

# INTRAVENOUS IMMUNOGLOBULIN ATTENUATES DIABETES INDUCTION IN MICE

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## INTRAVENSKI IMUNOGLOBULINI INHIBIRAJU RAZVOJ DIJABETESA KOD MISEVA

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### ABSTRACT

*Type 1 diabetes mellitus is an autoimmune disease in which pathologic autoreactive T cells attack the insulin-secreting pancreatic islets of Langerhans. Intravenous immunoglobulin has been shown to have a therapeutic effect in some autoimmune diseases. The therapeutic effect of intravenous immunoglobulin has not been tested in type 1 diabetes mellitus models.*

**Objectives:** We examined the effect of intravenous immunoglobulin (IVIG) on the development of immune-mediated diabetes induced by administration of multiple low doses of streptozotocin (SZT) in susceptible C57BL/6 male mice.

**Methods:** Diabetes was induced by five daily injections of streptozotocin. Mice were treated daily with either 50 mg/kg or 200 mg/kg body weight IVIG for 15 days. Control animals received equivalent doses of human serum albumin. Glycaemia and glycosuria were evaluated daily, and serum levels of TNF $\alpha$ , IL-17 and HbA1c were determined on day 21.

**Results:** Assessment of glycaemia ( $p < 0.001$ ), glycosuria ( $p < 0.01$ ), and HbA1c levels demonstrated that treatment with 200 mg/kg IVIG significantly attenuated diabetes induction. Calculation of Pearson's correlation coefficients indicated an inverse correlation between HbA1c levels and IVIG dose ( $p < 0.04$ ). Finally, serum levels of TNF $\alpha$  and IL-17 were significantly lower in IVIG-treated mice than in control mice ( $p < 0.05$ ).

**Conclusion:** Our results show for the first time that IVIG may attenuate diabetes induction by reducing serum levels of proinflammatory cytokines.

**Keywords:** Diabetes mellitus, intravenous immunoglobulin, TNF $\alpha$ , IL-17

### SAŽETAK

*Dijabetes melitus tip 1 je autoimuna bolest u kojoj patološki, autoreaktivni T limfociti oštećuju Langerhansova pankreasna ostrvca. Pokazano je da intraveniski imunoglobulini imaju terapijski efekat kod mnogih autoimunih bolesti. Terapijski efekat imunoglobulina u modelu dijabetes melitusa tip 1 nije ispitan. Ciljevi: Mi smo ispitali efekat intravenskih imunoglobulina na razvoj dijabetes melitusa izazvanog niskim ponovljenim dozama streptozotocina kod osetljivih C57BL6 miševa.*

**Metode:** Dijabetes je izazivan sa pet dnevnih injekcija streptozotocina. Korišćene su dve doze intravenskih imunoglobulina (50mg/kg, i 200mg/kg telesne mase) svakodnevno 15 dana. Kontrolne životinje dobijale su istu dozu humanog serumskog albumina. Glikemija i glikozurija mere se dnevno, dok se nivo serumskog TNF $\alpha$  i IL-17, kao i nivo HbA1c određivao 28.dana

**Rezultati:** Primena većih doza intravenskih imunoglobulina (200 mg/kg,) značajno je smanjila pojavu dijabetesa, što je praćeno kroz vrednosti glikemije ( $r < 0,001$ ), glikozurije ( $r < 0,01$ ) i nivoa HbA1c. Pirsonova korelacija pokazala je inverznu korelaciju između nivoa HbA1c u krvi i doze intravenskih imunoglobulina ( $R < 0,04$ ). Konačno, serumski nivo TNF $\alpha$  i IL-17 je bio značajno snižen nakon primene intravenskih imunoglobulina ( $r < 0,05$ ).

**Zaključak:** Naši rezultati su po prvi put pokazali da primena intravenskih imunoglobulina suprimiraju indukciju dijabetesa verovatno smanjenjem nivoa serumskih proinflammatory citokina.

**Gljučne reči:** Dijabetes melitus, intraveniski imunoglobulini, TNF $\alpha$ , IL-17

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