ORIGINAL ARTICLE

The impact of timing of insemination in relation to ovulation on the cycle pregnancy rate of intrauterine insemination and intrauterine tuboperitoneal insemination in unexplained infertility

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Abstract *Objective:* 1 – To compare the cycle pregnancy rate of intrauterine insemination (IUI) to that of intrauterine tuboperitoneal insemination (IUTPI) in unexplained infertility. 2 – To assess the effect of timing of insemination in relation to ovulation on the cycle pregnancy rate of IUI and IUTPI. *Design:* Prospective randomized study. *Main outcome measures:* 1 – Cycle pregnancy rate of IUI and IUTPI. 2 – Cycle pregnancy rate of preovulatory and postovulatory insemination. *Material and methods:* Two groups (A and B), each group included 160 women with unexplained primary infertility. Group A were treated by IUI and group B by IUTPI after controlled ovarian stimulation (COS) with sequential clomiphene citrate and human menopausal gonadotropin. Ovulation was by i.m. HCG. At the time of insemination the occurrence of ovulation was checked by transvaginal sonography. *Results:* After the first treatment cycle 17 patients of group A (10.62%) and 28 patients of group B (17.50%) had ongoing pregnancies (*p* = 0.0413). After the second treatment cycle 12 patients of group A (8.39%) and 18 patients of group B (19.63%) had ongoing pregnancies (*p* = 0.0442). After the third treatment cycle 11 patients of group A (8.39%) and 14 patients of group B (12.28%) had ongoing pregnancies (*p* = 0.0433). After the three treatment cycles 40 patients of group A (25%) and 60 patients of group B (37.50%) had ongoing pregnancies (*p* = 0.033) and the overall cycle pregnancy rate of group A was 9.21% and group B 14.81%

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($p = 0.0324$). In group A the cycle pregnancy rate of preovulatory insemination was 7.20% and postovulatory 9.76% ($p = 0.041$). In group B the cycle pregnancy rate of preovulatory insemination was 17.70% and postovulatory 13.0% ($p = 0.0322$). Five out of 40 pregnancies (12.5%) in group A, and 4 out of 60 pregnancies (6.60%) in group B were twins ($p = 0.0431$). *Conclusion:* In unexplained primary infertility IUPI had significantly higher cycle pregnancy rate than IUI. Cycle pregnancy rate of IUI was significantly higher with postovulatory than preovulatory insemination. Cycle pregnancy rate of IUTPI was significantly higher with preovulatory than postovulatory insemination.

1. Introduction

Intrauterine insemination (IUI) is considered the first treatment option for unexplained infertility after failure of expectant treatment and before in vitro fertilization (1). The reported pregnancy rates per cycle usually varied between 8% and 22% (2), but very low (3.28%) pregnancy rates were also reported.(3) The rationale of IUI treatment is to increase the rate of conception in the couple of unexplained infertility by increasing the chance that maximum number of healthy sperm reaches the site of fertilization (3).

It was observed that the number of spermatozoa distribution within the fallopian tubes around ovulation after IUI was low. Only a median of 251 spermatozoa was recorded by flushing the tubes (4) and there was only a 49% chance of peritoneal spermatozoa to be found even when all semen characteristics were normal (5).

Many methods have been tried to improve the outcome of IUI including certain ovarian stimulation with improvement of pregnancy rate (2), perturbation 1 day before IUI (3) but Aboulghar et al. (6) found no significant difference in pregnancy rate with and without hydrotubation before IUI, Fallopian tube sperm perfusion (FSP) (7,8) and intrauterine tuboperitoneal insemination (IUTPI) (9) using 4 ml and 10 ml inseminate respectively. Four milliliters of inseminate carrying spermatozoa was not sufficient to fill the uterus and Fallopian tubes and did not reach the pouch of Douglas. Ten ml inseminate used for IUTPI filled the uterine cavity and allowed inseminate and spermatozoa to reach the fallopian tubes and enter the peritoneal cavity (9). Human menopausal gonadotropin (HMG) ovarian stimulation and IUI treatment had a pregnancy rate of 12% per cycle but multiple birth rates averaging 13% (5). Mildly stimulated (1–3 follicles) cycles might reduce the cost and multiple birth rates but may require more cycles for treatment (6). The efficacy of IUI/mild controlled ovarian hyperstimulation (mOCH) needs to be confirmed by larger studies (2).

The impact of follicle rupture at the time of insemination on the pregnancy rate in IUI is a debated issue (10). This factor has not studied in IUTPI.

This prospective study was designed to: 1 – Compare the cycle pregnancy rate of IUTPI/mCOH with those of IUI/mCOH. 2 – Estimate the association between the timing of insemination with IUI and IUTPI in relation to ovulation (preovulatory or postovulatory) and the cycle pregnancy rate in unexplained infertility

2. Material and methods

The study was carried out between June 2009 and July 2014 at Department of Obstetrics and Gynecology, Tanta University, and a private infertility clinic in Tanta, Egypt. The study was prospective including 320 women with the diagnosis of unexplained primary infertility. They were divided into two groups, A and B, 160 women in each group. The two groups were matched for age, body mass index (BMI) and duration of infertility. They were randomized for treatment by IUI/mCOH (group A) or by IUTPI/mCOH (group B). All patients were complaining of primary infertility for at least 3 years but not more than 6 years. Unexplained infertility was diagnosed after a normal basic fertility evaluation was proved. This evaluation consisted of general and gynecological examinations which were normal. Menstrual pattern was normal, regular cycles of 24–35 days and ovulatory. Spontaneous ovulation was checked by folliculometry and detection of a corpus luteum as well as normal midluteal serum progesterone concentration of $\geqslant 10$ ng/ml. Serum prolactin, thyroid hormones, thyroid stimulating hormone (TSH) and testosterone were normal. If any abnormality detected the case was excluded. Chlamydia detection tests were negative. Normal patent fallopian tubes and normal endometrial cavity were demonstrated by hysterosalpingography (HSG) and by laparoscopy because of suspected tubal disease and to assure the absence of endometriosis and pelvic adhesions.

On day 3 of the menstrual cycle serum FSH was estimated and transvaginal ultrasonography was done to exclude any abnormal uterine findings, to count the antral follicles in the ovaries and to rule out ovarian cysts prior to mCOH. Ovarian reserve was normal as denoted by day 3 FSH < 10 mIU/ml and the total antral count, number of antral follicles, 2–8 mm mean diameter in the two ovaries > 10 (1). Age of all participants was $\leqslant 30$ years and their body mass index was < 25 kg/m^2. The husbands had $\geqslant$ 5th percentile of semen parameters according to World Health Organization criteria, 1999 (11): volume 2 ml, concentration 20 million/ml, progressive motility *a* and *b* 50%, normal morphology with strict criteria $\geqslant 4\%$. The protocol of the study was approved by the committee of Medical Ethics of Tanta University Hospitals. Details of the study were explained to all participants and they signed on an informed consent.

2.1. Exclusion criteria

Patient report with thyroid and other endocrine disorders, liver and renal diseases, diabetes mellitus, previous pelvic