

Hipertrofi ventrikel akibat induksi hipoksia sistemik kronik, analisis ekspresi protein apelin-13 dan BNP-45 serta hubungannya dengan stres oksidatif. = Ventricular hypertrophy due to induction of chronic systemic hypoxia, analysis of apelin-13 and BNP-45 protein expression and its relation to oxidative stress.

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Abstrak

**ABSTRAK**

Latar Belakang: Hipertrofi jantung dapat timbul akibat stres patologis misal hipoksia yang merupakan respon jantung sebagai mekanisme homeostatis yang diperlukan untuk menormalkan stres dinding ventrikel kiri dan mempertahankan curah jantung. Hipoksia sistemik kronik merupakan stres lingkungan yang berat. Respon spesifik jantung terhadap stres jantung terlihat pada peningkatan kadar peptida di dalam plasma, yang membantu jantung dalam menghadapi beban yang meningkat. Menurut sejumlah peneliti, kadar Apelin berhubungan erat dengan disfungsi ventrikel. Apelin merupakan preproprotein dengan 77 asam amino yang disekresikan dari keluarga adipokine, berperan dalam mempertahankan performa jantung pada beban tekanan kronik. Pada tingkat molekular, respons adaptasi diperantarai oleh perubahan ekspresi gen. Tujuan penelitian: Menganalisis pola ekspresi gen Apelin dan gen BNP pada hipertrofi ventrikel akibat induksi hipoksia sistemik kronik dengan mengukur konsentrasi Apelin-13 dan konsentrasi BNP-45. Penelitian bersifat eksperimental menggunakan 28 ekor tikus Sprague-Dawley jantan, umur 8-12 minggu yang dibagi dalam 7 kelompok n=4 ekor/kelompok, terdiri dari kelompok kontrol normoksia, O<sub>2</sub> atmosfer dan kelompok perlakuan hipoksia dalam sungkuphipoksia, 8 O<sub>2</sub>, masing-masing selama 6 jam, 1, 3, 5, 7 dan 14 hari. Parameter stres oksidatif akibat hipoksia jantung, dilakukan dengan pengukuran kadar malondialdehid MDA dan histopatologi dengan pewarnaan HE. Selain itu juga dilakukan pengukuran protein Apelin-13 dan BNP-45 menggunakan metoda ELISA dan pengukuran ekspresi relatif mRNA Apelin dan BNP-45 jantung, menggunakan real time RT-PCR kuantitatif dengan rumus Livak. Hasil penelitian: ekspresi relatif Apelin-13 di jantung menurun pada awal hipoksia dan kemudian meningkat mulai hari ke-3 sampai hari ke-14. Peningkatan kadar MDA yang signifikan terjadi sejak hipoksia 7 hari. Korelasi MDA terhadap peningkatan ekspresi relatif Apelin adalah kuat  $r=0.750$  dan signifikan  $p=0.000$ . Korelasi BNP-45 terhadap Apelin-13 adalah sangat kuat  $r=0.943$  dan signifikan  $p=0.000$ . Dapat disimpulkan bahwa adanya peningkatan MDA, peningkatan ekspresi relatif dan protein Apelin-13 dan peningkatan ekspresi relatif dan protein BNP-45 pada jaringan jantung mempunyai korelasi yang signifikan dan kuat, sesuai dengan peningkatan lamanya perlakuan hipoksia.

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**ABSTRACT**

Background: Cardiac hypertrophy can result from pathological stress eg hypoxia as a response to ventricular wall stress and to maintain cardiac output. Chronic systemic hypoxia is a severe environmental stress. During cardiac stress certain peptides are release by the heart into the plasma, which help the heart to compensate the increased myocardial load. According to several authors, apelin levels are increased during cardiac dysfunction. Apelin is a preproprotein with 77 amino acids from adipokine, which contributes to

maintaining cardiac performance at chronic stress loads. At the molecular level, the adaptation response is mediated by changes in gene expression. Objective: To analyze the expression pattern of Apelin-13 and BNP-45 on ventricular hypertrophy due to induction of chronic systemic hypoxia by measuring Apelin-13 and BNP-45 concentrations. The experimental study used 28 male Sprague-Dawley rats, 8-12 weeks old divided into 7 groups 4 per group, consisting of control group normoxia, atmospheric O<sub>2</sub> and 4 hypoxia treatment groups, which underwent systemic hypoxia in hypoxic chamber containing 8 oxygen, respectively for 6 hours, 1, 3, 5, 7 and 14 days. The presence of oxidative stress due to cardiac hypoxia was determined by malondialdehyde MDA and cardiac structural alteration was examined by HE staining. Apelin-13 and BNP-45 proteins were determined using the ELISA method and the relative expression of cardiac Apelin and BNP-45 mRNA were determined using quantitative RT-PCR real time with Livak formula. Results: Relative expression of Apelin-13 in the heart decreased early in hypoxia and then increased from day 3 to day 14. Significant increases in MDA levels occurred after 7 days hypoxia. There was a strong and significant correlation between MDA levels and Apelin relative expression  $r = 0.750$ ,  $p = 0.001$ . Similar results were obtained for of BNP-45 and Apelin-13  $r = 0.943$ ,  $p = 0.001$ . From the results, it can be concluded that during chronic systemic hypoxia there was an increase in oxidative stress, relative expression and Apelin-13 proteins and relative expression and BNP-45 protein of the rat cardiac tissue.