

# Efikasi Atorvastatin 80 MG Dalam Menghambat Edema Miokardium: Kajian Regulasi Folistatin-Like Protein 1 Pada Pasien Bedah Pintas Arteri Koroner = Efficacy of 80 mg Atorvastatin on Myocardial edema Following Coronary Artery Bypass Surgery in Relation with Follistatin-Like Protein-1

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## Abstrak

Edema miokardium dapat menyebabkan disfungsi miokardium. Pada operasi bedah pintas arteri koroner (BPAK), proses inflamasi dan reperfusion injury menyebabkan edema miokardium. Berbagai cara telah dilakukan untuk menghambat edema miokardium namun belum ada yang terbukti efektif. Statin merupakan obat yang memiliki efek pleiotropik sebagai anti inflamasi. Penelitian pada subjek hewan menunjukkan bahwa statin dapat mengurangi edema miokardium. Sebagai respons terhadap kondisi stress, jantung mengeluarkan berbagai sitokin seperti follistatin-like 1 (FSTL1). FSTL1 berperan dalam proses edema miokardium. Untuk mengurangi edema miokardium pasien BPAK dilakukan pemberian Atorvastatin 80 mg selama 2 minggu sebelum operasi.

Penelitian dilakukan secara uji klinis tersamar ganda pada pasien berusia 40–65 tahun yang menjalani operasi BPAK. Dilakukan dari Februari 2017 hingga Maret 2018 di rumah sakit jantung dan pembukuh darah Harapan Kita. Subjek penelitian diacak ke dalam dua kelompok, kelompok Atorvastatin dosis 80 mg dan Atorvastatin dosis 10 mg. Pemeriksaan edema miokardium dilakukan dengan MRI pada hari ke-6 pascaoperasi. Pemeriksaan FSTL1, PKA, PKB dan hs-CRP diambil dari plasma darah 1 hari sebelum operasi, hari ke-1 dan hari ke-6 pasca operasi. Parameter MRI yang dinilai adalah nilai T2 relaxation time. Sebanyak 20 pasien termasuk dalam kelompok Atorvastatin 80 mg dan 20 pasien dalam kelompok Atorvastatin 10 mg. Terdapat 7 subjek yang drop out. Pemeriksaan MRI mendapatkan nilai T2 relaxation time yang lebih rendah pada kelompok Atorvastatin 80 mg (50,11 ms vs. 59,03 ms,  $p = 0,01$ ). Tidak didapatkan korelasi yang bermakna antara FSTL1 dengan T2 relaxation time. Pemeriksaan FSTL1, PKA dan PKB tidak berbeda secara bermakna antara kedua kelompok sedangkan kadar hs-CRP lebih rendah serta bermakna secara statistik pada kelompok Atorvastatin 80 mg.

Simpulan: Pemberian Atorvastatin dosis 80 mg dapat menurunkan kejadian edema miokardium pasca BPAK dan menunjukkan efek antiinflamasi yang lebih baik dari pada Atorvastatin 10 mg.

.....Myocardial edema can cause myocardial dysfunction in many pathological states. During coronary artery bypass surgery (CABG), there is inflammatory system activation as well as reperfusion injury which can produce myocardial edema. Many efforts has been applied in order to prevent those process but none has proven effective. Statin is a drug with many pleiotropic effects as anti inflammatory. Animal study revealed that statin can decrease myocardial edema, In response to stress conditions, heart produced many cytokines, such as follistatin-like 1 (FSTL1). FSTL1 has a principal role in reducing myocardial edema. This study tried to find the effectiveness of Atorvastatin 80 mg, also known as high dose statin, in decreasing myocardial edema after CABG surgery.

Double blinded clinical trial was performed, in patients 40–65 years of age who underwent CABG surgery. This study was conducted from February 2017 until March 2018 at National Cardiovascular Centre Harapan

Kita. Subjects were randomized and divided in two groups, high dose Atorvastatin (80 mg) and low dose atorvastatin (10 mg). Myocardial edema evaluation using magnetic resonance imaging (MRI) was done in day-6 after surgery. FSTL1, PKA, PKB, and hs-CRP were evaluated before surgery, day-1 after surgery, and day-6 after surgery. T2 relaxation time was used as the MRI parameter of myocardial edema.

There were 20 patients treated with Atorvastatin 80 mg and 20 patients at Atorvastatin 10 mg. There were 7 subject who dropped out. MRI evaluation found lower T2 relaxation time in high dose group (50,11ms vs. 59,03 ms,  $p = 0,01$ ). There was no significant correlation between FSTL1 and T2 relaxation time. FTSL1, PKA and PKB in both groups were not statistically different but hs-CRP value was statistically lower in high dose group.

Conclusion: Atorvastatin 80 mg can decrease the incidence of myocardial edema after CABG surgery and shows a better anti-inflammatory effect than Atorvastatin 10 mg. The correlation between statin and FSTL1 in term of myocardial edema has not been defined yet.