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Original Article

Comparison of pregnancy rates between patients with and without local endometrial scratching before intrauterine insemination

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ABSTRACT

Objectives. – To determine the implantation success of local endometrial injury in patients undergoing intrauterine insemination following ovulation induction with gonadotropins as an infertility treatment.
Material and methods. – In this prospective randomized controlled trial, ovulation induction was performed with gonadotropins in 80 patients following intrauterine insemination. In 40 patients, local endometrial injury (scratch) was performed in the midluteal phase of the cycle preceding ovarian stimulation with a Novak curette to the posterior side of the endometrial cavity.
Results. – Fifteen pregnancies (37.5%) and 11 clinical pregnancies (27.5%) occurred in the intervention group, whereas eight pregnancies (20%) and five clinical pregnancies (12.5%) occurred in the control group. Although the pregnancy rates and clinical pregnancy rates were increased in the intervention group, no statistically significant difference was found between the intervention and control groups (pregnancy rates: $P = 0.084$; clinical pregnancy rates: $P = 0.094$).
Conclusion. – Performing local endometrial injury (scratch) in the cycle preceding ovulation induction in patients with a diagnosis of infertility and indication for intrauterine insemination increased the pregnancy and clinical pregnancy rates. This increase was not, however, statistically significant. More randomized, controlled, prospective studies with larger patient numbers are required before the use of iatrogenic induction of local endometrial injury can be recommended in routine clinical practice.

Introduction

Intrauterine insemination (IUI) with ovulation induction is a commonly used method in infertility clinics. The primary benefits of this method are increased pregnancy rates by increasing the number of dominant follicles, decreasing infertility arising from ovulatory dysfunction, allowing insertion of sperm into the uterine cavity at an optimal time for fertilization, and eliminating the cervical factor as a cause of infertility [1]. Moreover, IUI is a cheap, noninvasive, and easy protocol compared with assisted reproductive techniques. For the treatment of patients with unexplained infertility, the first choice must be ovulation induction combined with IUI before using assisted reproductive techniques.

Embryo implantation is a crucial stage of most infertility procedures such as IUI. It has long been known that the endometrium must mature before implantation and must be ready for embryo adhesion. This maturation process occurs by stromal decidualization with the appearance of pinopodes and microvilli on the luminal epithelium, thus enabling endometrial receptivity [2,3]. This receptivity is an important factor in embryo adhesion and implantation. Many strategies have been suggested for improving it, the most important of which is local endometrial injury (mechanical trauma to the endometrium). This causes excretion of cytokines, growth factors, and adhesive molecules by modulating their gene expression, making implantation easier and increasing endometrial receptivity [2–4].

Recently, many studies have shown that use of local endometrial injury in patients with unexplained infertility before using assisted reproductive techniques causes a considerable increase in pregnancy rates [2,4–9]. The requirement for assisted reproductive techniques may therefore decrease in future. In the present study, our aim was to determine the implantation success of using local endometrial injury in patients with unexplained infertility who had IUI following ovulation induction with gonadotropins as an infertility treatment.

Material and methods

Patients

One hundred and twelve infertile patients who admitted to infertility polyclinic were evaluated for participation however

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23 of them did not meet the inclusion criteria and 9 of them rejected participation. Thus randomization between the study and the control groups was applied to 80 patients, which resulted distribution of 40 patients into each group. The study was carried out at the Gynecology and Obstetrics Clinic of Ataturk University Hospital because of infertility between June 2013 and December 2013.

It was designed as a prospective, randomized controlled study and was approved by the ethics committee of Ataturk University Medical Faculty. All patients were informed verbally and provided written informed consent. Patients who did not meet the criteria determined at the beginning of the study were excluded. Inclusion criteria were as follows: women between 19 and 35 years of age; body mass index in the normal range; no pathological problems as determined by ultrasonography; a basal follicle-stimulating hormone level of < 10 mU/mL; and normal levels of thyroid-stimulating hormone, luteinizing hormone (LH), prolactin, and estradiol on the third day of the menstrual cycle. All patients included had normal hysterosalpingogram results or a normal tubal passage confirmed by laparoscopy. Patients who had systemic or endocrinological diseases were excluded, as were those with submucous myoma, endometrial polyps, a uterine septum, or a uterine anomaly determined by hysterosalpingography, hysteroscopy, or laparoscopy. In additional, spermiogram results had to be normal according to the World Health Organization criteria or at least 5% normal according to the Kruger criteria, and the total progressive motile sperm count had to be at least 1 million. All patients who matched these criteria were randomized and classified into two groups: the control group and the intervention group (Fig. 1).

Treatment protocol

Patients in both groups who were on the third day of their menstrual cycle were started on ovulation induction with gonadotrophins (Gonal-F 900 pen, 75 IU subcutaneous per day). Women in the intervention group underwent local endometrial injury (scratch) in the midluteal phase (days 21–25 of the cycle) preceding ovarian stimulation. The scratch was performed by the same investigator, with a Novak curette, to the posterior side of the endometrial cavity under sterile conditions. The women in the control group did not undergo an endometrial scratch before the ovulation induction cycle.

During ovulation induction, the follicle count and size was measured by transvaginal ultrasonography a few days apart. In addition, serum estradiol levels were measured and the gonadotrophin dosage was calibrated intermittently. When the dominant follicle (18 mm and above) arose after ovulation induction with gonadotropins, only if there was no ovarian hyperstimulation or multiple pregnancy risk, human chorionic gonadotropin (hCG) (Ovitrelle, single dose, 6500 IU hCG, subcutaneous) was administered to all patients in both groups. Thirty-six hours after ovulation, IUI was performed in patients by the same investigator under sterile conditions. Those patients who had not undergone IUI or whose cycles were canceled for any reason were excluded from the study. The criteria for cycle cancellation were the presence of premature luteinization (serum progesterone ≥ 1.7 ng/mL during ovulation induction), premature LH peak (LH ≥ 12.1 mIU/mL during ovulation induction), multiple pregnancy risk (follicle count > 4 on the day of hCG), or risk of ovarian hyperstimulation. The serum beta-hCG level was measured 14 days after IUI and pregnancies were determined. After 5–7 weeks of pregnancy, transvaginal ultrasound was used to determine the presence of a gestational sac and a fetal heartbeat; clinical pregnancy was considered if both were present.

Statistical analysis

SPSS version 21.0 was used to analyze statistical data. We used descriptive statistics to express the data (mean ± SD) in the study. To compare quantitative data, we used the Student's t test for normally distributed variables and the Mann-Whitney U test for non-normally distributed variables. The Chi^2 test was used to compare qualitative data. Statistical significance was set at $P < 0.05$.

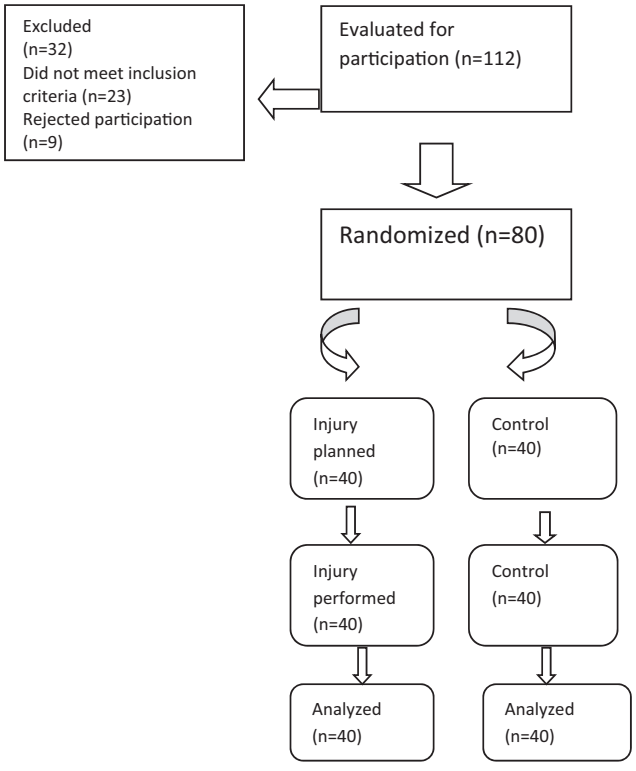

Fig. 1. CONSORT flow diagram.

Results

Eighty patients undergoing IUI were included in our study. We randomized them into two groups: 40 women in the intervention group and 40 women in the control group. The results showed that the groups were similar. No significant difference was found between the two groups in terms of patient age ($P = 0.839$), primary or secondary infertility, mean duration of infertility, menstrual invention, earlier medical treatments, number of menstrual cycles before undergoing medical treatment, or mean total progressive motile sperm count. Moreover, there was no statistically significant difference between the intervention and control groups in terms of endometrial thickness, basal hormone levels, mature follicle count, size of the largest mature follicle, or determination day of the mature follicle. The control and intervention groups also had similar incidences of having primary or secondary infertility ($P = 0.431$) (Table 1).

In the intervention group, 15 pregnancies (37.5%) and 11 clinical pregnancies (27.5%) occurred, whereas in the control group, eight pregnancies (20%) and five clinical pregnancies (12.5%) occurred among 40 patients in the two groups. Although the pregnancy and clinical pregnancy rates were increased in the intervention group, no statistically significant difference was found between rates in the intervention and control groups (pregnancy rates: $P = 0.084$; clinical pregnancy rates: $P = 0.094$) (Table 2).

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