

Inhibin A as a Marker of Ovulation in Patient Undergoing ICSI Using Antagonist Protocol

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Abstract: The aim of this study was to measure serum inhibin A concentrations from women undergoing ICSI using antagonist protocol in order to determine its prognostic value in the outcome of intracytoplasmic sperm injection/embryo transfer cycles. A total of 30 women following ovarian stimulation and intracytoplasmic sperm injection were included. Blood serum samples were drawn at the day of chorionic gonadotropin administration. There was correlation between inhibin A level and the number. Of oocyte retrieved but not with fertilizing capacity of Oocyte and pregnancy rate. It can be concluded that inhibin A could be considered as a marker of ovarian response, but not seem to be related to the pregnancy outcome in ICSI cycles of healthy women.

Key words: Inhibin A • Antagonist protocol • Pregnancy rate

INTRODUCTION

The last three decades have been marked by a blooming of assisted reproduction techniques. The advent of *in vitro* fertilization (IVF), controlled ovarian hyperstimulation (COH) and intracytoplasmic sperm injection (ICSI) are concomitant with an increase in the intensity of research into reproductive physiology [1]. IVF cycles provide unique opportunities to investigate reproductive processes such as folliculogenesis, ovulation and implantation, as it is easy to collect biological samples *e.g.* blood and follicular fluids (FFs) under controlled and carefully monitored ovarian function. The imperative necessity for the optimization of IVF attempts has led many scientific teams to study the usefulness of circulating or intrafollicular concentrations of several cytokines and hormones as prognostic markers for the outcome of IVF cycles [2-4]. Inhibin A is a heterodimer protein and does not begin to increase until just after the increase in oestradiol in the late follicular phase, suggesting secretion by the dominant follicle. Inhibin A secretion is regulated by LH and is associated with paracrine/autocrine action on oocyte maturation. Moreover, it is related to follicular development and size, serving as a marker of follicular maturation after IVF cycles [5].

The aim of this work is to study the usefulness and prognostic value of serum inhibin A in the outcome of intracytoplasmic sperm injection/embryo transfer cycles.

MATERIALS AND METHODS

The present study was a prospective study, conducted at the Obstetrics and Gynecology Department of Kasr El-Aini Hospital, Cairo University, Egypt in the period between 2013 and 2014. Thirty (30) women presenting by infertility and undergoing ICSI using antagonist protocol were recruited from the fertility clinic. Their age ranged from 20-40 years old.

Inclusion Criteria:

- Indication for ICSI treatment.
- The presence of one or two functional ovaries.
- Previous history of Good response to ovarian stimulation.
- Normal uterine cavity by hystroscopy.
- Basal serum FSH levels ≤ 13 IU.

Exclusion Criteria:

- Abnormal uterine cavity.

- Basal serum FSH levels >13 IU.
- Poor responders to ovarian stimulation according to the existence of at least two of the following criteria:
 - Advanced age (more than 40 years).
 - Antral follicles count <5.
 - Prior history of poor response to controlled ovarian hyperstimulation (peak E2 <500 pg/ml and/or ≤3 oocytes retrieved).
- Untreated endocrinologic disease.
- Azoospermia.

Methodology: Informed consent was obtained from all participants and procedures were previously reviewed and approved by the ethical committee of the department. All participants were subjected to the Following:

- At first history was taken from all participants in the form of age, gravidity and parity, symptoms they complain from and the past medical and surgical history (Hypertension, diabetes, breast tumours, previous cesarean section or myomectomy or any previous abdominal surgery for any other cause).
- General and gynecological examination (Abdominal, pelvic and per vaginal) was done.
- Laboratory tests were done: for the female partner D3 FSH, LH, PRL, TSH and AMH and for the male partner, semen analysis.

Women were treated with a GnRH antagonist protocol with cetrotide (Cetrorelix, merck serono) and received rFSH (Gonal f, merck serono) injections from cycle day 3 and daily injection of cetrotide will be given to all patients when lead follicles are 13 to 14 mm in mean diameter. injection of 10.000 IU of hCG will be given to all patients to trigger ovulation when the appropriate number of mature follicles will be visualized. The initial dose of FSH was 150 IU and the dose will then be adjusted according to the patient response. Cycle monitoring was conducted by transvaginal ultrasound and serial E2 (Every 48 hours) starting from cycle day 3 of the stimulated cycle until the day of the hCG trigger and in that day serum inhibin A will be measured.

Biochemical Study: Blood sample taken at the time of follicular maturation for for measurment of inhibin A by ELISA using inhibin a ELISA kit (BECKMAN COULTER, CA 92821, U.S.A).

Statistical Analysis: Data were statistically described in terms of mean ± standard deviation (± SD), median and range, or frequencies (number of cases) and percentages when appropriate. Comparison of numerical variables between the study groups was done using Student *t* test for independent samples. For comparing categorical data, Chi square (χ^2) test was performed. Exact test was used instead when the expected frequency is less than 5. Correlation between various variables was done using Pearson moment correlation equation for linear relation in normally distributed variables and Spearman rank correlation equation for non-normal variables. *P* values less than 0.05 was considered statistically significant. All statistical calculations were done using computer program SPSS (Statistical Package for the Social Science; SPSS Inc., Chicago, IL, USA) version 15 for Microsoft Windows (2006).

RESULTS

The study included 30 patients suffering from infertility. Treatment resulted in a success rate of 57.1%, i.e. 16 patients got pregnant. Data presented in Table 1 show the serum inhibin A, E2, number of follicles by ultrasound assessment, number of retrieved oocyte, number of M2 oocyte and number of transferred embryo in the examined patients.

There was no correlations between inhibin A and the pregnancy rate ($p=0.069$). although There was correlation between inhibin A and number of oocyte retrieved ($p=0.001$) as shown in Fig. 1.

Data presented in Table 2 show the correlation between the serum inhibin A and number of oocyte retrieved and pregnancy test result.

Table 1: Serum inhibin A, E2, number of follicles, number of retrieved oocyte, number of M2 oocyte and number of transferred embryo in the examined patients

E2(pg/ml) (Mean ± SD)	3.909 ± 2
Inhibin A (pg/ml) (Mean ± SD)	609.49 ± 240.8
Number of follicles (Mean ± SD)	14.20 ± 5.09
Number of oocyte retrieved (Mean ± SD)	13.67 ± 5.6
Number of M2 (Mean ± SD)	11.43 ± 4.5
Number of transferred embryo (Mean ± SD)	3 ± 1

Table 2: Correlation between the serum inhibin A and number of oocyte retrieved and pregnancy test result

Item	Inhibin A	
	Correlation coefficient	P value
Number of oocyte retrieved	0.578	0.001
Pregnancy test	0.348	0.069

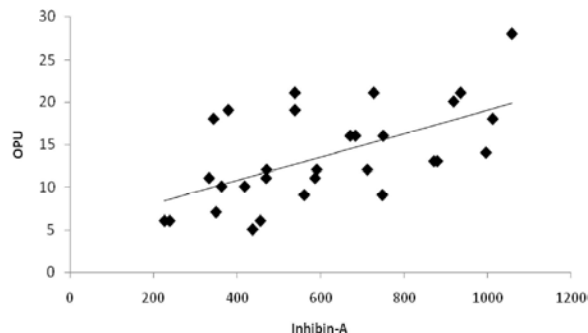


Fig. 1: Correlation between inhibin-A (pg/ml) and number of oocyte retrieved.

DISCUSSION

In our study we use inhibin A as a marker for follicular maturation. Wen *et al.* [6] showed that the inhibin A concentration in follicular fluid was increased with increasing the follicular size but there was no correlation to the fertilizing capacity of retrieved oocyte. In our study there was correlation between inhibin A level and the number of oocyte retrieved but not with fertilizing capacity of oocyte and pregnancy rate. Similar findings were achieved with a recent prospective study showed that higher levels of inhibin A and B were associated with the likelihood to retrieve oocytes at the time of OPU, but not with oocyte quality and fertilization competence [6]. Similarly, Fried *et al.* [7] observed that inhibin B in FF and serum was strongly correlated to the number of oocytes retrieved, but not with the IVF outcome, so that inhibin could be considered as a marker of ovarian response, but not of oocyte or embryo quality. Ocal *et al.* [8] found that high levels of inhibin A and B in the FF were associated with increasing fertilization and pregnancy rates. On the other hand, Lau *et al.* [9] found that a positive correlation between good quality oocytes and FF levels of Activin A, but not with inhibins A and B. His researches were not further developed, so the role of Activin A as a marker of oocyte quality and its relationship with inhibin family needs further investigation.

CONCLUSION

Inhibin A could be considered as a marker of ovarian response, but not seem to be related to the pregnancy outcome in ICSI cycles of healthy women.

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