



EMERGENCY MEDICINE: **Human Intravenous Immunoglobulin**

Overview

Human intravenous immunoglobulin (IVIg) is a plasma product taken from the human donor population, each vial includes sterilized and highly purified immunoglobulin from >1000 donors which contains IgG and trace amounts of IgA, IgM, CD4, and CD8. IVIg was first used in people in the 1950s for treatment of immune deficient conditions and was given IM, which caused painful irritation. The IV preparation was used in the 1980s for treatment of hypogammaglobulinemia in two children with concurrent ITP and was found to increase platelet numbers. IVIg is now FDA approved for use in humans for primary/secondary immunodeficiencies, Kawasaki disease, allograft rejection, chronic inflammatory demyelinating polyneuropathy, autoimmune dermatologic diseases, and is used off-label for many other conditions.

IVIg has many possible uses as a pro-inflammatory and anti-inflammatory agent in human medicine, even after 50+ years research is still on-going. Judicious use of IVIg in veterinary medicine with adequate client education may be beneficial. Further studies on the efficacy and safety of IVIg use in vet med, specific MOAs and possible production of recombinant IVIg with increased concentration to increase supply and decrease cost, may increase future possibilities for use of this immunomodulatory therapy.

Mechanism of action

Pro-inflammatory at low dose, anti-inflammatory at high dose. The specific mechanism of action (MOA) is unknown but there are many proposed mechanisms which likely work synergistically and vary depending on the specific immune response for each condition. Possibilities include modulation of Fc receptors, inhibition of complement cascade/cytokine network activation, and neutralization of autoantibodies. Incomplete understanding of many of the diseases IVIg is used to treat makes understanding the MOA inherently more difficult. While this is frustrating because knowing the specific MOA would help to tailor therapy and may increase the possibility of recombinant preparations with higher concentration of the active immunoglobulin, it is also encouraging in the sense that broad range MOAs may increase the possibility that it can help in diseases with unknown pathophysiology.

Usage in veterinary medicine

IVIg is used most commonly as an immunosuppressive therapy in refractory cases of ITP, IMHA, and dermatologic diseases such as pemphigus foliaceus, severe adverse cutaneous drug reactions, and erythema multiforme. There may be potential for use in sudden acquired retinal degeneration as well as myasthenia gravis and other neuropathies. IVIg must be obtained through human hospitals and is given at a dose of 0.5g/kg as a single IV infusion over four to six hours after pre-medication with diphenhydramine. Possible adverse effects include anaphylactic shock, pulmonary edema from fluid overload,

hypertension during infusion, acute renal failure (via immune complex deposition within the glomerulus and possible sucrose nephropathy), thromboembolism, and possibly aseptic meningitis (reported in human patients). At Michigan Veterinary Specialists, the use of IVIg is assessed by our clinicians on a case by case basis.

Pros & cons

Benefits of IVIg therapy include potent short-term immunomodulation which allows time for traditional immunosuppressive therapies to work. It's also a potential treatment option for educated owners to attempt in immune-mediated diseases which are not responding to traditional therapies or in diseases with typically poor prognosis, and as an area for future research. Some undesirable components of IVIg therapy include the high cost (\$1,000 to \$2,000 to the client per treatment) and it is difficult to obtain due to lack of sufficient product for demand. In addition, there is risk of adverse effects, the lack of set guidelines for use, and in some cases a lack of proven efficacy.

Questions?

Our 24/7 Emergency and Critical Care service is open year round and staffed by excellent doctors and technicians. MVS attracts the top veterinarians from Canada and the United States for its positions and the ER doctors have access to specialists 24 hours a day, 7 days a week.

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