

# Anatomy of Ovarian Stimulation Protocol for IVF

## **Anatomy of Ovarian stimulation Protocol for IVF**

Understanding the anatomy of ovarian stimulation Protocol for IVF or how is the ovary stimulated to produce multiple eggs, helps you understand different medications you are administering prior to IVF. Understanding the endocrine make up of a woman is essential before selecting and optimizing a protocol including

- i. ovarian reserve (and predicting before starting treatment if she is a high, average or low responder)
- ii. Age and what is a reasonable response for a pregnancy to ensues
- iii. Differentiating between PCOS, hypothalamic amenorrhea and normal ovulatory women.
- iv. Other gynecologic problems e.g endometriosis
- v. other factors that may lower the response : prior ovarian surgery, medical disorders, chemotherapy exposure ..
- vi. What are the specific aims of IVF in addition to pregnancy e.g PGD..

After evaluating these factors for each woman, different options are selected for stimulation prior to IVF. There is o place for one protocol fits all. Its a diligent thinking of what works best, one patient at a time.

## **Adjuvants**

These are medications given prior to menses or during the cycle to improve response to gonadotropins

Estradiol: oral or vaginal to synchronize the follicles, so that they are equal before starting stimulation so that they end the cycle close to each other at the time of egg retrieval

Antagonist: to prevent a premature growth of follicles prior to starting stimulation so that we obtain a synchronized group of follicle.

Oral contraceptive pills: we do not use birth control for timing of the cycle most of the time but sometimes to obtain a regular group of follicles before starting stimulation

Testosterone: testosterone gel for 2-3 weeks has been shown in randomized clinical trials likely because of sensitizing the ovary to the effects of stimulation medication. No other androgen preparation has been demonstrated to improve pregnancy outcome including DHEA.

Clomid or letrozole: these oral medications may improve response through release of internal FSH from the master gland.

Other medications suggested to improve response with weak evidence that they actually improve the pregnancy rates e.g Growth Hormone

## **Prevention of premature ovulation**

One landmark improvement in stimulation protocols is the addition of medicine that prevents the master gland in the brain from triggering ovulation prematurely. Two options are available agonist or antagonist

Agonist in a short protocol (flare lupron) or long protocol

Antagonist starts during the cycle when the largest follicle

reach 14mm and estradiol level 300pg/mL

Each have its advantages and merits and they are generally used for women with different endocrine environment. Antagonist protocols gained more dominance in the past decade.

## **Gonadotropins**

Two main types of gonadotropins exist in the US; Pure FSH and a mixed FSH + LH preparation. FSH is the main stimulating medicine but in some women the addition of LH improves the response. Many women receive mixed FSH and LH protocols.

The dose of such medicine starts at the highest dose then is drops gradually, the step down protocol. The initial dose depends on egg reserve, weight and expected response. Usually the maximum starting dose is a total of 450 units.

*Some reproductive endocrinologists recommend Minimal stimulation IVF* in select patients. There is no proof that the concept one healthy egg is correct. As a matter of fact many women produce many healthy eggs in the same cycle. There is no evidence that cycle for cycle they produce comparable pregnancy rate. Proponents of multiple stimulation recommend multiple cycles to produce multiple embryos.

## **Ovulation Trigger**

When your reproductive endocrinologist perceive that the eggs are close to maturity, she or he employs a triggering agent to finalize follicle maturity and prepare the eggs for retrieval. Two agents are available

hCG given in muscle or under the skin. Its associated with higher incidence of ovarian hyperstimulation.

Agonist (Lupron) trigger given under the skin and has a short duration of action. It prevents ovarian hyperstimulation syndrome.

## **The Length of Stimulation**

In general, shorter the stimulation the better the outcome. The earlier the the trigger shot is administered the better the quality of the eggs. Longer stimulation increases the exposure of eggs to gonadotropins and likely lower the quality of eggs.

## **Luteal phase Support**

Every woman stimulated for IVF require luteal phase support as progesterone production after retrieval is defective. Two preparations exist

Progesterone in the muscle. This is the classic way of supplementing progesterone. Its very stable but require injections and also can cause allergy.

Vaginal progesterone. Recently introduced, used twice a day using an applicator in the vagina.

*Many aspects of stimulation protocol need to be considered in each patient to ensure optimal stimulation of the ovaries, best possible egg yield and subsequently the highest number of good quality embryos and highest pregnancy rate. Sometimes changing the protocol is better for women than to continue with a protocol that is less productive and associated with low pregnancy rate. The talent, care and experience of reproductive endocrinologist is central to selection appropriate stimulation regimen*