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TITLE

IMMUNOMODULATION BY BIOLOGIC INTRAVENOUS IMMUNOGLOBULINS IVIG: IMMUNE THROMBOCYTOPENIA ITP AS A MODEL FOR THE LAST 30 YEARS

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The first publication on biologic intravenous immunoglobulin (IVIG) administration for children with immune thrombocytopenia ITP (Imbach et al., The Lancet 1981;1:1228-1231) evoked targeted immunomodulation in patients with inflammatory and autoimmune disorders. We update the development of the immunomodulatory effects of IVIG over the last 28 years. The biologic drug: IVIG is extracted from the pooled plasma of 10,000-100,000 blood or plasma donations. The safety of IVIG is controlled by ongoing careful selection and deferral of donors, by testing and validation of donated blood, and plasma as well as during the steps of production including the purification processes. The key patient in 1981 was a boy with severe ITP and secondary hypogammaglobulinemia due to long-term immunosuppressive treatment. Following administration of IVIG the boy's platelet counts started to increase and in a subsequent pilot study of 13 consecutive children with ITP, but without hypogammaglobulinemia, the same phenomenon was observed. Since then, there have been controlled clinical trials of IVIG in patients with ITP as well as in other inflammatory or autoimmune disorders. Examples of documented immunomodulation are: in hematology: graft versus host disease,, allograft recipients, autoimmune lypmphoproliferative syndrome…, in neurology: Guillain-Barré syndrome,. myasthenia gravis, multifocal motor neuropathy, remitting-relapsing multiple sclerosis,… in dermatology: autoimmune mucocutaneous blistering diseases, pemphigus, Stevens-Johnson syndrome... Extensive studies on the mechanisms of action of IVIG have documented the immunomodulatory interaction in the disturbed immune response in these patients. Today, the clinical efficacy and marketing success of IVIG has resulted in high demand for the product, although the mechanisms of action of IVIG remain far from being completely clear. Nonetheless, the worldwide annual use of IVIG increased remarkably, from 300 kg to 70,000 kg over the last 28 years. The peer reviewed scientific, original articles on "IVIG" (see PubMed) listed at total of 31'715 publications until August 2009. Thus, the human derived product IVIG challenged therapeutic approaches from immunosuppression to biologic immunomodulation in many inflammatory and autoimmune disorders.