Low effectiveness of inducing beta cell mass destruction as a model of type 1 diabetes on murine model by Streptozotocin infusion

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Background: Type 1 diabetes (T1D) is an autoimmune disease leading to the loss of over 90% of the β -cells mass. Studies to assess the effectiveness of potential therapies are often conducted in a mouse model with chemically induced T1D. Predominantly, streptozotocin (STZ) is employed for this purpose. It is selective for β -cells and causes preferential accumulation in β -cells after entry through the GLUT 2 receptor and destruction of cells. This study aims to determine whether this model of T1D leads to the destruction of over 90% of β -cells when using different STZ induction protocols.

Methods: The studies were carried out on BALB/c mice. Groups differed in the STZ dose or the method of administration. Doses ranging from 140–400 mg kg⁻¹ have been tested. Controls were performed for 21 days. Immunohistochemical staining of pancreatic, kidneys and liver were performed and the body weight of animals was monitored.

Results: Dose <300 mg kg⁻¹ cannot effectively destroy over 90% of the beta-cells mass. Despite high glucose levels, C-peptide levels were high. There were only two variants of STZ administration where animals where the destruction of beta-cell mass was considered as over 90%. STZ dose of 300 and 400 mg kg⁻¹ reduced concentration of C-peptide to the values <0.6 ng/mL. Unfortunately, mortality in those groups was 100% within 2 weeks after induction of diabetes. Histological analysis showed damage of pancreatic islets and changes both in the glomeruli and liver tissue.

Conclusions: STZ is not an efficient method for induction of diabetes with over 90% destruction of beta cells in the murine model. C-peptide concentration should be considered as the most reliable indicator for diabetes diagnosis. 100% mortality in high-STZ groups is due to general inflammation of internal organs but not due to high glucose levels.

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