Efek External Counterpulsation (ECP) Terhadap Kadar miR- 92a di Sirkulasi Pasien Angina Refrakter akibat Penyakit Jantung Koroner = External Counterpulsation (ECP) effect on miR-92a circulating level in Refractory Angina Patients due to Coronary Artery Disease

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Abstrak

Latar Belakang : External counterpulsation (ECP) ditunjukkan dapat mengurangi gejala angina dan memperbaiki kualitas hidup pasien penyakit jantung koroner (PJK) dengan angina refrakter. Efek protektif jangka panjang ini dipikirkan merupakan efek dari peningkatan pulsatile shear stress pada endotel vaskular sehingga terjadi perbaikan pada fungsi endotel. Dalam proses ini, sekelompok miRNA berfungsi meregulasi ekspresi gen dan dipengaruhi oleh shear stress, diantaranya adalah miR-92a yang bersifat proatherosklerosis. Tujuan : Mengetahui pengaruh ECP terhadap kadar miR-92a di plasma pada pasien PJK dengan angina refrakter. Metode : Sebanyak 50 pasien PJK dan angina refrakter direkrut dan diacak ke salah satu dari kelompok terapi ECP atau sham (1:1), dan menjalani 35 sesi yang berdurasi 1 jam tiap sesi. Terapi sham serupa dengan terapi ECP namun memberikan tekanan yang jauh lebih rendah. Level miR-92a di sirkulasi diukur di plasma darah sebelum dan sesudah selesai seluruh terapi, kemudian besar perubahan pada kedua kelompok dibandingkan. Hubungan antara keluaran klinis seperti keluhan angina, kapasitas fisik dan ejection fraction (EF) ventrikel kiri dengan kadar miR-92a juga dinilai.
Hasil : miR-92a di plasma meningkat bermakna pada kelompok ECP [+5.1 (+4.2 s.d +6.4) menjadi +5.9 (+4.8 s.d +6.4), p value <0.001] dan sham [+5.2 (+4.1 s.d +9.4) menjadi +5.6 (+4.8 s.d +6.3), p value 0.008]. Besar perubahan dan fold changes cenderung lebih besar pada kelompok ECP namun tidak berbeda bermakna secara statistik dibandingkan kelompok sham. Kadar miR-92a post intervensi berkorelasi signifikan dengan rasio diastolik/sistolik selama terapi dan perbaikan EF pasca intervensi. Selain itu, perubahan miR-92a berkorelasi positif dengan perbaikan kapasitas fisik.
.....Background : Noninvasive modality External counterpulsation (ECP) can improve angina frequency and exercise capacity in refractory angina (RA) patients. The long term benefit is thought to be the result of increase in shear stress on vascular endothelial cells resulting in improvement of endothelial dysfunction. In this process, a group of miRNA regulating gene expression in relation to shear stress is called flow-sensitive miRNA, among them is miR-92a. Aim : To evaluate ECP effect on plasma miR-92a level in RA patients. Method : Fifty subjects with RA were enrolled and randomized to either one of ECP or sham therapy (1:1 randomization). Each therapy session was one hour, for a total of 35 sessions. As a control, sham gave same sensation as ECP but with lower pressure. Plasma miR-92a level was measured before and after therapy and delta changes was compared between group. Secondary clinical outcome such as angina class, physical capacity and left ventricle Ejection Fraction (EF) were also measured and correlated with miR-92a level. Result : Plasma miR-92a level increased in both treatment groups [in ECP group +5.1 (+4.2 to +6.4) to +5.9 (+4.8 to +6.4), p value <0.001, in sham group +5.2 (4.+1 to 9.4) to +5.6 (+4.8 to +6.3), p value =0.008]. There was higher delta increase and fold changes in ECP group, however the difference did not reach statistically significant. miR-92a level post intervention correlated significantly with Diastolic/Systolic ratio during intervention and improvement in ejection fraction (EF) post intervention. Moreover, changes in miR-

92a correlated positively with improvement in physical capacity. Conclusion : ECP did not cause significant different increase of miR-92a compared to sham.