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NUH Women's Centre
Is My Answer

Intravenous Immunoglobulin Therapy in Recurrent Pregnancy Loss

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Miscarriages are common, affecting up to 15% of couples trying to establish a family. Recurrent Pregnancy Loss (RPL) however, is a challenging clinical condition that affects up to 5% of these couples. Up till today, no explanation is found in up to 50% of couples with RPL. Immune dysfunction has been increasingly implicated as a cause in this group as research in this arena has uncovered in the past two decades.

To date, many tests to evaluate immune dysfunction are still available only in the research setting. However, evidence shows that immunotherapy in the form of intravenous immunoglobulin (IVIG) may benefit some women with RPL.

What is Immunologic RPL?



It is the loss of a natural or IVF (in-vitro fertilisation) pregnancy due to abnormal function of the immune system (immune dysfunction).

What is IVIG?

IVIG is an injection of immunoglobulin (pooled-plasma protein) from blood donors. It is a solvent treated, freeze-dried preparation, containing more than 95% highly purified immunoglobulin G (IgG).

IVIG was first used in 1952 to treat patients with hereditary forms of low immunity (eg. Agammaglobulinemia). Over the decades, it has also been used in the treatment of various auto-immune diseases such as systemic lupus erythematosus, immune thrombocytopenia, and myasthenia gravis, among others.

How does IVIG help my pregnancy?



Studies have shown that Natural Killer (NK) cells play a crucial role in early pregnancy in terms of implantation of the embryo and placental development. However, some women with RPL have been shown to have higher blood NK cells of the aggressive type. Instead of helping with the implantation process, such NK cells cause miscarriages.

Studies have shown that IVIG has the capacity to reduce NK cell aggressiveness and has anti-inflammatory effects. It also has been shown to help in women with “sticky blood syndrome” (antiphospholipid syndrome) by lowering the levels of the sticky blood antibodies and reducing inflammation that promotes clotting in the placenta.

A recent study showed that IVIG if given before pregnancy, was effective in those with one live birth as well as those with no previous live births.

It must be recognised that IVIG **cannot help all** patients with RPL. It has the greatest benefit in those with abnormal immune tests, high NK cells and higher number of miscarriages.

What are the side effects of IVIG?

Severe side effects of IVIG are rare in well selected patients. Most commonly, mild side effects such as fever, headache, muscle aches, and nausea may occur in up to 10% of patients.

Recognised side effects



Minor Reaction (Most common)

- Headache
- Muscle aches
- Fever < 38.5°C
- Chills
- Light-headedness
- Nausea
- Vomiting

Moderate Reaction (Uncommon)

- Fever > 38.5°C
- Blood pressure changes
- Breathlessness
- Skin rashes

Severe Reactions (Rare)

- Occurs in patients who are unfit, elderly, overweight, have other serious medical problems*
- Acute kidney failure (usually reversible)
- Severe allergic reactions
- Transmission of blood-borne pathogens*

* non-reversible

Is this treatment safe in pregnancy?



Data from trials suggest that IVIG has an acceptable safety profile for both mother and the foetus.

Who cannot receive this treatment?



Patients who have pre-existing heart or kidney disease; as well as those with diabetes, low levels of serum IgA should not receive this therapy.

What is the treatment regime like?



Generally, most overseas centres that use immunotherapy for RPL recommend a monthly infusion preferably before conception or embryo transfer and it should be continued throughout pregnancy up to 28 weeks.

What are the costs involved?



The treatment averages S\$2,500 per infusion. Therefore the other causes of RPL such as chromosomal or genetic need to be ruled out before this therapy is undertaken.

Do I need to undergo any tests?



Please consult your doctor for more information.

@The information provided is not exhaustive. Further discussion with your physician is strongly recommended.