

Effect of genistein on expression of pancreatic SIRT1, inflammatory cytokines and histological changes in ovariectomized diabetic rat

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ABSTRACT

Objective(s): Genistein is reported to have anti-diabetic and anti-inflammatory functions, in particular, direct effects on β -cell proliferation and insulin secretion. In this study, we investigated the anti-inflammatory effect of genistein on the pancreatic β -cells in ovariectomized diabetic rat.

Materials and Methods: Forty female rats were divided into four groups: sham, bilateral ovariectomy (OVX), OVX.D (OVX+diabetes) and OVX.D.G (OVX.D+genistein). After bilateral ovariectomy, rats in the diabetic groups were fed high-fat diet (HFD), *ad libitum* for 4 weeks, and then a low dose of streptozotocin (STZ) (30 mg/kg) injected intraperitoneally. Genistein (1 mg/kg/day; SC) was administered for 8 weeks. At the end of 8 weeks, pancreas tissue was removed and used for western blotting and Hematoxylin-Eosin staining.

Results: Treatment with genistein declined inflammation and tissue injury, and this decline was correlated with the expression of SIRT1. OVX and OVX.D significantly increased Nf- κ B and IL-1 β expression and decreased SIRT1 levels compared to sham group ($P<0.05$). Significant reduction of Nf- κ B and IL-1 β , and increasing of SIRT1 were observed during genistein treatment ($P<0.05$).

Conclusion: Estrogen deficiency alone or with HFD increased pancreatic inflammation. However, subcutaneous administration of genistein prevented from these inflammatory changes in the pancreas of a surgery animal model of ovariectomy with or without diabetes. Our results support the potential preventing effect of genistein from pancreatic injury.

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Introduction

Diabetes, which is characterized by a deficit in β -cell mass, is developing to epidemic proportions. However, the mechanisms underlying β -cell destruction are not clear, it has been suggested that cytokines may be involved. In diabetes, cytokines are important mediators in the impaired function and destruction of pancreatic β -cells (1, 2).

Many pieces of evidence have demonstrated that the reduction in ovarian function with menopause or surgical is related with spontaneous rises in pro-inflammatory cytokines. The pro-inflammatory cytokines that have obtained the more attention are interleukin (IL)-1 β , and tumor necrosis factor (TNF- α). Estrogen deficiency has also been revealed to augment the responsiveness of cells to these cytokines by up-regulating cytokine receptors (3).

During the inflammatory process, pro-inflammatory cytokines such as IL-1 β and TNF- α are secreted by immune cells affecting the pancreas and contribute to

β -cell dysfunction and apoptosis (4). Activation of the transcription factor Nf- κ B is necessary for cytokine-induced β -cell death (5). SIRT1 belongs to family of histone/protein deacetylases (class III) and may play an important role in the inflammation. SIRT1 is expressed in the endocrine cells of the Langerhans islets. Furthermore, the effect of SIRT1 is inhibition of Nf- κ B by deacetylating p65; it can protect β -cells from cytokine (6).

Phytoestrogens, such as genistein, are naturally occurring plant estrogens that are suggested for use in postmenopausal women. These compounds have a chemical structure similar to human estrogen and have the ability to attach the estrogen receptors (7). Studies have demonstrated that phytoestrogen genistein has anti-diabetic effects; it has in particular direct effects on β -cell proliferation, insulin secretion and anti-apoptotic effects (8). Genistein decreases many pro-inflammatory mediators and some pro-inflammatory cytokines such as TNF- α , IL-1 β , and IL-6. These effects of genistein involved in the protection of human pathological processes (9).

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