Pro-inflammatory Cytokine Interleukin-6 is Upregulated in Early Stage Type 1 Diabetic Rats

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ABSTRACT

Type 1 diabetes (T1DM) is an autoimmune disease characterized by systemic inflammation. T1DM patients are at a higher risk of cardiovascular disease and chronic inflammation, and this is reflected by increased levels of circulating pro-inflammatory cytokines IL-6, IL-1β, and TNF-α. However, the time point at which these pro-inflammatory cytokines become elevated is not known. **PURPOSE:** The purpose of this study was to determine the concentration of circulating pro-inflammatory cytokines IL-6, IL-1β, and TNF-α in the early stage of T1DM. **METHODS:** We injected (i.p) 50mg/kg of Streptozotocin (STZ) or the vehicle (CTL) into male and female Sprague Dawley rats and waited one to three weeks before drawing blood. Blood was drawn from the carotid artery into a serum separator vacutainer, centrifuged, and then the serum was aliquoted into tubes and frozen at -80°C for subsequent batch analyses. A rat cytokine multiplex kit (RADPKMAG, EMD Millipore) was used to determine cytokine concentrations in the aliquoted samples. Samples were analyzed using a Luminex 200 instrument (Luminex Corp) according to manufacturer’s instructions. **RESULTS:** STZ rats had significantly higher blood glucose (CTL=200±15 mg/dl, n=14; STZ=523±14 mg/dl; n=14; p<0.01) and % HbA1c (CTL=4.3±0.1%, n=10; STZ=8.7±0.7%; n=11; p<0.01) than CTL rats. STZ rats had significantly lower insulin (CTL=1259±500 pg/ml, n=8; STZ=200±182 pg/ml, n=14; p<0.01) than CTL rats. We found that serum IL-6 was increased in STZ rats (222±205 pg/ml; n=11; four samples with undetectable concentrations were excluded) compared to CTL rats (116±69 pg/ml; n=10; one sample with undetectable concentration was excluded), p=0.06. In contrast, we found that IL-1β (STZ: 4.9±4 pg/ml, n=14; CTL: 4.6±3 pg/ml, n=7, p>0.05) and TNF-α (STZ: 15.6±12 pg/ml, n=14; CTL: 14.3±9 pg/ml, n=13, p>0.05) were not significantly different between STZ and CTL. **CONCLUSION:** We conclude that serum IL-6 concentrations are trending toward being greater in the early stage of T1DM. However, serum levels of IL-1β and TNF-α do not appear to be elevated at this stage of the disease. Further studies are needed to determine if concentrations of pro-inflammatory cytokines fluctuate during the progression of the disease.