

Optimizing Stimulation Protocols



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Optimizing an IVF protocol is an important part of an ART cycle. In general, there are three major components to the success of an IVF cycle – the patient and her partner, the IVF lab and the physician input. Optimizing the stimulation protocol is integral to achieving the best possible outcome. Before selecting an IVF protocol, one must assess a woman's ovarian reserve.

Ovarian reserve can be best evaluated utilizing AMH, random day 3 FSH and E2 levels, AFC, ovarian volume measurements and inhibin-B measurements. AMH is perhaps the most reliable in predicting a patient's response. The granulosa cells of pre-antral and small antral follicles produce AMH. It is not cycle dependent and therefore, more convenient than most measurements of ovarian reserve.

Identifying patients as poor, average or potentially high responders is an important part of determining the dosage and methods of medications for an ART cycle. Stimulation often involves both FSH and LH, although treatment with pure FSH protocols is usually successful as

there are often tonic, low-levels of endogenous LH present. In studies comparing FSH vs HMG, there appears to be a slight advantage to protocols utilizing HMG. There are probably no differences in agonist vs antagonist protocols in terms of success; however, antagonist protocols have an added measure of safety in that they allow for a GnRH-agonist trigger as a means to lower the risk of OHSS. Timing of when to trigger is important and can have significant impact on an IVF cycle outcome. Poor responders are typically defined by the Bologna criteria requiring 2 of 3 to be present: (1) age > 40 years old (2) prior poor response or (3) an abnormal ovarian reserve test.

There are many protocols to try with the poor responder- none has been shown to be superior. Growth hormone has been shown to improve the response in poor responders. Although in states like NY, the use of GH other than the treatment of diseases as recognized by HHS can be considered a felony. Studies have shown that even when the response is very low (<3 follicles), IVF has superior success rates to cancellation to an IUI cycle. When a patient is judged to be a high-responder, steps should be taken to prevent the development of OHSS. These include low dose medications, GnRH-agonist trigger, "freeze-all" techniques and coasting. If GnRH-agonist triggers are utilized, luteal support of E2 and P4 are required. Finally, modifying a cycle after a failed IVF cycle may help improve the subsequent cycle's outcome.