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Bridging the patient education gap: Moving from OI to IVF

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DISCLOSURES

Jennifer Barocas, RN, FNP, discloses no relationships.

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Margaret Post, RN, reports that she has served as a consultant for Schering-Plough and Ferring Pharmaceuticals.

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When a woman using ovulation induction is deemed a candidate for in vitro fertilization, the resulting change in medication regimens can seem daunting. With the objective of simplifying this process for patients and caregivers alike, several seasoned clinicians in the field of fertility were asked to share their experiences in a roundtable discussion. The following summary of that discussion ranges across a number of issues, including teaching insights, cost considerations, and variations among practices.

SHUBIN I'd like to start with an instructive case. A 35-year-old woman in a same-sex relationship using donor sperm came to our center after several unsuccessful attempts at ovulation induction (OI) elsewhere, 2 of the cycles with Clomid. We started her on Follistim, 50 IU/d, with microtitration. She produced just one follicle with no resultant pregnancy. In her second cycle, we switched her to Bravelle, 75 IU/d, due to financial reasons, and she produced 2 mature follicles and had a positive pregnancy, which resulted in a missed abortion due to a trisomy. In the third cycle, we gave her Bravelle at 150 IU/d for the first 3 days and then reduced the dose to 75 IU/d. She produced 4 mature follicles, but no pregnancy resulted. Due to her advanced maternal age and history of trisomy, it was decided that in vitro fertilization (IVF) with genetic screening would offer her the greatest success for a clinical pregnancy with live birth.

Since we were adding Menopur to her IVF treatment protocol, keeping her on Bravelle helped make the transition from OI to IVF smooth. It also kept the cost down. The patient produced 10 eggs: 6 were fertilized and 3 were screened as chromosomally normal.

For patients who start on Bravelle during timed intercourse cycles or intrauterine insemination cycles, we tend to keep them on Bravelle when they move on to IVF, and they receive Menopur as well. The IVF process is inherently stressful, and we have found that the option of giving one injection for at least the first 4 to 6 days helps relieve anxiety, minimizes injection training time, and reduces call-backs with questions.

JOSSIM In the last year, we have gone to Menopur and Ganirelix for OI

There may be discussion of off-label or otherwise nonapproved uses of products and/or devices.



patients. One of our patients taking that combination converted to IVF and did very well. We now use Menopur and Ganirelix most often so patients can convert easily to IVF if necessary.

LASKOWSKI During OI cycles at our center, most patients use a mixed protocol. Bravelle/Menopur is generally the combination of choice, given the ease of instruction and administration. This is also more efficient for us in that, if a patient moves forward with IVF, medication instruction is partially completed.

ZAGAMI When we do an all-injectable OI cycle at our center, the nurses generally pick the follicle-stimulating hormone (FSH). I prefer Bravelle with its Q-Cap mixing method. It helps simplify self-administration if we move patients on to IVF and the mixed protocols with Menopur. Some of our doctors have been opting for a straight hMG Menopur injectable cycle for OI, and one of our doctors has also started using Lupron with Menopur.

Medication choices in moving to IVF

SHUBIN When you go from OI to IVF, do you use the same FSH or do you switch brands?

ZAGAMI We generally use the same FSH.

SHUBIN Do you ever find that patients want to switch to a different FSH because it seems more proactive if they have already failed a timed intercourse, intrauterine insemination, or IVF cycle?

ZAGAMI No, they seem more comfortable staying on the same medication. There's so much anxiety to begin with, and the idea of switching and possibly becoming confused about a new regimen can add to the anxiety.

BAROCAS Selections are patient specific. But in New York State it's also insurance specific, with mandates determining which medications we can use. We often start patients on Follistim because we can titrate the dose.

LASKOWSKI The same is true in Illinois. Many patients, for example, are required to use Follistim. However, because a large majority of our patients use a mixed protocol, we still instruct patients in mixing Follistim with Menopur for one injection.

SHUBIN How many of your patients use the pens with microtitration?

BAROCAS For OI cycles, it's around 70%. When patients are older or we expect them to be poorer responders, we may go straight to a Bravelle/Menopur combination with the hope that we can convert them to IVF if they do well enough. But very often we're starting off more slowly.

SHUBIN If patients do not have insurance coverage for their fertility medications, do you ever go straight to Bravelle for financial reasons because it is the least expensive per 75 IU?

BAROCAS Absolutely. If a patient has no coverage for medication, Bravelle is our first-line choice.

POST It's very similar at our center, with choices being driven either by insurance or by patients' out-of-pocket costs. We

have patients who use Follistim and Gonal-f in their OI cycles, with Ovidrel. Many times in the IVF cycles we use a mixed protocol.

SHUBIN Do you switch them over to Bravelle when you do the mixed protocol?

POST Sometimes Bravelle. At other times it's Gonal-f and Menopur. Patients do like to stay with something they have tried, but it's not that much of an issue if they have to switch. The Q-Cap is easy to use once they're instructed in its use.

JOSSIM We pretty much use Bravelle/Menopur exclusively. Most of our patients are paying out of pocket, so we use Follistim or Gonal-f infrequently. Our patients love the mixed protocol in the single injection.

Instructing patients

SHUBIN Injection training occurs at the time of baseline ultrasound assessment; IVF calendars are reviewed and patients are taught how to mix and inject their FSH and hMG. Patients start these injections in 1 to 3 days. If we switch their FSH medications to another brand, our nurses will spend 20 minutes or more in injection training. Keeping patients on the same FSH from cycle to cycle minimizes our time spent with each patient, allowing us to help more patients. How do you handle injection training when you're switching FSH?

BAROCAS We teach injection technique in groups, and we mix OI and IVF patients. So, even if we end up switching OI patients to IVF, they've received instruction and we'll do a brief refresher with them. Group training is less than desirable. But we have far too many patients for one-on-one instruction.

POST We have 2 separate classes for our OI and IVF patients. It is part of the pre-cycle requirement that they attend, and we seldom waive it. We still use intramuscular (IM) hCG and progesterone for IVF, so they need that instruction. Anybody who needs individualized attention can get it at that point during their cycle. Most of the time they're well prepared from the classes. We also have a monitoring nurse available Monday through Friday to review medication mixing and administration techniques.

BAROCAS There is extra time required to instruct some patients when switching medications. However, web-based instruction is very helpful in this regard. If we know ahead of time, we let patients know they can visit, say, www.ferringfertility.com and watch a video of the technique. When they come in, we can go over it with them again. The fact is, some patients will even need retraining for the same thing they were doing before.

ZAGAMI I agree. The ease with which patients deal with their medications varies with the individual. For the most part, though, I find that keeping patients on the same medication makes for a smoother transition from OI to IVF.

JOSSIM We do individual teaching; we don't have the volume that many of you do. We spend probably an hour consulting with each couple, and then we do a review with them on the

IVF start day. The nurses take calls 24 hours a day and we get very few calls on mixing issues. We use the pens only infrequently. The calls we do get, however, regard the pens.

SHUBIN Do you mix injections together? I know some centers will mix Follistim, Gonal-f, Menopur, and Lupron in a single vial and then inject.

LASKOWSKI We do mix Follistim and Gonal-f with Menopur. Menopur is mixed initially using Q-Cap with 1 mL diluent. The Q-Cap is removed and Follistim/Gonal-f is injected directly into the top of the syringe. With this method, we know the patient is getting the prescribed dose.

POST We usually do not mix Follistim and Menopur because the Follistim vial holds just half a milliliter, and if you're mixing large amounts, the dilution is not right. We went back to the Follistim pen, but again, it's such a minute amount that if you put it in the vial, you don't know how much the patient is actually getting. We still give 2 injections, and patients don't complain about them. The only thing they complain about is the IM progesterone injections. So we don't get a lot of phone calls regarding 2 injections.

ZAGAMI Gonadotropins are together in one injection. We do not mix those with the agonist or the antagonist. We do use Menopur. And we'll add Ganirelix at the end of an OI cycle if we know we're going to convert a patient into IVF. And there are select patients for whom we'll recommend a straight hMG OI cycle.

SHUBIN Do you think if they knew that they could do one injection, they would prefer that over the 2 injections?

POST The staff at our center has talked about that. One of the IVF centers mixes Lupron, Ganirelix, or Cetrotide with their stimulation medications. And we just didn't feel comfortable with that. If a patient misses something, we can't be sure what they missed.

BAROCAS There are 10 doctors in our practice and each one has a different philosophy on this matter. With patients who are savvy, we may teach them to mix everything but Ganirelix or Cetrotide, which is always a separate injection for us. But most of our patients are doing separate injections unless they're using the Bravelle/Menopur combination.

SHUBIN If you have a nervous patient, will you pick Bravelle and Menopur to provide a single injection?

BAROCAS Yes, we will.

ZAGAMI We have 18 physicians and they pretty much let the nurses choose the medications. They'll give us the FSH and hMG dosing. If patients have to be on a different drug—say, Gonal-f or Follistim—I will not teach them to mix those with the Menopur. I tell them only to mix the Bravelle with the Menopur.

SHUBIN When you're mixing several vials—say, 4 Bravelle and 2 Menopur—do you still have patients use a Q-cap but add more water? Or do you have them draw it up with a needle?

ZAGAMI We stay with the Q-cap and they're able to mix that with 1 mL.

POST Yes, we're using the 1 mL and going right through with all of the vials that they will need to mix.

LASKOWSKI We use 1 mL diluent, up to a total of 6 vials of a Bravelle/Menopur combination.

JOSSIM If our patients have a BMI greater than 30, they get IM administration.

SHUBIN Do you find that teaching the Follistim/Gonal-f regimen is as easy as teaching Bravelle or Menopur?

ZAGAMI I don't think it's as easy. For one thing, the Gonal-f pen is hard to use. I don't mind the Follistim pen, but I don't use it. I prefer the Q-Cap mixing method. When I'm teaching a class and we get to the hCG injection, patients will ask, "Don't you have a Q-Cap for that?" It's just hard for a lay person to use a needle and syringe and try to get that last drop out of the vial. They don't understand the concept of holding a needle vertically. The hardest thing I find with patients is teaching them to mix with a needle and syringe for hCG. A single teaching technique also lowers patient anxiety.

JOSSIM When the Follistim formulation changed from powder to the pen, we found the pen was very hard to teach. Patients had to learn more than one technique with a mixed protocol. It also led to more shots per day and wasted medication if not used.

SHUBIN Do you have to retrain them in injection technique when you switch them from OI to IVF, if it's a following cycle or a subsequent cycle when using the same FSH or hMG?

ZAGAMI We do retrain patients if they're going from OI to IVF, because of the addition of drugs such as Lupron or Ganirelix, and to accommodate their trigger shot and hCG injections.

SHUBIN At baseline ultrasound, we teach them how to give the first 5 days of medications, usually just FSH, hMG, and Lupron (Lupron flare protocol) if they are using it. Patients will have an ultrasound either after 4 or 5 days of stimulation and are then taught how to inject Ganirelix or Cetrotide if applicable. We teach patients their injections as they come; we call it "baby steps." Do you also teach injections incrementally, or do you teach them everything at once?

ZAGAMI Everything at once. They tend to remember, and we really don't get many questions about mixing or medications. We also give them a booklet that reiterates everything in detail. And we, too, encourage patients to use online resources such as www.ferringfertility.com or the sites hosted by pharmacies. We also have a monitoring nurse who does not have a case load. She's available every morning to answer the phone and handle any questions patients have during the first cycle. And she reviews the beginning protocol with them, too, so our primary nurses can focus on their cases.

JOSSIM On average, our patients come in about every 3 days during their cycling. We're fortunate to have 8 nurses. One of us is always available, and I think it's comforting for patients to have that resource.

Endometrial support

SHUBIN We have minimized our use of IM progesterone. We reserve it for patients who have used it in subsequent cycles and changing them would create more anxiety, or for patients



with significant vaginal bleeding whose vaginal absorption of a suppository or gel would be compromised. We are primarily using Endometrin, micronized progesterone capsules, and Crinone.

BAROCAS We're moving to the endometrial delivery as well, and patients are happy about that.

LASKOWSKI We also use Endometrin unless patients have a history of early bleeding. Patients frequently say their biggest concern is that they would have to use IM progesterone. They have heard horror stories about its administration and are elated when told they can use Endometrin.

SHUBIN With vaginal progesterone delivery, the one caveat is that serum progesterone levels decrease dramatically, and you can't panic about it. I wish we would stop drawing serum progesterone levels because they are not an accurate portrayal of how much progesterone absorption is actually occurring. Through pharmacokinetic studies, we know that with even just 2 suppositories a day, the patient is getting 10 times more progesterone in the uterus than they do with 50 mg in an IM progesterone injection. If levels are less than 20 ng/mL, we educate our patients and encourage them not to go online to see what their progesterone levels "should be."

LASKOWSKI The decrease in progesterone levels was very difficult for us to get used to initially. However, having seen many successful results, we no longer draw a midluteal serum progesterone on patients using Endometrin. The progesterone is checked with the first beta.

JOSSIM Our clinic started using Crinone in October, and we've had a number of patients report bleeding. So, we've returned to the IM route, and we'll revisit the matter soon.

ZAGAMI We use endometrial delivery 3 times daily until a pregnancy test is positive, and then we go to twice daily.

LASKOWSKI We use Endometrin 3 times a day through 12 weeks of pregnancy.

SHUBIN Do any of your centers use estrogen supplementation after egg retrieval?

ZAGAMI No, we don't.

POST We will supplement estrogen if the patient's serum level is low. One week following retrieval of eggs, we have a patient return to measure the estrogen/progesterone level. If they've dropped a significant amount, we will start estrogen supplementation.

SHUBIN Are you finding that patients panic when IM progesterone injections are added to their treatment regimen? Since we are shying away from IM progesterone, I don't get many complaints. However, we do IM hCG with our IVF cycles, as opposed to subcutaneous in OI cycles. I do see patients panic when they see the difference in the needle size.

BAROCAS Patients hate IM. They're fine with the subcutaneous route.

ZAGAMI We use the IM hCG. We did a year-long study in which we switched IVF patients to Ovidrel for a subcutaneous hCG injection, and we lowered the pregnancy rate. That result, we concluded, was due to this population having a

higher BMI. We're back to using the IM hCG for all of our patients across the board.

Dealing with patient anxiety

SHUBIN How do you try to minimize patients' anxiety and their stress during their IVF cycle?

LASKOWSKI We explain to each patient that we will take her step by step through the IVF process and that we are only a phone call away. It's also very important to have a positive attitude with patients and try to impart confidence in them. We tell them that many patients are overwhelmed initially but then realize at cycle conclusion, if using Menopur/Bravelle, the injection portion of the cycle was not nearly as intimidating as they thought it was going to be.

BAROCAS A lot of TLC. We don't have primary nurses, but we still manage to individualize care. Each nurse has a different personality, and patients find the right nurse to help guide them through the process. Whenever patients visit the office, we try to teach them as much as we can. And we do have nurses on call.

SHUBIN Do you think their anxiety is primarily due to the need for multiple injections, the IVF process, or the stress of just trying to get pregnant?

BAROCAS All of those factors have an impact. That there are more injections with IVF is tough. Very often we're going directly from Clomid to IVF, and not even doing other injectable cycles with an intrauterine insemination.

Patient advocacy

SHUBIN I think we all agree that using one injection in a mixed protocol reduces patient anxiety, the time needed for injection teaching, and time spent with patients on phone calls to review medications or offer reassurance. But we're not always the ones selecting the protocols.

BAROCAS I think supervising physicians would be amenable to alternatives if we advocated for patients. A nurse's comfort level with particular medications has a lot to do with it.

SHUBIN I do notice anxiety when patients first see the 2 vials, the Q-Cap, the syringe, and the needle. It looks like a lot. But once I show them how to use it, their attitudes change.

BAROCAS I think, again, it reflects nurses' comfort levels. Yes, just looking at a pen suggests simplicity, but its use does require a number of steps. You have to fill the pen, and there is going to be overfill. There are a lot of details to pay attention to. Newer nurses in the field really like the pens. Those of us who have been in the field longer are comfortable mixing medications, and patients can reach that same comfort level.

LASKOWSKI Patients continually look to us for guidance, and if we are calm and clear in our instruction, I think this helps to build patient confidence. Injection instruction with Bravelle/Menopur and Q-Cap provides a mixing/injection method that is clear, concise, and understood with few issues. ⁿ