Selenium-Enriched Bifidobacterium Longum DD98 Combined with Pioglitazone Alleviates Type 2 Diabetes Mellitus in Mice

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Abstract

Pioglitazone is a commonly used drug for the treatment of type 2 diabetes mellitus (T2DM). However, long-term use of high-dose pioglitazone induces edema in a subset of patients. Probiotics and selenium (Se) have both shown antidiabetic activities. We previously reported a Se-enriched probiotic Bifidobacterium longum DD98 (Se-DD98) that may synergize the effects of selenium and probiotics. The present study aimed to investigate the combined effects of Se-DD98 and low-dose pioglitazone in the treatment of T2DM. A T2DM mouse model was established through a high-fat diet and intraperitoneal injection of streptozotocin (STZ). After three-week treatments of a combination of Se-DD98 and pioglitazone, fasting blood glucose, insulin, glycosylated hemoglobin, and lipid levels in T2DM mice decreased significantly ($p<0.05$). The combined therapy also enhanced the activities of antioxidant enzymes and decreased the expression of inflammatory factors. After the combination of Se-DD98 and pioglitazone, compared with pioglitazone alone, the three antioxidant enzymes of hepatic T-SOD, GPx, and CAT in mice were elevated by 30.62%, 35.60%, and 35.18%, respectively, and MDA was reduced by 60.75% ($p < 0.05$), and the expression of IL-6 and TNF-α mRNA were reduced by 44.99%, 31.30% ($p < 0.05$). Furthermore, Se-DD98 and pioglitazone combination showed significantly improved antidiabetic effects compared to the treatment of pioglitazone alone and the combined treatment of pioglitazone with the regular probiotic DD98 or inorganic selenium supplement Na2SeO3. Our studies support that the combined therapy of Se-DD98 and pioglitazone effectively mitigates T2DM risk, regulates glycolipid metabolism, improves insulin sensitivity, and alleviates tissue damage in diabetic mice. This could be a candidate way to delay type 2 diabetes progression and prevent pioglitazone-induced edema.

Keywords

Selenium-Enriched Probiotics, Type 2 Diabetes Mellitus, Glycolipid Metabolism, Oxidative Stress, Inflammation