Introduction to immunoglobulins

An immunoglobulin or antibody is a Y shaped protein that is produced by plasma cells (from B-cells lymphocytes) and helps to identify and neutralise foreign objects such as bacteria or viruses. These foreign objects are referred to as antigens. Antibodies are formed when the body encounters an antigen and are specifically produced just to fight one type of antigen. You can measure antibodies in the blood after a vaccination to see if the patient has responded to the vaccine. Immunoglobulins also enhance phagocytosis, aid in the neutralization of viruses, and activate the complement system.

Immunoglobulins are extracted from plasma donations. To minimize the risk of transmission of blood borne infections, all donors are tested for some critical blood borne viruses such as hepatitis B and C viruses or HIV. During the plasma fractionation process, independent viral inactivation steps effectively remove or eliminate both enveloped (e.g. hepatitis B and C viruses and HIV) and non-enveloped (e.g. hepatitis A virus and parvo virus B19) viruses. The methods used to prepare immunoglobulin products and to remove viruses vary slightly between companies. A list of products is provided in Appendix 1.

There are several subcutaneous products (16% product to a 20% product) available in Europe, one of them is facilitated immunoglobulin and requires the administration of recombinant human hyaluronidase prior the infusion. There are several IV products available in Europe with concentrations ranging from 5% to 10%. Each product has different levels of IgA and different stabilizers. Research to develop new products is a continuing process.

Replacement therapy

The indications for immunoglobulin therapy vary. Many patients with primary or secondary immunodeficiency are unable to produce (enough) properly working immunoglobulins. Genetic or acquired defects in the cells producing immunoglobulins lead to a failure or a reduction in the amount of antibodies in the blood. Immunoglobulin replacement therapy can help these patients fight infections. There are numerous genetic conditions that can cause primary immunodeficiencies (1), and further information can be found on the INGID webpage (www.INGID.com). Secondary immunodeficiency is caused by damage to the immune system by an extrinsic or environmental factor, such as chemotherapy, monoclonal antibody therapy or bone marrow transplantation, or by severe immunoglobulin loss due to diarrhoea, for example (2).

In replacement therapy, the starting dose is usually 0.4–0.6 g/kg body weight (BW) per 4 weeks. Some countries administer immunoglobulins at an interval of 3 weeks; please check your local guidelines. There is conflicting evidence that some patients with low immunoglobulin A might have high titres of anti-IgA antibodies that may cause adverse events or non-IgE-mediated anaphylaxis. Therefore, the first infusions (during 4–8 weeks) must always take place in a

hospital setting; this time should also be used for patient education. After that, it is safe to continue the treatment at home (3, 4).

Immunomodulatory therapy

Immunomodulatory therapy is used in neurology, haematology and dermatology indications. In Europe, approved indications for immunomodulatory therapy with immunoglobulins are immune-modulated thrombocytopenia, Kawasaki's disease and Guillain-Barré syndrome. Some of the products are also approved for chronic inflammatory demyelinating polyneuropathy (CIDP) and multi motor neuropathy (MMN). Immunomodulatory therapy is also often used off-label in patients with myasthenia gravis or multiple sclerosis (MS), for example. The starting dose for immunomodulatory therapy is in the range 1.0–3.0 g/kg BW (5). As doses are significantly higher than in replacement therapy the risk of adverse events is higher. Extra care should be taken with these patients (6, 7).

The choice of administration route, frequency and treatment location for each individual patient needs to be carefully assessed. It should remain flexible during different stages of life and it requires on-going assessment in partnership with the patient.

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