High fat diet induces disc degeneration in mouse: a preliminary study

INTRODUCTION

Intervertebral disc degeneration (IVDD) is considered as a major cause of the chronic low back pain, a serious disease that raises a high cost during the lifetime of patients. The pathogenesis of IVDD is largely unknown currently. A correlation of IVDD with obesity has been proposed, and epidemiological studies have indicated a close association of overweight with the increased risk of the number of degenerated lumbar discs, especially among the young population. Overweight was also reported to increase the risk of recurrent herniation of nuclear pulposus after lumbar microdiscectomy. However, no direct evidence has yet been established for a direct causal relationship between obesity and disc degeneration. In this preliminary study, we subjected male C57BL/6J mice to high fat (HF) diet and characterized the impact of diet-induced obesity on IVDD in comparison to mice fed on normal chow (NC) diet.

METHODS

The use of animal was following the animal protocol that was approved by IACUC at University of Virginia. Male C57BL/6J mice at 8 weeks of age were purchased from Jackson Lab and fed on HF or NC diet for 9 weeks. Radiographical imaging was performed, and the disc height rate was calculated as reported previously. The lumbar spines from animals on HF or NC diets were sectioned for Safranin O staining. Three discs from the upper (from L1/L2 to L3/L4) or lower (from L4/L5 to L6/S1) lumbar were mixed together for sulfated glycosaminoglycan (sGAG) assay by a colorimetric method. For gene expression analysis, cells were prepared by enzymatic digestion of disc tissues and cultured in alginate bead for 7 days followed by harvesting and total RNA isolation. Target gene mRNAs were determined by real-time RT-PCR. Data from 4 repeats were expressed as mean ± SD, and statistical significance was determined by Student’s t-test.

RESULTS

HF diet remarkably increased body weight (Fig. 1) with no significant impact on disc height rate (Fig. 2). However, discs from HF mice showed a thinner layer of outer AF and a more dehydrated NP than that of NC mice (Fig. 3). Furthermore, discs from HF mice produced less proteoglycan than NC mice, evidenced by sGAG level normalized to either DNA content or tissue weight (Fig. 4). Consistently, expression of matrix protein aggrecan in cultured disc cells from HF mice was significantly lower than that from NC mice (Fig. 5).

DISCUSSION

The results suggest that disc degeneration was accelerated in obese mice induced by HF diet, and this model is useful for studying the pathogenesis of obesity-induced disc degeneration. Whether the disc degeneration was induced directly by obesity or by the secondary effects of obesity is still unknown. The cellular mechanisms of disc degeneration associated with obesity need further investigation. Further experimentation is needed to identify and dissect the roles of mechanical and biochemical factors caused by obesity. For example, it has been reported that circulating level of leptin, a key regulator of appetite and adiposity, is greatly elevated in the HF diet-induced obese mice. Additionally, leptin was proposed to play a significant role during disc degeneration. Therefore, our future efforts will focus on the role of leptin in the pathogenesis of IVDD, using the leptin-deficient obese mice.

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REFERENCES


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