

Patient Information: Treatment with Gonadotropins

Introduction

Infertility is defined as a couple's inability to fall pregnant after twelve months of unprotected intercourse. After twelve months one would normally expect around 84% of couples to fall pregnant. This increases to only 92% after two years. Certainly, some completely normal couples will simply take longer to fall pregnant but this is outside the norm. Gonadotropins encompass two hormones, LH and FSH which stand for luteinizing hormone and follicle stimulating hormone. Clomiphene citrate (brand name Clomid) may also encourage ovulation in certain circumstances. However, it is not the panacea and in some situations can be counter-productive. There are very specific indications or reasons for using each of these drugs.

Before you Commence your Infertility Treatment

Before any treatment begins a couple should undergo a thorough evaluation. This not only helps me to determine what kind of treatment is needed but helps to establish an underlying reason for treatment. I will also try to get a very clear of the treatment goals and a time frame over which you wish to fall pregnant. Obviously some couples will have a greater degree of urgency than others, and this depends on underlying causes, length of time that the couple have already been trying and their potential for fertility as measured by such factors as ultrasound, and blood testing which may indicate ovarian reserve or ability to produce eggs. The male partner's evaluation will include history, sometimes physical examination and always a semen analysis. Semen quality varies from time to time, and just because semen quality may have been enough to produce a pregnancy on a previous occasion, this does not mean that semen quality is still adequate.

What are Gonadotropins?

LH and FSH are produced by the pituitary gland, a small gland at the base of the brain which produces hormones that control the way the body works. These two hormones stimulate the ovaries in women to produce a follicle, or large blister, which may contain an egg. LH and FSH used to be naturally derived however now they are produced synthetically and are therefore thought to be completely safe from transmitting infections. They must be injected under the skin in order to be effective. Generally speaking preparations containing only FSH are used.

Reasons for using Gonadotropins

Generally speaking there are two classes of women who need gonadotropins. The first is those that do not ovulate at all. The second are those who are ovulating, however they need treatment in order to produce more eggs in preparation for an IVF cycle. In women who ovulate normally, gonadotropins may also improve her chance of becoming pregnant by stimulating the ovaries to produce more than one egg. If the underlying problem is polycystic ovaries then generally speaking Clomid will be the first thing to try. The advantage of Clomid is that it may be safely used without complex monitoring, the dosage regimen is straightforward, and there is much less (although not zero) chance of multiple pregnancies. If a woman has tried Clomiphene, and not commenced ovulation, or if Clomiphene has been tried and a pregnancy not resulted then it is common to move on to FSH preparations in order to induce ovulation.

How Gonadotropins are used

There are a number of methods for using these drugs, the dosing and timing alters. The first thing to understand is that the first day of a period is considered to be day 1 of the cycle, by definition. Women may vary considerably in their response to FSH injections. Some respond to a very low dose such as 25 or 50 international units (IU) per day, and others have little response to as much as 450. There is, generally speaking very little reason to go higher than this as higher doses do not necessarily result in a better response. In the average patient the greater the dose of FSH, the greater is the likelihood of growth of many follicles and the greater the likelihood of multiple gestation, if intrauterine insemination or timed intercourse is used. However development of many follicles is desirable in IVF cycles, although it is possible to overdo it. When more than 20 eggs are harvested at the time of vaginal pick up (see notes elsewhere) there is a higher chance of a condition called ovarian hyperstimulation syndrome. In most cases the gonadotropin or FSH injection is given once per day, in the evening. After a few days of injections you will be asked to have a pelvic ultrasound and also blood tests to measure hormone levels. The ultrasound is intended to track the development of follicles on

your ovaries. Blood tests and ultrasounds may need to be repeated through these stimulation cycles. For women who do not ovulate on their own and, are having injections in order to produce the follicle it is desirable to achieve a single follicle of approximately 15-18mm in size. Sometimes, if multiple follicles develop then the intended course of action is intrauterine insemination or timed intercourse, the cycle may need to be cancelled due to the risk of multiple pregnancies. In some cases however the cycle may be converted to an IVF cycle, so that we can control the number of embryos that are placed back in the uterus.

Then, when blood testing and ultrasound indicate that the ovaries are ready, you will be instructed to give an injection of HCG (Ovidrel) to trigger ovulation. This causes the final step in maturation of the egg, before ovulation would normally occur and renders the egg mature for trans-vaginal pick up (VPU).

Ovarian Hyperstimulation Syndrome (OHSS)

This is a condition where the ovaries become moderately to severely enlarged with many follicles, the symptoms of which are abdominal pain, dehydration, decreased urine output, increased blood "thickness" with attendant risk of deep venous thrombosis, electrolyte imbalances, and sometimes difficulty with breathing. At its most mild, OHSS may present something like severe mid cycle pain and at its very worst can be life threatening. Fortunately these days with tight control of IVF and stimulation cycles, this is very uncommon, however it does occasionally occur.

Intrauterine Insemination

This can either be done by timed intercourse or artificial intrauterine insemination by husband or donor. It is intended, to bypass difficulties such as low sperm count, difficulty ejaculating, or a very narrow cervical opening. It requires knowledge of when a woman is ovulating and patent (not blocked) fallopian tubes. Clearly if the fallopian tubes are blocked then there is no way for the egg to reach the uterus and intrauterine insemination will fail. At its best however it brings pregnancy rates up to somewhere near natural pregnancy rates per cycle which is around 25% with normal intercourse. This compares very unfavourably with results going through IVF, and so therefore, because ovarian hyperstimulation and intrauterine insemination represents most of the difficulty of a conventional IVF cycle, but has much lesser results, an IVF cycle is generally preferable.

Procedure

Intrauterine insemination is usually performed around one day after the woman has injected her HCG. A speculum is inserted into the vagina, and a long thin plastic tube is inserted through the cervix in order to administer the prepared sperm sample. This only takes a few minutes, may cause some mild cramping but has no other ill effects.

What Happens Next?

Pregnancy testing. About two weeks after intrauterine insemination or timed intercourse, a blood test for pregnancy is usually done. Generally speaking, urine pregnancy tests are positive from around about the time of the first missed period. This corresponds to a time two weeks after ovulation, or around one month since the last period. However in a very early pregnancy home unit pregnancy testing may be erroneously negative. The blood test is much more sensitive. If in the first blood test the HCG level is <5 the woman is not pregnant. We would like to see an $HCG > 10$. This test may be repeated after two days to confirm that levels are increasing. Ordinarily for the first month or so we would expect a doubling of HCG levels every 48 hours.

Ultrasound

If the pregnancy test is positive a pelvic ultrasound will be scheduled three or four weeks after ovulation. This corresponds to a normal gestation of five or six weeks at which stage it should be possible to see a gestational sac and probably also an embryonic heart beat.

Arranging Pregnancy Care

When the blood tests are positive and the ultrasound demonstrates that all is well at this very early stage it is now time to start organizing pregnancy care. I would be very happy to advise you about this.

