



Intravenous immunoglobulins exposed to heme (heme IVIG) are more efficient than IVIG in attenuating autoimmune diabetes

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Abstract Intravenous immunoglobulins (IVIG) are known to have a therapeutic effect in some autoimmune diseases. We examined the effect of IVIG and heme-exposed IVIG on the development of immune mediated diabetes induced in C57BL/6 mice by multiple low doses of streptozotocin. IVIG were used in a dose of 200 mg/kg daily for 15 days. Treatment with IVIG resulted in significant attenuation of diabetes induction as evaluated by glycemia, glycosuria and HbA1c level. Interestingly, heme-exposed IVIG had a still stronger antidiabetogenic effect. Serum levels of proinflammatory cytokines TNF- α , IFN- γ and IL17 were lower in IVIG treated animals when compared with controls, while IL10 level was higher. The number of CD4⁺Foxp3⁺ cells was higher in pancreatic lymph nodes of heme-exposed IVIG treated mice. Our results show that IVIG may downregulate diabetes induction possibly by favouring induction of T regulatory cells and suggest enhanced effect upon heme-binding to IVIG.

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1. Introduction

Intravenous immunoglobulins (IVIG) are a therapeutic preparation of normal pooled human IgG obtained from plasma pools of a large number of healthy donors that possess multiple immunomodulatory and anti-inflammatory proper-

ties [1,2]. Initially used in treating primary and secondary immune deficiencies, intravenous immunoglobulins are increasingly used for the treatment of diverse autoimmune and systemic inflammatory diseases including immune thrombocytopenia, Guillain-Barré syndrome, chronic inflammatory demyelinating polyneuropathy, myasthenia gravis, dermatomyositis, Kawasaki's syndrome, etc. [3]. The mode of action of IVIG is complex and involves several mechanisms, such as modulation of Fc receptors, interference with the complement and cytokine network, regulation

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