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Published in:
Diabetologia

Publication date:
2015

Document Version
Peer reviewed version

The effect of a short-term high-fat overfeeding on plasma levels of acylcarnitines in young, healthy men with low or normal birth weight

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Background and aims: Low birth weight (LBW) subjects have an increased risk of developing type 2 diabetes later in life compared with normal birth weight (NBW) subjects. Also, an impaired oxidation of fatty acids and a subsequent accumulation of lipid species have been implicated in the pathogenesis of type 2 diabetes. Acylcarnitines are markers of an incomplete beta-oxidation in mitochondria. Here, we investigated whether LBW and NBW subjects had different plasma levels of acylcarnitines after a control diet and a high-fat, high-calorie diet and whether they changed these levels in response to overfeeding. Also, we examined whether the levels were related to insulin secretion and/or sensitivity.
Materials and methods: Twenty LBW (0-10th percentile) and twenty-six NBW (50-90th percentile) young, healthy men were in a random order given a three-day control diet and a five-day high-fat, high-calorie diet. After these challenges, we measured fasting plasma levels of forty-five acylcarnitine species by tandem mass spectrometry and assessed differences in these levels between birth weight groups or diets by unpaired or paired t-tests, respectively, or Wilcoxon signed rank tests. Also, we performed intravenous glucose tolerance tests and hyperinsulinaemic euglycaemic clamps to assess insulin secretion and sensitivity and evaluated associations between levels of acylcarnitines and these measures by regression analyses adjusted for age, body mass index, and birth weight.
Results: LBW subjects had higher plasma levels of eight acylcarnitine species, of these five hydroxyl- (OH)/dicarboxyl- (DC) species, as well as of total acylcarnitines and total OH-/DC-acylcarnitines after the control diet compared to NBW subjects, but no differences were seen after the high-fat, high-calorie diet. Furthermore, LBW and NBW subjects decreased levels of twelve species and increased levels of three or four species, respectively, and additionally decreased the level of total acylcarnitines in response to overfeeding. Also, the level of total OH-/DC-acylcarnitines was inversely associated to the serum level of insulin and hepatic insulin resistance after the control diet.
Conclusion: LBW subjects had a higher plasma level of total acylcarnitines after the control diet compared to NBW subjects, which indicates that they have an incomplete beta-oxidation of fatty acids in mitochondria. Also, their higher level of total OH-/DC-acylcarnitines suggests that they have a higher omega-oxidation of fatty acids in endoplasmic reticulum and/or an incomplete beta-oxidation of OH-/DC-fatty acids. LBW and NBW subjects decreased the level of total acylcarnitines in response to overfeeding, which may be a normal response to an acute overfeeding followed by an overnight fast with a minor release and oxidation of fatty acids in this less fasted state. Acylcarnitines do not seem to adversely affect insulin secretion or action. On the contrary, the level of total OH-/DC-acylcarnitines was inversely associated to insulin resistance, which suggests that omega-oxidation may be a scavenger pathway for oxidation of fatty acids that could accumulate as lipid species that impair insulin signalling.
Supported by: Danish Innovation Foundation, EFSD/Lilly, EU 6th Framework EXGENESIS