SHORT COMMUNICATION

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In Vitro Fertilization in Patients with Ovarian Endometrioma

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Purpose: To assess the influence of ovarian endometrioma during IVF.

Methods: Patients were submitted to cystectomy by the laparoscopic route for exeresis of ovarian endometrioma. Group I ($n = 28$) consisted of patients without ovarian endometrioma and group II ($n = 14$) consisted of patients with recurrence of ovarian endometrioma during IVF.

Results: Fertilization and cleavage rates were higher in group I and the pregnancy rate per transfer was similar in the two groups.

Conclusions: The presence of endometrioma during IVF causes a worsening of oocyte fertilization and embryo cleavage but does not affect the pregnancy rate per transfer.

KEY WORDS: Endometrioma; in vitro fertilization; ovarian cystectomy; ovulation induction.

INTRODUCTION

Endometriosis is a common and enigmatic disease which has been related to a decline in fertility. However, the mechanism of infertility continues to be a matter of debate and controversy. Ovarian endometriomas can be seen as an invagination of endometriotic tissue and are frequently treated by surgery. Literature data have suggested that ovarian endometriomas might affect the response to ovarian stimulation and oocyte retrieval and implantation rates (1–4).

In infertile women, ovarian endometriomas require surgery and laparoscopy has become the gold standard. In our service, the laparoscopic route with exeresis of the endometrioma is used to maintain the maximum possible amount of ovarian parenchyma. In a recent study, Hemmings *et al.* (5) suggested that exeresis of endometriomas may be deleterious to the

normal residual parenchyma of the ovary, and Hsin-Yi Ho *et al.* (6) concluded that ovaries previously submitted to this treatment show a poorer response to controlled ovarian hyperstimulation. On the other hand, Donnez *et al.* (7) observed that vaporization surgery of endometriomas was not deleterious for in vitro fertilization (IVF) rates. Khamsi *et al.* (8) compared fertilization rates and embryo quality between patients whose embryos had been exposed to endometriotic fluid during oocyte retrieval and patients without endometriomas and detected similar results. Tinkanen *et al.* (9) observed that the presence of a small endometrioma does not affect the success of IVF.

The objective of this study was to determine whether the presence of an ovarian endometrioma in women submitted to IVF affects the final fertilization rates.

MATERIALS AND METHODS

A retrospective study was conducted on patients seen at the Human Reproduction Sector, University Hospital of Ribeirão Preto, University of São Paulo, from January 1994 to December 2002. Included in the study were infertile women who had been submitted to diagnostic laparoscopy and assisted reproduction techniques at our service and who had been diagnosed with ovarian endometriomas at some time during the procedure.

Endometriosis was classified during laparoscopy according to the revised scheme of the American Fertility Society (rAFS). Endometriomas had their capsule removed and content drained, followed by washing of the peritoneal cavity. Peritoneal endometriosis was treated by electrocoagulation of affected focal points.

The patients were divided into two groups: group I ($n = 28$) consisted of patients who, after laparoscopy and exeresis of the endometrioma, were submitted to IVF/ICSI, and group II ($n = 14$) consisted of patients in whom the presence of ovarian endometriomas with a mean diameter smaller than 4 cm was detected during IVF/ICSI cycles despite previous exeresis.

Group I consisted of 28 patients with a mean age of 32.36 years (24–41 years); 57% ($n = 16$) presented the male factor of infertility, 67.8% ($n = 19$) had associated diseases other than endometrioma, and 10.7% ($n = 3$) were treated with gonadotropin-releasing hormone (GnRH) analogs after surgical treatment. Group II consisted of 14 patients with a mean age of 31.43 years (24–36 years); 50.0% ($n = 7$) presented

Table I. IVF Data for Groups I and II Patients

Variable	Group I (without endometrioma)	Group II (with endometrioma)	<i>p</i>
Age (years)	32.29 ± 3.86	31.43 ± 3.75	0.4613
Previous treatment	10.7%	28.5%	0.1967
Male factor	57.14%	50.0%	0.7483
Associated diseases	67.8%	64.2%	1.000
FSH units (IU) used	2401 ± 861.4	2746 ± 901.7	0.2341
No. of retrieved follicles	9607 ± 5.5	9857 ± 4.3	0.8836
% Retrieval	50.9%	54.9%	0.3734
% Fertilization	62.11%	50.15%	<0.0020
% Cleavage	75.92%	64.23%	0.0124
No. of embryos	3250 ± 3051	2286 ± 3049	0.6022
Pregnancy rate per transfer	40%	28.5%	1.000
No. of transferred embryos	2214	1643	0.2406
Endometrium (mm)	11.89 ± 2.615	10.77 ± 1.787	0.2524

the male factor, 64.2% ($n = 9$) had associated diseases other than endometrioma, and 28.5% ($n = 4$) were treated with GnRH analogs as complementary treatment. The patients were submitted to a controlled ovarian hyperstimulation protocol including long-term pituitary blockade with a GnRH agonist and recombinant FSH at the dose of 225–300 IU/day. When at least one follicle with a mean diameter larger than 18 mm was observed, human chorionic gonadotropin was administered at the dose of 10,000 IU, and the patients were submitted to oocyte aspiration 35 h later.

According to resolution No. 1358/92 of the Federal Council of Medicine, a maximum number of four embryos were transferred 72 h after oocyte aspiration using an easy Fridman catheter guided by ultrasound. The patients received luteal phase supplementation and the diagnostic test for pregnancy was performed after 14 days.

For statistical analysis, quantitative variables were compared by Student's *t* test and Fisher's exact test was used for proportions.

RESULTS

The groups were homogenous in terms of patient age (32.36 years for group I and 31.43 years for group II), previous treatment with GnRH analogs (10.7% for group I and 28.5% for group II), presence of the male factor of infertility (50% for group I and 57.14% for group II), and other associated diseases (67.8% for group I and 64.2% for group II). No difference between groups was observed regarding the number of FSH units used for ovulation induction (group I = 2401 IU FSH and group II = 2746 IU FSH), number of retrieved follicles (group I = 9607 and group II =

9857), retrieval rate (group I = 50.9% and group II = 54.9%), number of day 3 embryos (group I = 3250 and group II = 2286), number of transferred embryos (group I = 2214 and group II = 1642), endometrial thickness on the day of transfer (group I = 11.89 mm and group II = 11.0 mm), or pregnancy rate per transfer (group I = 40% and group II = 28.5%) (Table I).

The fertilization rate (group I = 67.9% and group II = 48.5%) and cleavage rate (group I = 87.9% and group II = 70.0%) were higher in the absence of endometriomas ($p < 0.0020$ and $p = 0.0124$, respectively).

In the group of patients submitted to IVF in the presence of endometrioma, oocyte retrieval was also compared between the ovary with endometrioma and the healthy contralateral side. The oocyte retrieval rate (number of oocytes per punctured follicle) was 65.9% in the ovary with endometrioma and 92% in the ovary without endometrioma ($p = 0.0005$) (Fig. 1).

Fig. 1. Rate of oocyte retrieval in the ovary with endometrioma and in the healthy contralateral ovary of group II patients ($p = 0.0005$).

DISCUSSION

In this study, two highly homogenous groups in terms of patient age, endometrial quality at the time of embryo transfer and number of embryos transferred were obtained for the analysis of the impact of the presence of ovarian endometrioma on the outcome of assisted fertilization. The presence of the male factor of infertility, the association with diseases other than endometriosis, or previous clinical treatment for endometriosis also did not differ in this population, thus facilitating the interpretation of the repercussions of endometriomas on infertility treatment.

Classically, alterations in the production of interleukins, other cytokines, and growth factors are known to occur in the presence of endometriosis, in addition to an increase in the number of apoptotic bodies in granulosa cells, changes in the inflammatory response and autoimmune factors and interference with steroid levels, possibly having a negative impact on follicular growth, oocyte quality and implantation rates during assisted reproduction cycles (10–12).

However, the literature reports that oocytes exposed to endometrioma fluid during aspiration have no effect on early embryo development (8), and that the presence of small endometriomas during the assisted fertilization cycle also has no effect on the success of treatment (9,13).

In this study, the presence of endometrioma at the time of aspiration (group II) caused a decline in ovarian reserves as demonstrated by the smaller number of retrieved follicles and aspirated oocytes when compared to the contralateral healthy ovary. However, the fact that no differences in the number of retrieved follicles or oocytes obtained were observed between groups I and II might be explained by the influence of the healthy ovary in the group of patients with endometriomas, altering the final outcome.

Oocyte quality was better in the group of patients without endometriomas, as shown by the higher rates of fertilization and embryo cleavage. However, the pregnancy rates per embryo transfer were similar in the two groups. This is due to the fact that pregnancy in an IVF cycle is multifactorial, and some parameters cannot be evaluated clinically, such as endometrial receptivity, immunologic factors, and intrinsic embryo properties.

The same surgical technique was used for all patients studied and therefore the possibility of dam-

age to the ovarian parenchyma was present in both groups.

On the basis of these findings, we may conclude that the presence of endometriomas during ovarian hyperstimulation for assisted reproduction leads to worse results regarding oocyte fertilization and embryo cleavage although it does not affect the pregnancy rate per embryo transfer.

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