Atorvastatin memodulasi ekspresi gen tumor necrosis factor interferon- dan interleukin-4 pada jaringan katup dan appendiks atrium kiri penderita penyakit jantung rematik = Atorvastatin modulating gene expression of tumor necrosis factor interferon- and interleukin-4 in cardiac valves and left atrial appendage of rheumatic heart disease

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Abstrak

[Latar Belakang : Penyakit jantung rematik (PJR) merupakan komplikasi paling serius dari demam rematik (DR). Penelitian terbaru telah menyoroti adanya inflamasi kronis yang ditandai tingginya kadar CRP, keterlibatan limfosit T serta sitokin inflamasi seperti TNF-, IFN- dan IL-4. Obat yang memiliki efek anti inflamasi adalah penyekat HMG KoA reduktase, yang mampu menurunkan kadar TNF- dan IFN- serta meningkatkan kadar IL-4.
Tujuan : Untuk membuktikan efek atorvastatin dalam menurunkan ekspresi gen TNF- dan IFN-, serta meningkatkan ekspresi gen IL-4. Menilai hubungan antara penurunan ekspresi gen TNF- dan IFN- dengan peningkatan ekspresi gen IL-4.
Metode : Penelitian ini merupakan studi eksperimental. Pasien dengan penyakit katup jantung dengan etiologi rematik yang akan menjalani tindakan perbaikan/penggantian katup diberikan perlakuan atorvastatin/plasebo 6 minggu sebelum operasi, dilakukan pemeriksaan ekspresi gen TNF-, IFN- dan IL-4 pada jaringan katup dan Appendiks Atrium Kiri (AAK) yang dieksisi saat operasi, menggunakan alat Real Time PCR.
Hasil : Dari 53 responden, dengan rerata usia 35 tahun, 70% di antaranya adalah perempuan. 25 responden mendapatkan atorvastatin. Kelompok Atorvastatin memiliki ekspresi gen TNF- di AAK yang lebih rendah dengan p 0,005 (95% CI 0,05-0,58), setelah disesuaikan dengan jenis kelamin dan fraksi ejeksi. Namun tidak terdapat perbedaan yang bermakna secara statistik dari ekspresi gen IL-4 dan IFN- di AAK antara kedua kelompok responden, begitu pula dengan seluruh sitokin pada jaringan katup.
Kesimpulan : Pemberian atorvastatin dapat mengurangi inflamasi pada jaringan appendiks atrium kiri penderita penyakit jantung rematik yang ditandai dengan rendahnya ekspresi gen TNF- namun tidak terbukti mengurangi inflamasi pada jaringan katup. Terdapat hubungan antara penurunan ekspresi gen TNF- dan IFN- dengan peningkatan ekspresi gen IL-4.;Background : Rheumatic Heart Disease is the most troublesome complication of
rheumatic fever. Recent trials emphasized ongoing chronic inflammation represented by CRP, TNF-, IFN- and IL-4,. HMG CoA reductase inhibitor was agent with antiinflamatory effect, suppressing TNF- and IFN- and increasing

IL-4.
Objectives : This study was to prove the effect of atorvastatin in suppressing gene expression of TNF- and IFN-, and also effect of atorvastatin in increasing gene expression of IL-4. Knowing correlation between suppressed TNF- and IFN- gene expression and increased IL-4 gene expression.
Method : This study was designed as an experimental study. Patients with valvular dysfunction due to rheumatic process planned to underwent cardiac valves repair/replacement operation were given atorvastatin/placebo 6 weeks before. Gene expression method was used to check mRNA TNF-, mRNA IFN- and mRNA IL-4 level from excised valves and Left Atrial Appendage (LAA).
Result : 53 patients were enrolled. Proportion of women was 70% and age average was 35 years old. Atorvastatin group had lower gene expression TNF- level in LAA with p 0,005 (95% CI 0,05-0,58), after adjusted with gender and ejection fraction. But there were no differences of IL-4 and IFN- gene expression in LAA, either all inflammation cytokines in valves.
Conclusions : Atorvastatin reduced inflammation in LAA patients with Rheumatic Heart Disease by suppressing TNF- gene expression but didn’t proved reducing inflammation in cardiac valves. There was correlation between supressed gene expression of TNF- and IFN- with increased gene expression of IL-4 level., Background : Rheumatic Heart Disease is the most troublesome complication of rheumatic fever. Recent trials emphasized ongoing chronic inflammation represented by CRP, TNF-α, IFN-γ and IL-4,. HMG CoA reductase inhibitor was agent with antiinflamatory effect, suppressing TNF-α and IFN-γ and increasing IL-4.
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