

Ekspresi hypoxia inducible factor-1, mioglobin dan b-type natriuretic peptide-45 pada jantung tikus sebagai respons adaptasi pada paparan hipoksia hipobarik intermiten = The expression of hypoxia inducible factor 1 myoglobin and b type natriuretic peptide 45 in heart rat tissue as adaptive response on intermittent hypobaric hypoxia exposure

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Abstrak

Latar Belakang : Penelitian ini menganalisis respons adaptasi jaringan jantung pada paparan hipoksia hipobarik intermiten (HHI) pada tikus. Faktor transkripsi HIF-1 penting untuk mengatasi keadaan hipoksia, terdiri atas 2 subunit yaitu HIF-1 dan HIF-1 yang dalam keadaan hipoksia membentuk heterodimer dan mengatur ekspresi sejumlah gen target untuk mengatasi keadaan hipoksia. Hipoksia akan menyebabkan jantung mengalami beban yang meningkat berupa hipertrofi ventrikel. Jantung akan mengatasi keadaan tersebut melalui pembentukan Mb dan BNP-45.

Metode : 25 ekor tikus jantan Sprague-Dawley dibagi dalam 5 kelompok dan 4 kelompok dipaparkan HHI menggunakan hypobaric chamber di Lakespra Saryanto TNI AU, selama 50 menit dengan variasi ketinggian, interval intermiten 1 minggu, 4 kali perlakuan (hari 1, 8, 15 dan 22). Dilakukan pengukuran protein HIF-1 dan Mb (ELISA), ekspresi relatif mRNA Mb dan BNP-45 (real time RT-PCR satu langkah). Hasil : Kadar protein HIF-1 meningkat pada paparan hipoksia hipobarik dan terus menurun hingga induksi hipoksia hipobarik intermiten 3 kali (ANOVA, $p=0,0437$). Ekspresi mRNA dan protein Mb meningkat pada paparan hipoksia hipobarik dan terus menurun hingga induksi hipoksia hipobarik intermiten 3 kali (ANOVA, $p=0,0283$; $0,0170$), dan keduanya berkorelasi kuat (Pearson, $r=0,6307$). Ekspresi mRNA BNP-45 meningkat pada paparan hipoksia hipobarik intermiten 1 kali dan terus menurun hingga induksi hipoksia hipobarik intermiten 3 kali (ANOVA, $p=0,0314$). Hasil uji korelasi juga menunjukkan hubungan yang kuat antara protein HIF-1 dengan ekspresi mRNA Mb, namun sangat lemah dengan ekspresi mRNA BNP-45. Kesimpulan : Terjadi respons adaptasi HIF-1, Mb dan BNP-45 pada paparan hipoksia hipobarik intermiten pada jantung tikus. Protein HIF-1 meregulasi ekspresi Mb dan BNP-45.

Background: The study analyzed the adaptive responses of heart tissue after induction of intermittent hypobaric hypoxia (IHH) in rat. The transcription factor HIF-1 is important to overcome hypoxia condition, which consist of 2 subunits: HIF-1 and HIF-1 in a state of hypoxia form heterodimers and regulate the expression of a number of target genes to overcome hypoxia. Hypoxia, especially continuous one, may lead the heart to hypertroptive state. The heart will overcome the situation through the establishment of Mb and BNP-45.

Methods: Twenty five male Sprague-Dawley rats were exposed to IHH in a hypobaric chamber in Indonesian Air Force Institute of Aviation Medicine, for 50 minutes at various altitudes, 1 week interval for 4 times (day 1, 8, 15 and 22). HIF-1 and Mb protein were measured with ELISA. mRNA expression of Mb and BNP-45 were measured with one step real time RT-PCR.

Results: HIF-1 protein levels increased after induction of hypobaric hypoxia and continues to decrease after induction of intermittent hypobaric hypoxia 3 times (ANOVA, $p=0.0437$). mRNA expression and protein of Mb increased after induction of hypobaric hypoxia and continues to decrease after induction of intermittent

hypobaric hypoxia 3 times (ANOVA, $p=0.0283$; 0.0170), and both are strongly correlated (Pearson, $r=0.6307$). mRNA expression of BNP-45 increased after induction of intermittent hypobaric hypoxia 1 time and continues to decrease after induction of intermittent hypobaric hypoxia 3 times (ANOVA, $p=0.0314$). Correlation test results also showed a strong relationship between HIF-1 protein with mRNA expression of Mb, but very weak with mRNA expression of BNP-45.

Conclusions: Adaptive response of HIF-1, Mb and BNP-45 occurs after induction of intermittent hypobaric hypoxia in rat heart. HIF-1 protein regulated the expression of Mb and BNP-45.