Antihyperlycemic action of angiotension II receptor antagonist, valsartan, in streptozotocin-induced diabetic rats

陳保羅

Chan P;Wong KL;Liu IM;Tzeng TF;Yang TL;Cheng JT

摘要

Abstract

In the present study, we use valsartan, a highly selective antagonist for angiotensin(1) (AT(1)) receptor subtype, to investigate the effect of AT(1) receptor on the plasma glucose metabolism in streptozotocin-induced diabetic rats (STZ-diabetic rats). METHODS: The plasma glucose concentration was assessed by glucose oxidase method and plasma insulin was measured using enzyme-linked immunosorbent assay. Systolic blood pressure (SBP) was determined by the tail-cuff method. The intravenous glucose challenge test (IVGCT) was carried out to evaluate the effect of valsartan on the glucose utilization in vivo. The mRNA levels of the subtype 4 form of glucose transporter (GLUT4) in soleus muscle and phosphoenolpyruvate carboxykinase (PEPCK) in the liver were detected by Northern blotting analysis. Moreover, the protein levels of GLUT4 in isolated soleus muscle and hepatic PEPCK were investigated using Western blotting analysis. RESULTS: A single intravenous injection of valsartan decreased the plasma glucose concentrations in a dose-dependent manner in STZ-diabetic rats. Plasma glucose-lowering action of valsartan also observed in normal rats although in a way not so effective as that in STZ-diabetic rats. Valsartan at the dose of 0.2 mg/kg that produced the maximal plasma glucose-lowering activity in STZ-diabetic rats is also effective to lower the SBP. However, oral treatment with nifedipine or nicorandil in STZ-diabetic rats at the dose sufficient to decrease SBP showed no change of plasma glucose. Otherwise, infusion of saralasin (10 microg/kg per min) into STZ-diabetic rats produced a plasma glucose-lowering activity similar to that by valsartan at 0.2 mg/kg. Moreover, valsartan (0.2 mg/kg) significantly attenuated the raise of plasma glucose induced by IVGCT in normal rats. Repeated intravenous administration of valsartan (0.2 mg/kg) in STZ-diabetic rats resulted in the lowering of plasma glucose after 3 days. The mRNA and protein levels of GLUT4 in the soleus muscle were increased after repeated intravenous administration of valsartan in STZ-diabetic rats for 3 days. Moreover, similar repeated treatment with valsartan reversed the elevated mRNA and protein levels of PEPCK in the liver of STZ-diabetic rats. CONCLUSIONS: These results suggest that the plasma glucose-lowering activity of AT(1) receptor antagonism was associated with an increase in the glucose utilization in peripheral tissue and/or a reduction in hepatic gluconeogenesis in the absence of insulin.