11-Keto-β-Boswellic Acids Prevent Development of Autoimmune Reactions, Insulitis and Reduce Hyperglycemia During Induction of Multiple Low-Dose Streptozotocin (MLD-STZ) Diabetes in Mice.

Shehata AM[1], Quintanilla-Fend L[2], Bettio S[2], Jauch J[3], Scior T[4], Scherbaum WA[5], Ammon HP[1]

Abstract

The aim of the work was to study whether or not 11-keto-β-boswellic acids prevent induction of autoimmune reactions, insulitis, and hyperglycemia in the model of multiple low-dose streptozotocin (MLD-STZ) diabetes. Using male mice (n=6) diabetes was induced by daily i.p. injections of 40 mg/kg STZ for 5 days. In a second series together with STZ, daily i. p. injections of 11-keto-β-boswellic acid (KBA) and O-acetyl-11-keto-β-boswellic acid (AKBA) (7.5 and 15.0 mg/kg) were applied for 10 days. Thereafter, pro-and anti-inflammatory cytokines in the blood, histochemistry of pancreatic islets, and blood glucose levels were assayed. Five days after the last injection of STZ, a significant burst of pro-and anti-inflammatory cytokines in the blood, infiltration of lymphocytes (CD3) into pancreatic islets, and appearance of peri-insular apoptotic cells were observed. Plasma glucose increased significantly (124.4±6.65 vs. 240.2±27.36 mg/dl, $p<0.05$). Simultaneous treatment with KBA and AKBA significantly reduced pro-and anti-inflammatory cytokines (IFN-γ $p<0.01$, $p<0.01$; IL-1A $p<0.001$, $p<0.001$; IL-1B $p<0.001$, $p<0.001$; IL-2 $p<0.001$, $p<0.001$; IL-6 $p<0.01$, $p<0.001$; TNF-α $p<0.05$, $p<0.001$; IL-4 $p<0.01$, $p<0.001$; IL-10 $p<0.001$, $p<0.001$) in the blood. No infiltration of lymphocytes into pancreatic islets and appearance of peri-insular cells were detected. Moreover, KBA and AKBA reduced STZ-mediated increase of blood glucose on day 10 to 163.25±16.6 ($p<0.05$) and 187.6±19.5 mg/dl ($p<0.05$), respectively. In the model of MLD-STZ induced diabetes KBA and AKBA prevent cytokine burst, development of insulitis and reduce increase of blood glucose through "silencing" a forced-up immune reaction.