intervention

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Abstrak

Latar belakang: Remodeling jantung pasca Infark Miokard Akut (IMA-ST) dipercaya sebagai penyebab masih tingginya angka komplikasi gagal jantung walaupun sudah diberikan terapi standar dan tatalaksana revaskularisasi. Matriks ekstraseluler (EKM) memiliki peranan penting dalam proses remodeling. Nekrosis miokard menyebabkan peningkatan kadar matriks metalloproteinase (MMPs) yang akan mendegradasi EKM. Berbagai studi eksperimental, menunjukkan bahwa inhibisi MMPs memberikan manfaat pada proses remodeling. Doksisiklin merupakan penghambat MMPs poten yang telah memberikan efek menjanjikan terhadap remodeling pada hewan coba dan uji klinis tidak tersamar.
Tujuan: Mengetahui efek doksisiklin terhadap struktur dan fungsi ventrikel sebagai penanda remodeling pada IMA-ST yang telah menjalani IKPP.
Metode: Penelitian ini menggunakan desain uji klinis acak tersamar ganda. Pasien IMAST dengan keterlibatan anterior atau Killip 2-3 dengan onset kurang dari 12 jam yang menjalani IKPP terbagi secara acak pada grup Doksisiklin (2x100 mg tablet selama 7 hari) sebagai terapi tambahan dari standar tatalaksana dan grup kontrol. Pemeriksaan ekokardiografi dasar pada saat awal perawatan segera setelah IKPP. Ekokardiografi evaluasi dilaksanakan pada bulan ke 4.
Hasil: Terdapat 134 subjek yang masuk dalam penelitian ini. Setelah evaluasi lanjutan, terdapat 8 pasien drop out pada masing-masing grup karena meninggal dan lost to follow up 58 subjek masuk dalam Grup Doksisiklin dan 60 subjek Grup Kontrol. Karakteristik demografis dan klinis kedua grup homogen. Parameter ekokardiografi menunjukkan adanya peningkatan Left Ventricle End-Diastolic Volume Index (D LVEDVi) yang lebih rendah dibandingkan grup kontrol (9,2 (-21-45) mL/m2 vs 16 (-13-62) mL/m2, p=0,008). Selain itu, fungsi fraksi ejeksi (DLVEF) mengalami peningkatan pada grup Doksisiklin (2,36 ± 8,5 vs -2,6 ± 8,4; p 0,005). Persentase Adverse Remodeling lebih sedikit pada grup Doksisiklin. Rentang perbaikan Global Longitudinal Strain (DGLS) lebih besar pada grup Doksisiklin, walaupun statistik tidak bermakna. Angka rehospitalisasi tidak berbeda bermakna pada kedua grup.
Kesimpulan: Doksisiklin memberikan efek perbaikan terhadap struktur dan fungsi ventrikel kiri pada pasien IMA-ST yang telah menjalani IKPP
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Background: Cardiac remodeling after acute myocardial infarction with ST elevation

(STEMI) had been proved as the cause of the increased of heart failure complications despite standard therapy and revascularization management. Extra cellular matrix (ECM) has an important role in the remodeling process. Myocardial necrosis causes increased levels of matrix metalloproteinase (MMPs) which will degrade ECM. Various experimental studies, showed that MMPs inhibition provides benefits in the remodeling process. Doxycycline is a potential MMPs inhibitor that has a promising effect on remodeling in experimental animals and clinical trials.
Objective: To determine the effect of doxycycline on the structure and function of ventricles as a remodeling marker in STEMI that had undergone Primary Percutaneous Coronary Intervention (PPCI)
Methods: We conducted a double-blind randomized control trial. Patients with STEMI anterior or with Killip class 2-3 with onset of less than 12 hours undergoing PPCI were randomly assigned to the group that receiving Doxycycline (100 mg b.i.d for 7 days) as adjunctive therapy from standard management and the group without adjunct therapy. An initial echocardiographic examination was done after PPCI. Further evaluation was held in 4 months after PPCI with an echocardiographic examination, which will be compared between the initial examination and the evaluation.
Results: There were 134 subjects included in this study. After further evaluation, there were 8 patients drop out due to death and lost to follow up. Doxycycline group has 58 and 60 subjects in Control group. Demographic and clinical characteristics of both groups are homogeneous. Echocardiographic parameters showed change in Left Ventricle End-Diastolic Volume Index (D LVEDVi) significantly lower in Doxycycline group (9.2 (-21-45) mL/m2 vs. 16 (-13-62) mL/m2, p 0.008). In addition, the change of ejection
fraction (D LVEF) increased in the doxycycline group (2.36 ± 8.5 vs -2.6 ± 8.4, p 0.005).The percentage of Adverse Remodeling is smaller in the Doxycycline group (70% vs 83%) and the range of D Global Longitudinal Strain (DGLS) is greater in Doxycycline group, although both not statistically significant. Rehospitalization was not significantly different between two groups.
Conclusion: Doxycycline had effect in improving structure and function of the left ventricle in STEMI patients who have undergone PPCI