

ADVANCES IN IBD

Current Developments in the Treatment of Inflammatory Bowel Disease

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Inflammatory Bowel Disease, Women, and Pregnancy



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G&H How informed are clinicians, especially nongastroenterologists, about pregnancy and inflammatory bowel disease?

SK They are hardly informed at all. One reason is because management of inflammatory bowel disease (IBD) is usually the domain of the gastroenterologist, although this trend is changing. More and more internists are finding themselves responsible for the care of patients with IBD. IBD is still such a dynamic and ever-changing field of study, though, that even practicing gastroenterologists feel a need to be attending every IBD session presented at major meetings to keep up. So, family practitioners, internists, and obstetrician-gynecologists (OB-GYNs) may be naturally nervous about treating patients with IBD. Even OB-GYNs who specialize in high-risk pregnancies appreciate a very engaged, actively involved gastroenterologist when working with patients who have gastroenterologic challenges.

G&H What are some of the common misconceptions about IBD and pregnancy among patients?

SK The first misconception is that women with IBD cannot get pregnant—that somehow having that diagnosis is a contraindication to pregnancy—which is absolutely not true. Another misconception is that women who have IBD will automatically have a complicated pregnancy. This is also not true. Yet another misconception is that a patient needs to stop her IBD therapy if she wants to get pregnant; or else, once she learns that she is pregnant,

the patient is set up to fear that her IBD medication is going to cause pregnancy complications, although thiopurines at the doses used for management of IBD have been shown to be safe in pregnant patients. Thiopurine use for IBD is off-label, but US Food and Drug Administration–approved indications and dosages for thiopurines carry alarming pregnancy warnings in the labeling.

G&H What kinds of complications do women with IBD encounter, and how are they planned for?

SK Patients with IBD are at higher risk for venous thrombosis when not pregnant; so, it is no surprise that the risk of venous thrombosis increases during pregnancy, given that pregnant women are generally at increased risk for this complication. In terms of obstetric complications, patients with IBD are not at any more risk—other than for venous thrombosis—than are patients without IBD. IBD does not increase the risk of fatty liver of pregnancy, hyperemesis gravidarum, preeclampsia, or any other pregnancy-related syndromes. In terms of pregnancy outcomes, however, IBD increases the chance of small gestational age at birth, low birth weight, and preterm birth.

G&H How does the gastroenterologist prepare the patient who plans to become pregnant?

SK The patient will require a lot more follow-up than a patient without IBD. Disease activity during conception and pregnancy is a key factor in whether an IBD-related

adverse birth outcome might occur, but if disease is in remission, then increased risk is nil. Although there is no evidence that Apgar scores are decreased or that developmental milestones are not met in babies born to women with IBD, selecting a pediatrician who can expertly address adverse outcomes of pregnancy and developmental complications might be good planning.

Some gastroenterologists recommend that, on the very first visit when a woman receives a diagnosis of IBD, a discussion take place concerning IBD and pregnancy. I have not been an advocate of this practice because I think that there are many other more important issues that should be covered on that first visit. The patient may never have thought about pregnancy and may become overwhelmed if the gastroenterologist suddenly forces the topic on her. A more appropriate strategy might be to take time to speak to the patient about her life plans and thoughts about family planning after she has visited the office a few times, has been doing well on treatment, and is in remission. It is at this time that the patient has the opportunity to say something like, "Well, hold the phone; I'm working on my PhD, and I don't even have a boyfriend." My response then would be, "OK, if your situation or preferences change, come back, and let's talk."

If a woman tells me that having children is not a priority, I do not force the issue about IBD and pregnancy. Many male gastroenterologists insist that pregnancy and family planning issues must be addressed early. They also base treatment recommendations on whether the patient has 2 X chromosomes, but very many female patients are not interested in becoming pregnant; therefore, therapeutic choices should not be solely based on the chance that a pregnancy might possibly occur in these patients.

G&H What therapeutic agents are used or should be selected for women of childbearing potential?

SK It is important to recognize that a woman may have childbearing potential, but 1 out of every 7 couples in North America is infertile. I will reiterate that just because a woman has childbearing potential does not mean that medication decision-making should be predicated on that 1 factor. It is a factor if the patient tells you, "I'm engaged, and my fiancé and I want to start a family soon after the wedding." My response then is, "Okay, let's make sure your IBD is in remission before you become pregnant."

The only drug that absolutely cannot be used to manage IBD during pregnancy is methotrexate. Although thiopurines have labeling that causes concern, the bigger picture about the safety warning and also what is known about the safety of thiopurines in IBD needs to be explained to the patient. Thiopurine teratogenicity

was identified in animal studies but was associated with intrathecal or intra-abdominal injections of doses that were tens to hundreds of times higher than what is given orally to a patient. If a thiopurine is injected directly into the abdominal cavity, complications may arise, but when taken orally at the doses given for IBD—with the drug's relatively poor absorption—the amount that circulates in the serum really is negligible compared with the amount that laboratory animals were exposed to in toxicology studies.

G&H Can anti-tumor necrosis factor agents be used in women of child-bearing potential?

SK Anti-tumor necrosis factor (anti-TNF) agents, or biologics, are proteins, not medicines, and have been shown to be generally safe in pregnancy. The first-generation agent infliximab (Remicade, Janssen) and the second-generation agent adalimumab (Humira, AbbVie) cross the placenta, but certolizumab pegol (Cimzia, UCB Pharma), which is just a fragment of an antibody, does not cross the placenta, and this is stated in the labeling. Because certolizumab pegol does not cross the placenta, it is perceived as being "better" than the other 2 anti-TNF agents across the board for women. Again, this is not necessarily appropriate reasoning. A female patient may not be interested in pregnancy and may be very compliant with birth control and so may not require treatment focused on the possibility of pregnancy. Considering that most anti-TNF agents elicit a response for, at best, 3 to 4 years before the patient needs to be switched to another agent, it might be wise to use another anti-TNF agent in a patient who does not want to become pregnant now but may want to down the road, at which time, the gastroenterologist could start the patient on certolizumab pegol if she has concerns about fetal exposure to an anti-TNF agent.

G&H If a patient becomes pregnant while experiencing active disease, how is she managed?

SK Management depends on whether the patient has ulcerative colitis or Crohn's disease. It also depends on whether the flare developed while she was on standard therapy or whether the flare occurred because the patient stopped her medication. The first step is to treat her as if she was not pregnant and do what is appropriate to find out what is going on and then make treatment decisions based on the disease activity. Obviously, there are some caveats. Magnetic resonance imaging (MRI) would be chosen over computed tomography to avoid radiation exposure, and if the patient is in her first tri-

mester, a noncontrast MRI would be ordered because exposure to gadolinium is contraindicated. Then, the gastroenterologist should perform a physical examination, examine the patient's history, and do some stool studies. This is the way that a gastroenterologist would work up anybody's flare regardless of pregnancy status. If the flare occurred because the patient discontinued medication, the clinician would restart it and hope for the best. The disease should be treated as aggressively as needed; if corticosteroids are needed, they should be given, or an anti-TNF agent could be started during pregnancy to control the flare.

G&H Are there circumstances in which pregnancy is contraindicated in patients with IBD?

SK There are very few instances in which pregnancy would be contraindicated. If the patient is in immanent need of an operation, if she has symptomatic anemia, or if she has active malabsorption issues, pregnancy would be contraindicated because the fetus is, after all, feeding off the mother, and if the mother has low reserves, the fetus also would be at a loss.

G&H What is the effect of pregnancy on IBD?

SK A European study that was conducted about 7 years ago found that women with IBD who got pregnant had fewer IBD flares following their pregnancies than those who did not get pregnant. Since that time, some basic science has been done to show that pregnancy changes the environment of the maternal immune system and, potentially, the microbiota, as well. Indeed, there are circumstances in which IBD is treated with a pregnancy. The pregnancy downregulates the immune system so much that it puts the IBD into remission.

G&H What is your best advice for office-based gastroenterologists about how to address patients' concerns about IBD and pregnancy?

SK Gastroenterologists should discuss the prospect of pregnancy with a patient before it occurs, but they should not assume that every woman wants to become pregnant or is going to ever be pregnant. Unless the patient is insisting that she wants to become pregnant immediately, the gastroenterologist should treat the patient as if pregnancy is not an issue. When family planning concerns are ultimately discussed with patients, the message to those patients who are planning for pregnancy is that the best time to be pregnant is when they are well and that the physician-patient goal should be working toward this. If the patient becomes pregnant, especially before remission has been achieved, she needs to be advised to immediately inform her gastroenterologist so that she can be properly managed from the start.

Dr Kane has no conflicts of interest to disclose.

Suggested Reading

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