Ameliorative Effect of Adjunct Therapy of Metformin with Atorvastatin on Streptozotocin-induced Diabetes Mellitus in Rats

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Key words
- diabetes mellitus
- metformin
- atorvastatin
- lipid profiles
- oxidative stress

Abstract

Metformin has been used for the treatment of diabetes, whereas atorvastatin reduces the incidence of atherosclerosis and ischemic heart disease. Therefore, combined treatment with meformin plus atorvastatin may be beneficial in diabetic patients associated with cardiac disease. The present study was designed to evaluate the combination therapy of metformin and atorvastatin on streptozotocin-induced diabetes mellitus in rats. Blood pressure, serum insulin, glucose, lipid profiles and antioxidant enzymes in pancreatic tissues were measured. Histopathological examination of pancreatic tissues was performed. Streptozotocin treated rats showed significant decrease in body weight and body mass index. Streptozotocin-treated rats showed a significant increase in the levels of blood pressure, serum glucose, triglycerides, total cholesterol and thiobarbituric acid reactive substance as well as a significant decrease in the levels of serum insulin, high density lipoprotein and reduced glutathione in pancreatic tissues. Administration of metformin plus atorvastatin for a period of 14 days significantly improved these biochemical parameters near to normal. The protective effect of metformin plus atorvaststin against streptozotocin-induced diabetes was further confirmed by histopathological examination. The results of present study suggest that metformin plus atorvastatin possess antioxidant activity and has a significant protective effect against streptozotocin-induced diabetes mellitus.

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Introduction

Diabetes and its complications are a major health problem in modern societies. Diabetes mellitus (DM) comprises abnormalities of insulin action including insulin deficiency and insulin resistance. It is characterized by chronic hyperglyceamia with disturbances of carbohydrate, fat and protein metabolism resulting from defects in insulin secretion, insulin action or both [1]. It is commonly associated with endothelial dysfunction [2]. Various studies have reported that increased production of reactive oxygen species (ROS) resulting from metabolism of excessive glucose and free fatty acid as well as decreased expression of antioxidant enzymes have been responsible for deterioration of pancreatic β-cells [3]. Hyperglyceamia also enhances the oxidative modification of low density lipoprotein (LDL) which induces production of cellular adhesion molecules (CAM) and increase monocyte adhesion [4].

Streptozotocin (STZ) a naturally occurring broad spectrum antibiotic and is toxic to the insulin producing pancreatic β-cells. Oxidative stress may be responsible for deterioration of pancreatic β-cells. Thus, oxidative stress play a key role for the development of DM. Studies also reported that administration of STZ led to increase production of ROS resulting from metabolism of excessive glucose and free fatty acids, and decreased expression of antioxidant enzymes. Thus, STZ induced oxidative stress may play a major role for development of DM [2,3].

Metformin, a biguanide, is the most widely prescribed drug for the treatment of hyperglycaemia in type II diabetics [5,6]. It blocks hepatic gluconeogensis and increases hepatic insulin sensitivity as well as to a lesser extent insulin mediated glucose uptake in fat and muscle tissue [7]. Metformin has a potent antioxidant and anti-inflammatory properties [8]. In recent years, study reported that metformin exerts several pleiotropic effects including beneficial changes in blood rheology, serum lipid profile and putative