

18 Passive Immunisation

18.1 Introduction

Passive immunisation involves administering pre-formed antibody as human immune globulin to a recipient who is thought to have either no natural immunity to one or more infections, or has impaired antibody production. Human immune globulin preparations are prepared by fractionating large pools of plasma collected from blood donors to the New Zealand Blood Service. In New Zealand, blood donations are only collected from voluntary, unpaid donors who are in good health and who do not have any conditions identifiable by the standard questionnaire that all blood donors complete, and/or by the mandatory serological testing for HIV/AIDS, hepatitis B, hepatitis C and syphilis on each donation. Blood donations are only used if the tests show no evidence that these infections are present. CSL Bioplasma of Australia manufacture the immune globulins (immunoglobulins) for the New Zealand Blood Service.

18.2 Preparations available in New Zealand

There are two classes of immunoglobulin product available in New Zealand: human normal immunoglobulin for intramuscular use, and human normal immunoglobulin for intravenous use (IVIG). Both products have an excellent safety record in both Australia and New Zealand.

Human normal immunoglobulin for intramuscular use

Normal immunoglobulin is a sterile, preservative free, pasteurised solution containing 160 mg/mL human plasma proteins and 22.5 mg/mL glycine. The solution has a pH of 6.6. At least 98 percent of the protein is immunoglobulins (mainly immunoglobulin G, or IgG). Normal immunoglobulin is intended for intramuscular injection, and is available in 2 mL and 5 mL vials. It is prepared by Cohn cold ethanol fractionation of human plasma. The manufacturing process for normal immunoglobulin contains a specific viral inactivation step (pasteurisation at 60°C for 10 hours) to reduce the possibility of virus transmission.

Human normal immunoglobulin for intravenous use

The current human normal immunoglobulin for intravenous use in New Zealand is Intragam®P,¹ produced by CSL Australia. Intragam®P is a sterile, preservative free solution containing 6 g of human protein and 10 g of maltose in each 100 mL. The solution has a pH of 4.25. Isotonicity is achieved by adding maltose. At least 98 percent of the protein has the electrophoretic mobility of IgG. At least 90 percent of the protein is IgG monomer and dimer. Intragam®P contains only trace amounts of IgA (typically < 18 µg/mL). Intragam®P is intended for intravenous administration. It is made by chromatographic fractionation of large pools of human plasma obtained from voluntary blood donors. The protein has not been chemically or enzymatically

modified. The manufacturing process contains special steps to reduce the possibility of virus transmission, including pasteurisation (heating at 60°C for 10 hours) and incubation at low pH.

The sterile solution of immunoglobulin is prepared from a large pool of plasma. Both immunoglobulin products provide antibodies representative of those present in the general population: those against measles, varicella zoster, hepatitis A, and other viruses that are prevalent in the community.

Other immunoglobulin preparations

There are also a number of specific human immunoglobulin preparations available, including those for tetanus, hepatitis B, varicella zoster and anti-D. These are manufactured from plasma pools containing donations from individuals known to have high levels of the appropriate antibody. Presentation of these preparations is the same as normal immunoglobulin. The volume of the product will be determined by the potency for the appropriate antibody. In unusual circumstances, when supplies of specific immunoglobulin products are not available from the New Zealand Blood Service, commercial products from alternative donor sources may be supplied.

Other products are held in one or two centres for national use. For example, rabies immunoglobulin is held at Christchurch Hospital pharmacy and in Auckland by CSL NZ/Pro Pharma Ltd. The diphtheria antitoxin is held at the Auckland Hospital pharmacy.

18.3 Indications for use

Passive immunisation

For advice on the use of immunoglobulin products and specific dosages of these products, please contact a transfusion medicine specialist at the New Zealand Blood Service.

Human normal immunoglobulin is available for passive immunisation (pre- or post-exposure prophylaxis) against measles (see section 9.8) and hepatitis A (see section 14.8). It is not recommended for the prevention of rubella or mumps. Guidance on the use of specific preparations is provided in other sections of this Handbook: pre- or post-exposure prophylaxis against hepatitis B (section 3.8), tetanus (section 5.8) and varicella zoster (section 17.8).

Information on rabies is provided in the Ministry of Health publication *Health Advice for Overseas Travellers*, 1996 (see also Appendix 11 for additional websites). Information on a commercial preparation of rabies immunoglobulin is available from Medsafe, at the Ministry of Health.

Management of primary and acquired immune deficiency

Recurrent infections can occur in individuals who have low or absent levels of circulating immunoglobulins – so-called humoral immune deficiency. This can arise as a congenital disorder or can be acquired as a consequence of a number of diseases. Humoral immune deficiency can exist alone or as part of a wider immune deficiency syndrome. Immunoglobulin products can be used to prevent recurrent infections in these patients. In most clinical settings IVIG will be the product of choice for managing these patients.

For replacement therapy in antibody deficiency disorders, monthly administration of IVIG is given, usually at a dosage of 300–400 mg/kg of body weight. The dosage and frequency of infusion should be based on the effectiveness in the individual patient. In general, however, the aim of treatment should be to maintain the serum IgG at or above a level of 5 g/L. IVIG may also be used to treat Kawasaki disease, immune mediated thrombocytopenia, paediatric HIV infection, and conditions in adults such as chronic lymphocytic leukaemia and after a bone marrow transplant. It is important to consult a specialist physician/paediatrician for advice.

18.4 Storage and administration

Immunoglobulin products must be stored at +2°C to +8°C and must not be frozen. They should also be protected from the light. Always check and observe the manufacturer's expiry date before injecting the product. Discard unused portions of an ampoule. Record the batch number of the dose injected on the recipient's records.

Intramuscular human normal immunoglobulin should be given using a large (20 G) needle. This product should not be given intravenously because of the possible reactions discussed below.

18.5 Duration of effect

The half-life of immunoglobulin in the circulation is approximately three weeks. It is estimated that at the recommended doses, protective levels will be maintained for three to four weeks.

18.6 Expected responses and adverse reactions

Any severe or unexpected reactions to any immunoglobulin product should be reported on a form obtainable from the New Zealand Blood Service.

Local tenderness and muscle stiffness occasionally occur at the site of injection and may persist for several hours after intramuscular injection. An occasional recipient may react more strongly, with erythema or low grade fever. Systemic reactions, urticaria and angioedema may occur.

Reactions to IVIG tend to be related to the infusion rate and are most likely to occur during the first hour of the infusion. However, delayed reactions can occur, and include nausea, vomiting, chest pains and rigors. Systemic and local reactions are more common in those being treated for hypogammaglobulinaemia than in those with normal gammaglobulin levels who are being treated with immunoglobulin preparations for autoimmune conditions.

There have been occasional reports of renal failure following infusion of IVIG. These largely relate to sucrose containing products. Intragam[®]P, the product available in New Zealand, does not contain sucrose, but patients should be adequately hydrated prior to administration of Intragam[®]P. Renal function should be monitored in patients considered to be at increased risk.

Aseptic meningitis has been reported following treatment with IVIG. This may present up to two days following treatment. Anaphylactic reactions, although rare, have been reported following injection of immunoglobulin products, although anaphylaxis is more likely to occur following intravenous infusion (see below).

Immunoglobulin products may interfere with the immune response to live virus vaccines (see section 1.9 and Table 1.11). In general, live vaccines should be given at least three weeks before or up to six months after the immunoglobulin preparation. This does not apply to the yellow fever vaccine, because New Zealand blood donors are very unlikely to have antibodies to this virus. For travellers abroad this interval may not be possible.

18.7 Precautions and contraindications

Anaphylactic reactions have been reported following injection of immunoglobulin preparations, and anaphylaxis is more likely to occur following intravenous infusion. In highly allergic individuals, repeated injections may lead to anaphylactic shock. For this reason, adrenaline and other means of treating acute reactions should be immediately available.

Skin tests should not be conducted with immunoglobulin preparations. Intradermal injection of concentrated gammaglobulin may cause a local inflammatory reaction, which can be misinterpreted as a positive allergic reaction. Such allergic responses to normal immunoglobulin given in the prescribed intramuscular route are extremely rare, but may occur in those with immunoglobulin A (IgA) deficiency and in whom anti-IgA is present. Approximately 1 in 1200 individuals in New Zealand are IgA deficient, and a small percentage of these have anti-IgA present. All immunoglobulin preparations contain traces of IgA. If a patient is known to be IgA deficient with anti-IgA present, expert advice should be sought before administering these products. It is not current practice, and it is not recommended, to test for IgA deficiency or anti-IgA prior to administering intramuscular human immunoglobulin.

Reference

- 1 Medsafe. 2001. *Intragam[®]P Data Sheet*. URL: <http://www.medsafe.govt.nz>