



The Comparison of Area under the Curve of Serum Estradiol during Controlled Ovarian Stimulation between Long Gonadotrophin Releasing Hormone Agonist Protocol and Short Gonadotrophin Antagonist Protocol in Invitro Fertilization

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Abstract

Background: during stimulation, estradiol levels represent the dynamic hormonal interaction of follicle development. Some studies have been done to evaluate the influence of day-hCG estradiol assay and IVF outcome. However, this assay does not reflect the total exposure of estradiol throughout stimulation. Hence the concept of calculating the area under the curve (AUC) of estradiol during ovarian stimulation is thought to be a better parameter to evaluate total exposure of estradiol to the entire process of IVF. **Methods:** a retrospective analysis of data from a fertility center in a tertiary hospital. Between 2011-2016, there were long GnRH agonist cycles and short GnRH antagonist cycles eligible for analysis. Data including subject's characteristics, the level of estradiol on day-2, day-6, and day-hCG during controlled ovarian stimulation were obtained. Those data were plotted, and area under the curve of each subject was calculated. Statistical analysis was done using student t-test while $p < 0.05$ was considered significant. **Results:** there were no significant differences in subject's age (33.4 vs. 34.2 years, $p = 0.12$), day-3 of menstrual cycle FSH level (7.1 vs. 7.3 mIU/mL, $p = 0.64$), and day-3 estradiol level (35.1 vs. 36.5 pg/mL, $p = 0.61$). The estradiol level on day-5 of COS was

324.9 (273.1) pg/mL and 363.3 (293) pg/mL ($p = 0.36$), and at the day of hCG administration was 2461.8 (2283.7) ng/mL and 2558.2 (2043) ng/mL ($p = 0.76$). Estradiol area under the curve for long protocol and short protocol was 9205.2 (7683.7) pg/mL and 9732.9 (6893.9) pg/mL respectively ($p = 0.63$). Conclusion: our results indicate that there are no significant differences in the area under the curve of estradiol between two protocols.

Subject Areas

Gynecology & Obstetrics

Keywords

Area under the Curve, Controlled Ovarian Stimulation, Estradiol, Long Agonist Protocol, Short Antagonist Protocol

1. Introduction

Controlled ovarian stimulation (COS) is an important and integral part of *in vitro* fertilization (IVF) program, with the goal to obtain more oocytes in supraphysiological conditions. This may lead to higher pregnancy chance, and the spare embryos can be cryo-stored for future transfer [1] [2]. The COS protocol mainly consists of exogenous follicle-stimulating hormone (FSH) administration using long-agonist protocol, and short-antagonist protocol. The long-agonist protocol induces hypophyseal desensitization to prevent premature luteinization, and significantly reduce cycle cancellation. The oocyte yield was considered to be higher compared to the short antagonist protocol. However, in a specific patient group such as polycystic ovary syndrome (PCOS), on the other hand, the short antagonist protocol completely blocks pituitary GnRH receptors and induces reversible and rapid gonadotrophin secretion. This may be achieved by administration of GnRH antagonist drugs such as cetrorelix and ganirelix [3] [4] [5].

The ovarian response during COS should be monitored adequately [2] [6] [7]. During COS, the ovarian produces E2 in supraphysiological level, and this may reflect ovarian response. The goal of COS monitoring was to ensure adequate ovarian response while avoiding complication potentials *i.e.*, ovarian hyperstimulation syndrome or inadequate response due to inaccurate FSH dosage [2] [5] [8]. However, the serum E2 assay is mostly done by serial measurement during COS and may not reflect the actual exposure of E2. The area under the curve (AUC) concept, therefore proposed in several studies to calculate the amount of E2 exposure during COS [9] [10].

This study was aimed to compare the AUC during COS between long agonist- and short antagonist protocol. We hypothesized that there was no significant difference in AUC between two protocols, which may reflect the same efficacy of both protocols.