

Comparative study of effect of GnRH protocols on the quality and the quantity of oocytes retrieved and embryos form

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Abstract

Background: Correlation of GnRH long Agonist protocol and GnRH short Antagonist protocol-quality applying in Assisted Reproductive Technology, we studied which protocol is better to make good quality embryos, oocyte and out come of in-vitro fertilization and embryo transfer. GnRH has important part in manage ovarian stimulation. Effect of GnRH analogous on embryos and oocytes equality. GnRH Antagonist detected successful for ovarian simulation. Oocyte and quality of embryos are very crucial for positive result in in-vitro fertilization.

Objectives: The objectives include study of GnRH long Agonist Protocol, Study of GnRH Short Antagonist Protocol and to Correlate it's Effect on Quality of embryos and oocytes.

Methodology: This is invasive methodology giving intra muscular injection in both protocol long Agonist and Short antagonist then we check the follicles size and numbers under USG. Inj HCG given before 34hr of ovum pick up. Oocytes retrieved examined oocyte quality and numbers. Then we will perform ICSI or IVF then check embryos forms and grade in which protocol given good embryos. We transfer embryos blastocyst and morula stage. B-HCG done after 14 days of embryo transfer.

Keywords: Oocyte, GnRH analogue, Embryo quality, long agonist, short antagonist Pregnancy outcome. AMH test.

INTRODUCTION

Assisted Reproductive Technology is very useful for couples in several problems of infertility like anovulation, ovulatory disorder, dysfunction of hypothalamus-pituitary, and some regarding the endocrine disease. Ovarian hyperstimulation syndrome is one of the big issue of ovarian stimulation in cycles of in-vitro fertilization/intracytoplasmic sperm injection (1).

As we know for the success of in-vitro fertilization and embryo transfer the ovarian stimulation is a very important factor.

The quality of Embryos and oocyte plays crucial role in the positive result in in-vitro fertilization. Only well grade of embryos can give a positive outcome in IVF in terms of pregnancy (2). So many protocols are there in IVF and embryo transfer and these protocols are developed for IVF-ET treatment in the 1980s.(3)

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The main variance and the clinical feature of the protocol used with GnRH agonist and GnRH antagonist point up the major outcome and also these two protocols are used in ART. GnRH protocol can help for those couples having multiple failures in intrauterine insemination(2).

Ovarian stimulation with either GnRH agonist or GnRH Antagonist is a good analog for IVF. These analogs affect oocyte/embryo quality. Gonadotropin-releasing Hormones have an important role in ovarian stimulation. Gonadotropins are used to increase multiple follicles and manage ovarian hyperstimulation. While ovarian stimulation GnRH Analogs are administered to inhibit the premature luteinizing hormones surge. The patients taking treatment under Assisted Reproductive Technique (ART) will get benefit from GnRH agonist as it inhibits early luteinizing hormone (LH) surge(4). Therefore, the pregnancy rate increases because of increasing numbers of oocyte retrieval and this reduces the number of cycles. GnRH Antagonist aggressively blocks GnRH Receptors and can cause the quick defeat of GnRH Release. GnRH Antagonist helps to manage the ovarian stimulation cycle, the need for low follicle stimulation is protected from ovarian hyperstimulation syndrome(5)(6). This treatment is very smooth for patients because of lesser complications and short-term treatment. The major aim of the study of GnRH protocol in multiple-dose of injections in form of GnRH long agonist and GnRH short Antagonist effects on oocyte and embryo quality, embryo development, and IVF treatment outcome. GnRH Agonist and Antagonist protocol detected mild variation in these protocol like oocyte retrieval, immature embryos.(7)

Rationale:

Qiaohonglai ET AL studied about effectiveness of the GnRH protocol Agonist and Antagonist controlled Ovarian stimulation in Assisted Reproductive Technology cycles. period of April 2010 to October 2012 at center of Biomedical research Tongji Hospital Tongji medical college Huazhong University of Science and Technology. This Authors detected here both agonist and antagonist protocol studied in same patients during manage ovarian stimulation between these two protocol analyzed and failed to detect variation in two protocol in duration of ovarian stimulation. Finally outcome result is GnRH Antagonist protocol improving and development rate and good quality of embryos number of oocyte retrieved. patients had treatment under Agonist-105 and 88 patients had treatment under Antagonist. out of these patients got good outcome and improved in Short Antagonist protocol.(2-10)

An-cong wang ET AL study was effect of GnRH Antagonist protocol in Reproductive women in in-vitro fertilization/intra cytoplasmic sperm injection. period of study January 2014 to September 2015 at department of Reproductive Medicine Shandong provincial medical and health science and technology china.298 patients took treatment under Antagonist protocol the 108 patients age

was less than 35 years and left of patients has more then 35years here analyzed and detected Antagonist protocol well effected on oocyte retrieved and Succeed in beta HCG positive as well as depend on age and body mass index. Beta HCG positive rate was 38.93% and live birth rate was 26.85% (80/298).(11-17)

Raffaella depalo ET AL Studies on GnRH protocol Agonist and Antagonist compared outcome in-vitro Fertilization/Embryos transfer and Hormonal changes can occurs with each protocol. studied in 2012 at department of gynecology, obstetrics and Neonatology university of Bari “Aldo more” Bari Italy. Here indicate which able to defeat pituitary FSH and LH secretion is relate with raise pregnancy result as differentiate with the use of gonadotropins without a GnRH agonist. Antagonist are outcome stop in premature raise of LH and produce a less and low-cost ovarian stimulation compered to agonist protocol. finally many effectual GnRH Antagonist direct effects extra pituitary tissue i.e corpus luteum, endometriosis, ovary, embryos and Antagonist giving good dedication to new plan of action of stimulation the patients in which radio-chemotherapy cycle are required.

Martine Stimpfel et al the study was the effectiveness GnRH Agonist and Antagonist protocol of ovarian hyper stimulation in good prognosis patients. here analyzed and found in agonist and antagonist protocol changes in oocyte retrieval, immature oocyte, embryos between COH protocol there is no any changes in live birth rate. miscarriage and ectopic pregnancy between two protocol but here found high pregnancy rate show in GnRH mild Antagonist protocol comparing both Agonist and Antagonist protocol.so here showed GnRH Antagonist protocol may be good method of taking good prognosis patients.(17)

Objectives:

Aim: To Study the Effect of GnRH Protocols on Quality of Embryos and oocytes.

Hypothesis:

Type of ovarian Stimulation Protocol may be a key factor in increasing number and quality of Embryos and Ova.

NULL HYPOTHESIS

Type of Ovarian Stimulation Protocol may not be factor in increasing number and quality of Embryos and Ova.

Methods:

Study design:

Observational Study

Methodology:

Total 50 patients _ visited Wardha Test Tube Baby Centre, between 2020 to 2022, studied. Every one patient took once for long agonist and once for antagonist protocol. All patient had no any history of menopause. Patients with regular

menstrual cycle (between 26-31 days) and some patient getting treatment for infertility in female due to fallopian tube problems, endometriosis and thyroid problem, etc. In male unexplained or mix factors like oligospermia, asthenozoospermia, some other surgical procedure, varicocele, hydrocele, inguinal hernia. Patient not took any kind of oral contraceptive pills before the IVF cycle and did not process ovarian stimulation before this protocol cycle. The study was on comparative clinical and laboratory outcome taken between _ agonist protocol and _ antagonist protocol. All studies and subject approved consent form from the WTTBC (Wardha Test Tube Baby Centre).

GnRH LONG AGONIST PROTOCOL:

From day 21 of menstrual cycle, start administrating inj. leuprolide depote 3.75mg for endometriosis and reduce the pain. After that we will conduct USG and blood test to check hormonal levels. We will continuously administrating inj. leuprolide acetate for increasing ovarian reserve. And then we will take test for AMH level and also check a ovarian reserve by transvaginal ultrasound, if every thing will be in control, then we will stop administrating inj leuprolide acetate. After that, from day 3 of menses will start gonadotrophin inj. recombinant FSH at the same day USG done. <34year/old patients to advise two ampoule 150IU of GONAL-F daily which will help in ovarian development (mature) >34yrs old patients to advise 3 ampoule (225IU) daily. This dose will be fix for 5-days stimulation then later 5 days follow-up medication. Then transvaginal USG will be conduct. If patient has >2 follicles more than 14mm in size, then we will stop administrating inj. rFSH. Before 34hr ovum pick up we will trigger patients with inj. human chorionic gonadotrophin (Inj.HCG)1000IU.

GnRH SHORT ANTAGONIST PROTOCOL

USG done on day 3 of menstrual period inj HMG + rFSH same day of USG examination. The patients <34 214

2year old we Advise get two ampoule (150IU) of inj Gonal-f daily. The patient 00.34 year old with normal BMI advise to take three Ampoule of inj Gonal-f. same doses fixed for first 5day of stimulation ,later 5 days followed inj LA 0.5mg daily till day 2 of stimulation. trans vaginal examination done and identify follicular developments and size >2 follicles greater than 14mm. inj rFSH stop administrate inj Gonal-f .GnRH Antagonist inj Certoralix 0.25mg Fixed dose start from D6 for controlled ovarian stimulation and prevent premature ovulation After D6 of stimulation cycle the day of inj HCG 10,000 Administrate. Trans vaginal examination Done before 34hr ovum pick up.

OOCYTE RETRIVAL

Inj. cetorelix and Gonal-f will be continuously administration till 3 to 4 follicles gain >17mm. estradiol E2 and Serum concentration examed on the day of HCG administration. Oocyte retrieved after 34hr HCG injection administrated than ovum pick up (OPU) done in standard protocol.

EMBRYOS TRANSFER

Embryos transfer done 120hr later oocyte retrieval each patient 2 embryos transferred. injection progesterone (in oil) start intra muscularly daily 180mg/day from day one after oocyte retrieval for maintain for restore the hormone in body. After embryo transfer β -HCG done on 14th day under ultrasound examine done presence of gestational sac.

COMPARISON

The clinical and laboratory result in the middle of GnRH agonist and GnRH antagonist protocol. We differentiate an outline. The rFSH time and dosage in GnRH agonist protocol kind of bigger than GnRH antagonist protocol. But without enumeration separate search kind of greater oestrodial (E2) was detect for the agonist long protocol as a contrast with antagonist protocol. At the day of HCG given and no any changes in progesterone level, endometrial thickness and in follicles number, size ≥ 14 mm oocyte retrieval and rate of fertilization, cleavage and the number of embryo transfer allying these two protocol the good grade I and II embryos. Obtainal embryo kind of bigger in antagonist. Short antagonist abandon 02 out of 25 cycles and long agonist abandon 03 out of 50 cycles due to some reason poor quality of embryos or low grade of embryos and bleeding from uterine after medication. than reduce number of sperms like agospermia from husband and some missed follow up.

Setting:

Location : WARDHA TEST TUBE BABY CENTRE, AVBRH

Relevant dates, including periods of recruitment : 2021 – 2022

Participants:

INCLUSION CRITERIA

- Patients suffering from infertility.
- Patients with regular follow-up.
- Patient having history of fail IUI cycle

EXCLUSION CRITERIA

- Patient with diminished ovarian reserve (DOR).
- Patient with polycystic ovarian syndrome (PCOS).
- Patient with history of salpingo-hysterectomy and oophorectomy.
- Patient suffering from infections such as HIV, Hbs-Ag, HCV, etc.

Study size:

Sample size :

50 infertile couple

$$N = \frac{\chi^2 * N * p(1-p)}{C^2(N-1) + \chi^2 p(1-p)}$$

Total population = N=120during36 months

χ^2 = Chisquare value for 1 degrees at some desired probability level. This is 3.84 at 5% level of significance

P = 50% proportion

Q = 100 – p

= 50

C= Confidence interval of the one choice (95% CI)

= 0.05

N= $\frac{3.84*120*0.5*0.5}{(0.05)^2 *24+3.84*(0.5*0.5)}$

= 50

Expected Outcomes:

50 women will be included. We will use GnRH short antagonist protocol stimulation for 25 women, and other 25 women will stimulate using GnRH long agonist. Further we will check the quality of oocyte and embryo obtained by both the protocols. Thus, by using GnRH short antagonist protocol for stimulation may increase the quality of oocytes and embryos which leads to improve implantation rates in ART.

Discussion:

The main aim of this study is to check between GnRH long Agonist and GnRH short Antagonist protocol. After OPU, we will check the grade of oocytes retried and will compare oocytes retrieved from both the protocols. After comparing the quality of oocytes and embryos, we will decide which protocol is best over another.

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