Black tea prevents hyperglycemia and obesity in KK-A^y mice

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Summary

In this study, we investigated the preventive effects of black tea on obesity and hyperglycemia in KK-A^y diabetic mice. During the feeding period, the mice were given water or black tea. The levels of plasma glucose and insulin were increased in the group given water, but black tea suppressed these increases. Moreover, black tea lowered the weight of white adipose tissue (WAT) and plasma lipid levels. In mensenteric white adipose tissue, black tea decreased gene expression of inflammatory cytokines such as tumor necrosis factor-α (TNF-α), interleukin-6 (IL-6), and monocyte chemotactic protein-1 (MCP-1), which evoke insulin resistance, whereas black tea increased lipid-metabolizing enzyme such as acetyl-CoA carboxylase (ACC) and carnitine palmitoyltransferase-1 (CPT-1). These results indicate that black tea improves lipid metabolism and suppresses insulin resistance through the down-regulation of the expression of inflammatory cytokines in WAT.

Introduction

Obesity is a serious health problem in many countries, because it is implicated in various diseases including type 2 diabetes mellitus which are characterized by hyperglycemia [Kopelman (2000)]. Hyperglycemia follows insulin resistance, and it is reported that inflammatory cytokines evoke insulin resistance. For example, IL-6 inhibits insulin signaling in HepG2 hepatocyte [Senn, *et al*. (2002)], and TNF-α decreases the expression of glucose transporter 4 (GLUT4) in 3T3-L1 adipocyte [Long, *et al*. (1996)]. Black tea (*Camellia sinensis*) is consumed worldwide, and contains not only caffeine and catechins but also theaflavins. It is reported that black tea attenuates deposition of fat to WAT induced by intake of a high-fat diet in rats [Lin, *et al*. (2007)]. We previously demonstrated that black tea suppresses hyperglycemia by retaining GLUT4 expression in muscle of mice as well as green tea [Nishiumi, *et al*. (Submitted)]. However, its underlying mechanism is not fully understood. In this study, we, therefore, investigated the effects of *ad libitium* intake of black tea on fat accumulation and hyperglycemia in type 2 diabetic mice.

Materials and methods

All animal treatments in this study conformed to the "Guidelines for the care and use of experimental animals, in Rokkodai Campus, Kobe University". Male KK-A^y mice (4 weeks old) were purchased from CLEA Japan, Inc. (Tokyo, Japan). After acclimation for 1 week, mice were randomly divided into three groups. W and BT groups were given tap water or black tea, respectively, during the feeding period, and WBT group was given black tea after giving water for 5 weeks. After 9 weeks feeding, blood was collected from cardiac puncture under anesthesia. Mesenteric, epididymal, retroperitoneal, and subcutaneous WAT were entirely removed from the body.

Results and discussion

In this study, we investigated whether black tea contributes to suppress hyperglycemia and fat accumulation in KK-A^y mice. The body weight gain of BT group was suppressed compared with W group during the feeding period. In WBT group, more increase in body weight was attenuated by black tea. In both WBT and BT groups, the relative weight of total WAT were lower than W group, and black tea showed a significant effect in BT group. At the end of feeding, the levels of plasma glucose and insulin were increased in W group, but these increases were significantly suppressed in BT group, and a similar tendency was observed in WBT group. Plasma levels of triacylglycerol, free fatty acids, and

total cholesterol were reduced in both WBT and BT groups compared with W group. These results demonstrated that black tea prevents insulin resistance and hyperlipidemia, and improves these metabolic disorders. The effects of black tea on the gene expression levels of lipid-metabolizing enzymes in mesenteric WAT were examined by real-time polymerase chain reaction (RT-PCR) assay. Those of ACC, a rate-limiting enzyme of fatty acid synthesis, and CPT-1, a rate-limiting enzyme of β-oxidation of fatty acids, were increased in WBT and BT groups. These results indicated that intake of black tea improved lipid metabolism in WAT.

Inflammatory cytokines such as TNF-α, IL-6, and MCP-1 are produced in overblown adipocytes and decrease the expression of insulin receptor and glucose transporter in WAT [Borst, *et al*. (2005), Jiao, *et al*. (2009), Nishimura, *et al*. (2008)]. Thus, inflammatory cytokines cause insulin resistance. To elucidate the mechanism of hyperglycemia, the gene expression of TNF-α, IL-6, and MCP-1 in mesenteric WAT was measured by RT-PCR assay. The expression levels of IL-6 and MCP-1 in both WBT and BT groups were decreased compared with W group, whereas TNF-α was slightly reduced. These results indicate that black tea decreases the gene expression of inflammatory cytokines in WAT and suppresses the increase of the levels of plasma glucose and insulin. In conclusion, black tea improves lipid metabolism and suppresses insulin resistance through the down expression of inflammatory cytokines in WAT.

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