IVIG Treatment for Infertility
Targeting NK Cells in Pregnancy

© Elaine Moore

Nearly 80 percent of all reproductive problems in women are due to immune system problems; intravenous immunoglobulin therapy, used off-label, offers benefits.

Reproductive Medicine

According to Dr. Alan Beer, a pioneer in the field of reproductive medicine who died in 1996, up to 80 percent of problems with infertility are caused by immune system problems or autoimmune infertility. The most common cause is the autoimmune condition antiphospholipid syndrome. Other immune problems include blocking factors or incompatibility to specific HLA antigens, ovarian antibodies, and elevated levels of Natural Killer Cells.

What are Natural Killer (NK) Cells?

Lymphocytes are blood cells involved in the immune response, and Natural Killer (NK) cells are a subtype of lymphocytes that plays an important role in the immune system’s host response in destroying or lysing infectious and malignant cells. NK cells, which are large granular lymphocytes, become activated and proliferate when they receive signals from other immune system components such as interferon and various immune system cell receptors. The granules in the cytoplasm of NK cells contain a number of toxic proteins.

Natural Killer cells are present in the bloodstream and upon receiving appropriate signals they can occur in various organs. NK cells present in the endometrium of non-pregnant women work in conjunction with hormones to assist with ovulation ad reproduction. Levels of endometrial NK cells rise dramatically after ovulation. Several studies show that treatments aimed at reducing NK cell levels are beneficial in patients with immune-mediated fertility problems.

Natural Killer Cells are produced in the bone marrow and in the decidua. The decidua refers to the uterine lining (endometrium), which is composed of large cells that aid in implantation during pregnancy. The decidua is shed during menstruation and with the placenta during childbirth. NK cells produced in the decidua have a greater potential for toxicity than cell produced in the bone marrow. The NK cells produced in the decidua, which are phenotypically and functionally different from the NK cells of the bone marrow, produce large quantities of the cytokine Tumor Necrosis Factor (TNF) that are capable of killing the placental and fetal cells.

CD 56+ and 16+ NK Cells in Pregnancy
Natural Killers are identified by the proteins CD56+ with or without 16+, which serves as surface immune system markers. CD56+ NK cells are the dominant type of maternal immune system cell found in the uterine mucosa (inner lining) during formation of the placenta and they persist in large numbers at the implantation site. NK Cells are activated by a pregnancy that fails or by a fertilized embryo that begins to degenerate. The normal range of CD56+ NK cells in the blood circulation ranges from around 5-12 percent. Levels of 18 percent or higher are associated with poor reproductive outcome.

**Using Intravenous Immunglobulins**

However, critics point out that the NK cells of the decidua differ from the NK cells present in the blood, and that the activity of the NK cells is more important than the amount. Regardless, the use of intravenous immunoglobulin therapy to reduce NK levels has resulted in successfully pregnancies.

Normally, NK cells found in the endometrium help with vascular function, and they help sustain fetal trophoblasts. However, when there are problems with implantation or pregnancy itself NK cells activated. One of the goals in reproductive medicine is to reduce the number of NK cells with steroids, intravenous immunoglobulins (IVIg), or tumor necrosis factor-alpha blocking drugs such as Enbrel.

In one study of 47 women with various immunologic abnormalities and an average age of 37 years, a low dose of IVIg was given two weeks before anticipated conception and continued through either 12 or 30 weeks of pregnancy. In this study 75 percent of treated women had successful pregnancies, whereas the 7 women who did not use IVIg therapy all miscarried.

**Resources:**


The copyright of the article NK Cells in Pregnancy in Autoimmune Disease is owned by Elaine Moore. Permission to republish NK Cells in Pregnancy in print or online must be granted.