Scleroderma Association B.C.

INTRAVENOUS IMMUNOGLOBULIN AND SCLERODERMA

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Systemic sclerosis (or scleroderma) is an autoimmune disease in which the immune system is dysfunctional and attacks its own cells, leading to excessive scarring (fibrosis) of the skin and internal organs. Intravenous immunoglobulin (IVIg) is a blood product used to treat certain autoimmune diseases. In this article, we will discuss the role of this treatment in scleroderma.

WHAT IS INTRAVENOUS IMMUNOGLOBULIN?

IVIg is a blood product made from a mixture of antibodies that can be given intravenously (through a vein). Antibodies are proteins produced by the body to fight infections. IVIg is prepared from the blood of thousands of human blood donors and, therefore, contains a wide variety of antibodies.

WHAT IS THE MECHANISM OF ACTION OF INTRAVENOUS IMMUNOGLOBULIN?

IVIg is used primarily in two types of diseases: immunodeficiencies and autoimmune diseases.

In immunodeficiencies, the body does not produce enough antibodies, making it vulnerable to infections. In this situation, immunoglobulin treatments are used to replace the missing antibodies to help the body protect itself from infections.

In autoimmune diseases, the immune system is dysfunctional and produces antibodies that attack its own cells (autoantibodies). In this situation, the antibodies and other substances contained in IVIg could act by neutralizing the abnormal autoantibodies and interfering with the development and function of immune cells, including B-cells, which are responsible for producing the abnormal autoantibodies. IVIg might also act on fibrosis, by

interfering with small proteins in the blood (cytokines) that are involved in fibrosis formation. The mechanism of action of IVIg in autoimmune diseases is complex and only partially understood, but overall, IVIg appears to interfere with various components of the immune system and may be beneficial in the treatment of some autoimmune diseases.

HOW IS INTRAVENOUS IMMUNOGLOBULIN ADMINISTERED?

Immunoglobulins are administered intravenously, that is, through a vein. The total dose of IVIg required depends on the individual's weight and is usually divided over two to five days, with each infusion lasting several hours. This allows for a more gradual infusion, which reduces the risk of side effects. Each infusion cycle (over two to five days) may be repeated monthly and the total duration of treatment is determined by the specific disease under consideration and response to treatment. IVIg infusions are usually administered in a hospital medical day unit or infusion clinic.

ARE IMMUNOGLOBULINS EFFECTIVE IN THE TREATMENT OF SYSTEMIC SCLEROSIS?

A systematic review of the literature was published in 2021 summarizing clinical studies performed on IVIg treatments in systemic sclerosis from the years 2000 to 2020 (Agostini *et al*.) A total of 17 studies, including 182 patients, were identified.

Most of these studies reported the experience of patients with scleroderma who received IVIg treatments, but without a control group. These patients were treated with IVIg because of severe and refractory disease (unresponsive to conventional therapies), coexisting muscle inflammation (IVIg is used to treat myositis) and/or concomitant infections (thus precluding the use of conventional immunosuppressive therapies). IVIg has been used primarily to treat diffuse skin and muscle involvement, but also for severe joint (arthritis), cardiac (myocarditis/inflammation of the heart), pulmonary (inflammation of the lungs) and/or gastrointestinal manifestations. Improvements have been noted in many of these patients after one or more cycles of treatment, with rapid and sometimes sustained benefits.

Only one study was a randomized, placebo-controlled, double-blind clinical trial. This type of study is the best way to determine the efficacy of a treatment, because it allows the treatment to be compared to a control group (and thus compared to the natural course of the disease), eliminates the placebo effect (improvement in the disease related to the psychological benefit of receiving the treatment), and reduces the effect of confounding factors (by randomly separating the groups). In this study published in 2013 by Takahera *et al*., 63 participants with the diffuse form of systemic sclerosis from 17 medical institutions in Japan received an IVIg treatment or placebo. The results: the mean decrease in skin fibrosis score was not significantly different between the two study groups at 3 months after a single cycle of treatment. However, when a second cycle of treatment was given at 6 months to all participants who had not improved, a significantly greater reduction in skin fibrosis score was observed in the group that received 2 doses of IVIg compared to the group that initially received a placebo.

In summary, IVIg may be effective in the treatment of systemic sclerosis, given its potential effect on autoimmunity and fibrosis, and based on mostly uncontrolled studies reporting benefits in patients with severe and refractory disease. However, randomized controlled trials with a longer duration of treatment and larger numbers of participants would be required before a more definitive conclusion can be reached regarding the efficacy and role of IVIg in the treatment of systemic sclerosis.

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COULD I BENEFIT FROM TREATMENT WITH IMMUNOGLOBULINS?

As previously discussed, the efficacy of IVIg has not yet been definitively established and, therefore, this treatment is not commonly used in the treatment of systemic sclerosis. However, IVIg may be considered in certain specific situations, such as for severe skin, muscle, joint, heart, lung or gastrointestinal involvements that are refractory to conventional treatments. IVIg may also be considered when there is a contraindication or intolerance to conventional immunosuppressive treatments. For instance, IVIg is considered safer than immunosuppressive drugs for the risk of infectious complications. It should be noted, however, that current access to IVIg is limited due to a worldwide shortage of this blood product and its very high cost, and may require special authorization.

WHAT ARE THE POSSIBLE RISKS OF INTRAVENOUS IMMUNOGLOBULIN TREATMENT?

Most patients who receive IVIg tolerate the infusion very well. However, some patients may experience side effects, such as headache, chills, fever, muscle aches, fatigue or nausea. These symptoms are usually mild and occur most often after the first dose. More serious side effects, such as an allergic reaction, heart or kidney failure, non-infectious meningitis or anemia, may occur but are very rare. Myocardial infarction (heart attack), stroke and thrombosis (blood clots) have been reported, but are very rare when the infusion is administered slowly over several days. Although IVIg is a blood product, the risk of infection is extremely low because the methods used to purify the immunoglobulins destroy bacteria, hepatitis viruses and other infectious organisms.

IN SUMMARY

IVIg is a blood product composed of a mixture of antibodies and have beneficial effects on autoimmunity and fibrosis. Studies have reported a beneficial effect of IVIg in some patients with severe scleroderma refractory to conventional treatments, but more clinical studies are needed before a more definitive conclusion can be made about their efficacy. Nevertheless, IVIg may be tried in certain specific situations, such as when other therapeutic options have failed or are contraindicated.

References:

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