Perbedaan respons adiposit terhadap pemberian pakan tinggi lemak pada kelompok tikus dewasa yang berbeda status gizi pada masa pertumbuhan = The adipocyte response to high fat diet in obese adult rats which differ in nutritional state during childhood

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Abstrak

Latar belakang: Prevalensi populasi gemuk dewasa terus meningkat di seluruh dunia, termasuk Indonesia. Hal ini penting terkait perkembangan penyakit degeneratif. Perbedaan perilaku adiposit dengan awitan obesitas yang dimulai sejak kecil atau sejak dewasa belum diketahui secara jelas. Penelitian ini bertujuan untuk menganalisis perbedaan jumlah, ukuran, tingkat hipoksia, glikolisis anaerobik, autofagi, biogenesis dan fungsi mitokondria adiposit viseral tikus coba.

Metode: Tiga puluh lima ekor tikus Sprague-Dawley jantan, usia 4 minggu, BB 65–110 gram, secara acak dibagi menjadi kelompok perlakuan 8 dan 28 pekan. Kelompok 8 pekan terbagi 3 kelompok: PRK8 (pakan rendah kalori 8 pekan), PTL8 (pakan tinggi lemak 8 pekan), PS8 (pakan standar 8 pekan) sebagai kontrol. Kelompok 28 pekan terbagi 4 kelompok: PRK28 (PRK 8 pekan + PTL 20 pekan), PS28 (PS 8 pekan + PTL 20 pekan), PTL28 (PTL 28 pekan) dan kontrol (PS 28 pekan). Jumlah dan ukuran adiposit dianalisis pada pekan 8 dan 28 (histopatologi). Pemeriksaan ekspresi mRNA Hif-1Î±, Hif-2Î±, Lc3 (RT-qPCR); kadar HIF-1Î±, HIF-2Î±, PGC1Î±, MnSOD, LC3 (ELISA); dan aktivitas LDH (pemeriksaan enzimatis) dilakukan pada akhir pekan 28.

Hasil: BB kelompok PRK8 lebih rendah dibandingkan PS8 (p = 0,008), BB kelompok PTL8 lebih tinggi dibandingkan PS8 (p = 0,008). Jumlah adiposit tidak berbeda bermakna, namun ukuran sel kelompok PRK8 lebih kecil dibandingkan PS8 dan PTL8 (p = 0,000). BB kelompok PRK28, PS28 dan PTL28 lebih tinggi bermakna dibandingkan kontrol. BB PTL28 didapatkan paling tinggi, namun kenaikan BB akibat pemberian PTL 20 pekan terjadi pada kelompok PRK28. Jumlah adiposit PRK28 paling sedikit namun paling hipertrofi. Kadar HIF-1Î± PRK28 meningkat dibandingkan PTL28 (p = 0,046) dan kontrol (p = 0,029). Kadar HIF-2Î± PRK28 meningkat dibandingkan PS28 (p = 0,045) dan PTL28 (p = 0,022). Adiposit PTL28 juga hipertrofi, disertai peningkatan ekspresi mRNA HIF-2Î±. Kadar PGC1Î± PRK28 meningkat dibandingkan PS28 (p = 0,000), PTL28 (p = 0,000) dan kontrol (p = 0,000). Aktivitas MnSOD PRK28 meningkat dibandingkan PTL28 (p = 0,038) dan PS28 (p = 0,015). Aktivitas LDH tidak berbeda bermakna pada seluruh kelompok. Ekspresi mRNA Lc3 PRK28 meningkat dibandingkan PTL28 (p = 0,037) dan kontrol (p = 0,047) namun tidak ada perbedaan pada kadar protein LC3.

Simpulan: Ditemukan perbedaan respons adiposit viseral pada kelompok tikus gemuk dewasa yang berbeda status gizi pada masa pertumbuhan. Adiposit tikus yang kurus pada masa pertumbuhan didapatkan hipertrofi dan hipoksia; disertai peningkatan gen autofagi, biogenesis dan fungsi mitokondria. Adiposit tikus yang

gemuk sejak kecil didapatkan hipertrofi disertai peningkatan ekspresi gen hipoksia.
<hr />Background: The prevalence of obesity in adults is increasing worldwide. This is problematic since obesity is associated with degenerative diseases. Nowadays, Indonesia is facing an interesting phenomenon, where there are adults who have been obese since childhood and others who conversely were undernourished while young. The biological differences of these two types of obesities are not well understood. This study aims to analyse the difference in the size, number, hypoxic state, anaerobic glycolysis, autophagic activity, biogenesis and mitochondrial functions of rat visceral adipocytes that differ in nutritional state at youth.

Method: Thirty five four-week-old male Sprague-Dawley rats were randomly divided into 8-week and 28-week treatment groups. The 8-week groups consist of groups given a low-caloric diet (LCD8), a high-fat diet (HFD8), a standard chow diet (SD8) as control. The 28-week groups consist of groups given LCD for 8 weeks + HFD for 20 weeks (LCD28), SD for 8 weeks + HFD for 20 weeks (SD28), HFD for 28 weeks (HFD28), and SD for 28 weeks as control. The size and number of visceral adipocytes were analyzed at week 8 and 28 by histopathological examination. The levels of Hif-1Î±, Hif-2Î± and Lc3 mRNA (RT-qPCR), HIF-1Î±, HIF-2Î±, PGC1Î±, MnSOD, LC3 (ELISA); and the lactate dehydrogenase activity (enzymatic analysis) were analyzed at week 28.

Result: The LCD8 significantly had the lowest BW and the HFD8 had the highest. There was no difference in the number of adipocytes, but the LCD8 adipocytes were tiny in size. At week 28, there was a significant increase of BW in all the treatment groups compared to control. The highest BW was found in the HFD28 group, but the highest BW increase was found in LCD28. The LCD28 had the least amount of adipocytes, but the size was the largest, with the significant increase of HIF-1Î± and HIF-2Î±. Although the HFD28 adipocytes were hypertrophic, there was an increase in the Hif-2Î± mRNA expression but not in the protein level. The PGC1Î± level and the MnSOD activity of the LCD28 were significantly higher than the other groups. There was no difference in the lactate dehydrogenase activity between all groups. The Lc3 mRNA of the LCD28 was increased significantly, but not in the level of LC3 protein.

Conclusion: There were differences in the visceral adipocyte characteristics of obese adult rats which differ in nutritional state at a young age. Adipocytes of the obese adult rats which were undernourished were hypertrophic, hypoxic, and had increased autophagic gene expression, biogenesis and mitochondrial functions. The adipocytes of rats which were obese since young were hypertrophic and had increased hypoxic gene expression.