Immune Globulin and Pregnancy

While the medical community believes the benefits of IG therapy outweigh the risks during pregnancy, dosing adjustments may be needed for immune-deficient patients.

By Leslie J. Vaughan, RPh

Many patients who are prescribed immune globulin (IG) therapy have concerns about whether the drug is safe during pregnancy. While there is no definitive answer to this, pregnancy is listed as a precaution for IG. For instance, WebMD states that "during pregnancy, this medication should be used only when clearly needed." Of course, IG is clearly needed by immune-deficient patients, as well as many autoimmune disease patients. The good news, then, is that most physicians believe IG is safe during pregnancy, and that its benefits outweigh its risks. In addition, there are many case reports of patients being treated with IG with no adverse effects to the fetus.

Benefits vs. Risks

Upon a medicine's approval, the U.S. Food and Drug Administration assigns it one of five pregnancy categories that indicate the potential of a drug to cause harm to the fetus if used during pregnancy (Table 1). Each category outlines whether clinical studies have shown any potential risks of the drug during pregnancy. IG falls under category C, which means that either no animal or human studies have been conducted or animal reproduction studies have shown drugs in this category to have an adverse effect on the fetus, but there are no well-controlled studies conducted on humans to date. IG's potential benefits may warrant its use despite potential risks.

The current belief in the medical community is that IG therapy is safe during pregnancy. But, the decision to continue to infuse IG during pregnancy is one that should be made with the treating physician, and it should be based on a risk-benefit analysis. A standard risk-benefit analysis considers all the benefits of using a medication and weighs those benefits against the risks of potential adverse events that may be caused by the medication. For women who are pregnant, the risk-benefit analysis should consider both the benefits of the medication and the risk of adverse events to both the mother and the developing fetus. For IG, the risk-benefit analysis should also include the risk of stopping the medication. For example, someone being treated with IG for an immune deficiency may be at increased risk of developing serious infections if IG is stopped during pregnancy. Ideally, a patient with a chronic condition being treated with IG or any other drug should discuss pregnancy with her physician well in advance of becoming pregnant. This will allow for the development of a solid treatment plan to support both the mother and the baby during pregnancy.

IG Dosing

Currently, there is no specific protocol published for IG therapy during pregnancy. According to Dr. Marc Riedl, associate professor of medicine in the division of rheumatology, allergy and immunology at the University of California, San Diego, "it's well-recognized that IgG trough levels will fall in the second and third trimesters due to placental transfer, blood volume and weight gain." So, he says it is advisable to begin checking the trough levels of those with an immune deficiency during the second trimester and to make dose adjustments to keep IgG levels well within the normal range. And, toward the end of gestation, it may be necessary to increase the frequency of the infusions. "In my experience, antibody deficient patients do very well during pregnancy with these relatively simple measures," says Dr. Riedl.

For patients with autoimmune conditions, IgG trough levels aren't a valid test for determining the correct dosing adjustments. Instead, the best indicator is to assess the specific symptoms related to the condition prior to pregnancy with the goal of maintaining the patients' symptoms at the same or improved levels. If during the course of pregnancy the patient declines clinically, the physician may consider a modest dose increase to regain control. According to Dr. Todd Levine, director of the department of neurophysiology at Good Samaritan Hospital in Phoenix, Ariz., he adjusts the IG dose for autoimmune disease patients only if symptoms get worse. Otherwise, he keeps his patients on the pre-pregnancy dose throughout gestation.

Case Studies

Several studies conducted in the past have assessed the safety of receiving IG during pregnancy. Most of these

Table 1. U.S. Food and Drug Administration Pregnancy Categories

The FDA-assigned pregnancy categories as used in drug formularies are as follows:	
Category A	Adequate, well-controlled studies in pregnant women have not shown an increased risk of fetal abnormalities.
Category B	Animal studies have revealed no evidence of harm to the fetus, however, there are no adequate and well-controlled studies in pregnant women. **or** Animal studies have shown an adverse effect, but adequate and well-controlled studies in pregnant women have failed to demonstrate a risk to the fetus.
Category C	Animal studies have shown an adverse effect and there are no adequate and well-controlled studies in pregnant women. **or** No animal studies have been conducted and there are no adequate and well-controlled studies in pregnant women.
Category D	Studies, adequate well-controlled or observational, in pregnant women have demonstrated a risk to the fetus. However, the benefits of therapy may outweigh the potential risk.
Category X	Studies, adequate well-controlled or observational, in animals or pregnant women have demonstrated positive evidence of fetal abnormalities. The use of the product is contraindicated in women who are or may become pregnant.
NA	FDA pregnancy rating not available

articles are small case studies of patients who were receiving IG for a chronic condition prior to becoming pregnant, and continued to receive IG during the course of their pregnancy. And, each of the studies found it was safe to continue IG therapy with no adverse events noted for the mother or the baby. Three of these studies focused on patients with common variable immune deficiency who were treated with IG during pregnancy and whether dose adjustments were needed. The common result from each of these studies found dosing adjustment was necessary during the course of the pregnancy to keep IgG trough levels at pre-pregnancy levels. The need for increased dosing in the late second and third trimesters is thought to be due to plasma volume expansion. The studies also found that babies born to immune deficient patients who continued IG therapy during pregnancy had adequate IgG levels after birth, whereas babies whose immune-deficient mothers were not treated throughout pregnancy had slightly lower birth weights and presented with lower IgG trough levels. The studies did note, however, that low birth weight babies did develop normally and did not have any long-term impact.

Communication Is Key

While there are no current studies directed at testing the safety of IG treatment during pregnancy, current practical experience has found IG to be safe and effective, and the benefits of IG therapy are believed to outweigh the risks. However, each patient is different. Therefore, close communication between the patient, the IG prescriber and the Ob/Gyn physician throughout the pregnancy will allow for timely dose adjustments when necessary. ■

LESLIE J. VAUGHAN, *RPh, is senior vice president of clinical services at NuFACTOR Specialty Pharmacy.*

Reference

1. Otugo, O, Chou, J, Ogundare, O, et al. Assessment of the Consistency of Pregnancy Labeling Across Therapeutic Classes. Onyeka et al; Office of Women's Health FDA Pediatric and Maternal Health Staff, Maternal Health Team, CDER. Accessed at www.fda.gov/downloads/scienceresearch/specialtopics/womenshealthresearch/ucm309188.pdf.

Sources

1. Clark, AL, and Gall, SA. Clinical Uses of Intravenous Immunoglobulin in Pregnancy. *American Journal of Obstetrics & Gynecology*, 1999 Jun;42(2):368-80. Accessed at www.ncbi.nlm.nih.gov/pubmed/10370855.
2. Osada, H, Morikawa, Y, Nishiwaki, T, and Sekiya, S. Intravenous Immunoglobulin Replacement Therapy for Common Variable Immunodeficiency during Pregnancy. *Archives of Gynecology and Obstetrics*, 1996;258(3):155-9. Accessed at www.ncbi.nlm.nih.gov/pubmed/8781705.
3. Schaffer, FM, and Newton, JA. Intravenous Gamma Globulin Administration to Common Variable Immunodeficient Women during Pregnancy: Case Report and Review of the Literature. *Journal of Perinatology*, 1994 Mar-Apr;14(2):114-7. Accessed at www.ncbi.nlm.nih.gov/pubmed/8014693.
4. Sorensen, RU, Tomford, JW, Gyves, MT, Judge, NE, and Polmar. SH. Use of Intravenous Immune Globulin in Pregnant Women with Common Variable Hypogammaglobulinemia. *American Journal of Medicine*, 1984 Mar 30;76(3A):73-7. Accessed at www.ncbi.nlm.nih.gov/pubmed/6424460.