ANDROLOGY

Is There Any Need for Diagnostic Laparoscopy in Couples Undergoing Intracytoplasmic Sperm Injection for Severe Male-Factor Infertility?

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Purpose: Our purpose was to determine whether there is a need for a preliminary diagnostic laparoscopy in couples undergoing intracytoplasmic sperm injection (ICSI) because of severe male-factor infertility.

Methods: In this retrospective study, the results of diagnostic laparoscopy in 342 women with a normal fertility workup undergoing ICSI were evaluated and sperm parameters were correlated with the findings at laparoscopy. Subgroups of patients were defined according to sperm quality, which was expressed as total normal motile count [TNMC = volume (ml) $\times$ concentration (10^6 /ml) $\times$ percentage progressive motility/100 $\times$ percentage normal morphology/100].

Results: When sperm morphology was evaluated according to Kruger's strict criteria, the probability of finding pathology on laparoscopy in the normal male group (16.7%) was statistically higher than that in the group with severely abnormal sperm (1.8%; $P < 0.01$).

Conclusions: There is no need to perform a preliminary diagnostic laparoscopy in the female partner if a full workup is normal in couples with severe male-factor infertility willing to undergo ICSI.

KEY WORDS: diagnostic laparoscopy; intracytoplasmic sperm injection; male infertility.

INTRODUCTION

Until the introduction of intracytoplasmic sperm injection (ICSI) in 1992, there was no effective treatment for infertile couples suffering from extreme oligoasthenoteratozoospermia (OAT). Assisted reproductive techniques (ARTs) such as intrauterine insemination and in vitro fertilization (IVF) were applied with limited success. Optimization of the female factor was important to improve couples' fecundity, and laparoscopy was part of the investigation.

Artificial insemination with donor sperm (AID) was the only valid alternative. It has been shown that in AID cycles performed for male-factor infertility, the pregnancy rate was significantly higher in patients whose husbands were azoospermic than in women whose husbands were subfertile (1–3). These authors showed that if husbands were oligoasthenoteratozoospermic, more pathology was found than in women whose partners were azoospermic.

Since 1992, ICSI has replaced AID for many couples (4–7). This retrospective study aims at investigating whether a preliminary diagnostic laparoscopy may have any role in couples undergoing ARTs for male-factor infertility.

MATERIALS AND METHODS

Three hundred forty-two women who underwent a diagnostic laparoscopy at the Center for Reproductive Medicine of the Dutch-speaking Brussels Free Univer-

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sity between January 1, 1993 and October 1, 1996 were included in this retrospective study. All patients had a normal infertility workup including a physical examination; a medical history without any antecedent of pelvic inflammatory disease, extrauterine pregnancy, endometriosis, or tubal sterilization; normal endocrinology, i.e., normal serum luteinizing hormone (LH), follicle stimulating hormone (FSH), thyroid stimulating hormone (TSH), prolactin, and androgen levels; and a normal ultrasonographic examination.

The diagnostic laparoscopy performed at our institution was considered abnormal when one or more of the following pathologies were found: severe endometriosis (degrees III + IV) (8), adhesions (degrees C + D) (9), hydrosalpinx, bilateral tubal occlusion, ovarian mass >3 cm or any size with solid components, and subserous myoma >5 cm. Sperm was evaluated by visual microscopic analysis by well-trained technicians according to World Health Organization (WHO) guidelines (1992) except in group B, in which morphology was evaluated according to strict criteria (10). Groups were selected according to the husband's semen profile from couples undergoing ARTs in whom the female partner had a preliminary laparoscopy. Subgroups of patients were defined according to sperm quality, which was expressed as the total normal motile count [TNMC = volume (ml) $\times$ concentration (10^6 /ml) $\times$ percentage progressive motility/100 $\times$ percentage normal morphology/100]. Because it has been proven that morphology is an important parameter to predict sperm's fertilization potential, we started to evaluate sperm morphology according to Kruger's strict criteria (11). Thus, the patients were divided into two groups because of the use of two systems to evaluate sperm morphology at two time periods. In the first group (group A; $n = 207$), sperm morphology was analyzed according to WHO guidelines. Patients in this group were divided into two subgroups according to sperm morphology: i.e., <30 or $\geq 30\%$ normal morphology. Those with a TNMC $< 6 \times 10^6$ were defined as group A1, and those with a TNMC $\geq 6 \times 10^6$ as group A2 (calculated according to the formula $2 \text{ ml} \times 20 \text{ mil/ml} \times 50/100$ progressive motility $\times 30/100$ normal morphology). In the second study group (group B; $n = 135$), sperm morphology was analyzed according to Kruger's strict criteria (11). Three subgroups were included according to sperm morphology: ≤ 4 , 5–14, and $> 14\%$ normal morphology. In group B1, the TNMC was $\leq 0.8 \times 10^6$; in group B2, the TNMC was between 0.8×10^6 and 2.8×10^6 ; and in group B3, the TNMC was $> 2.8 \times 10^6$ (calculated according to the formula $2 \text{ ml} \times 20 \text{ mil/}$

$\text{ml} \times 50/100$ progressive motility $\times \leq 4$ or 5–14 or $> 14/100$ normal morphology).

Statistical Analysis

The χ^2 and Fisher's exact probability test were used for comparison of the percentages of abnormal findings at laparoscopy for both groups (A + B). Receiver operating characteristic (ROC) analysis (Medcalc; Medcalc Software, Ghent, Belgium) was used to assess the clinical accuracy of the TNMC calculated with Kruger's strict criteria for morphology and to choose a decision threshold for TNMC to be used in predicting pathology at laparoscopy. The sensitivity, or the chance that a certain cutoff value for TNMC tests positive in the presence of abnormality at laparoscopy, and the specificity, defined as the chance that a certain cutoff value for TNMC tests negative when the laparoscopy was normal, were calculated. In the ROC curves the true positive rate (sensitivity) is represented on the y axis and the false positive rate ($100 - \text{specificity}$) is represented on the x axis of the curve. The area under the curve is a quantitative measure of accuracy. A variable was considered perfectly discriminative when the area under the curve equaled 1 (ROC curve that passes through the upper left corner) and clinically a powerful predictor when it was 0.9 or greater. When the area under the curve was 0.5 (ROC curve that goes from the lower left corner to the upper right corner) a variable was considered without any discrimination (12).

RESULTS

Seventy-six patients from group A ($n = 207$; WHO criteria) with poor sperm quality (TNMC $< 6 \times 10^6$) were defined as group A1. In this group five abnormal laparoscopies were observed (6.6%). In group A2, composed of 131 patients with normal sperm characteristics (TNMC $\geq 6 \times 10^6$), 10 pathologic findings were observed (7.6%) (Table I). The most frequent pathology found in group A was tubal blockage (9 of 15 patients). The comparison of the percentages of abnormal findings at laparoscopy done by χ^2 test revealed no statistically significant difference between the two subgroups (groups A1 and A2).

In group B ($n = 135$), classified according to Kruger's strict criteria, 57 patients had extremely poor sperm quality, with a TNMC $\leq 0.8 \times 10^6$ (group B1). Only one spouse revealed a pathologic finding at laparoscopy (1.8%) (left cornual myoma with curled tubes

Table I. Abnormal Laparoscopic Findings in Group A (Sperm Morphology According to WHO Criteria) (11)

Group	TNMC ^a	Abnormal laparoscopy
A1 (<i>n</i> = 76), TNMC < 6 × 10 ⁶	1.10	Tubal blockage
	2.07	Bilateral hydrosalpinx
	2.46	Tubal blockage
	3.06	Bilateral hydrosalpinx
	4.68	Endometriosis (grade IV, rAFS)
A2 (<i>n</i> = 131), TNMC ≥ 6 × 10 ⁶	9.48	Severe adhesions, hydrosalpinx
	10.63	Endometriosis (grade III, rAFS)
	12.48	Tubal blockage
	27.29	Endometriosis, tubal blockage
	31.42	Tubal blockage
	60.98	Hydrosalpinx
	93.74	Tubal blockage
	106.98	Severe adhesions, tubal blockage
	107.10	Tubal blockage
	256.41	Tubal blockage

^a Total normal motile count (TNMC) = volume (ml) × concentration (10⁶/ml) × percentage progressive motility/100 × percentage normal morphology/100.

and impaired patency using methylene blue dye). Group B2 (*n* = 24), with a TNMC = 0.8–2.8 × 10⁶, revealed two cases with abnormal laparoscopy (8.3%). Nine of 54 patients with normal sperm characteristics, classified as group B3 (TNMC > 2.8 × 10⁶), revealed abnormalities at laparoscopy (16.7%). The comparison of the percentages of abnormal laparoscopic findings in groups B1 and B2 and groups B2 and B3 by Fisher's exact probability test showed no statistically significant difference. However, the difference in the percentages of abnormalities at laparoscopy between the severe male-factor group (group B1) and the normal male group (group B3) was statistically significant (*P* < 0.01) (Table II).

The clinical accuracy of the TNMC with Kruger's criteria for morphology (group B; *n* = 135) for predicting the likelihood of pathology at laparoscopy, analyzed by ROC curve analysis with a sample size large enough to draw meaningful qualitative conclusions, showed an area under the curve of 0.72. The best cutoff level for TNMC, which is the decision level chosen to use this variable to predict abnormality at laparoscopy, was 2.15. The sensitivity at this cutoff value was 91.7%, and the specificity was 59.8% (Fig. 1).

DISCUSSION

In recent years ICSI has been developed as an alternative to AID and IVF for the treatment of couples

Table II. Abnormal Laparoscopic Findings in Group B (Sperm Morphology According to Kruger's Strict Criteria) (10)

Group	TNMC ^a	Abnormal laparoscopy
B1 (<i>n</i> = 57), TNMC ≤ 0.8 × 10 ⁶	0.00	Let cornual myoma, tubal blockage
B2 (<i>n</i> = 24), TNMC = 0.8–2.8 × 10 ⁶	2.44	Endometriosis (grade IV, rAFS)
	2.55	Endometriosis (grade IV, rAFS)
B3 (<i>n</i> = 54), TNMC > 2.8 × 10 ⁶	4.12	Unilateral tubal blockage, hydrosalpinx
	4.80	Severe adhesions, tubal blockage
	5.10	Severe adhesions, hydrosalpinx
	7.89	Hydrosalpinx, difficult patency
	9.10	Tubal blockage
	9.70	Severe adhesions
	10.17	Tubal blockage
	12.32	Tubal blockage
	54.05	Hydrosalpinx, difficult patency

^a Total normal motile count (TNMC) = volume (ml) × concentration (10⁶/ml) × percentage progressive motility/100 × percentage normal morphology/100.

with severe male-factor infertility (5–7). Before the application of ARTs, optimization of the female factor was of utmost importance. For this, diagnostic laparoscopy was essential. From AID studies it is well-known that the occurrence of female pathology is increased in the presence of OAT compared to azoospermia. Thus, in couples suffering from male-factor infertility the following rule applies: the better the male, the worse the female. Nowadays the question of whether

Fig. 1. Receiver operating characteristics (ROC) curve analyzing the value of sperm characteristics to predict abnormalities at laparoscopy for group B (sperm morphology analyzed according to Kruger's strict criteria).

there is a real need for a preliminary diagnostic laparoscopy in couples undergoing ICSI because of severe male-factor infertility is raised.

In this study, therefore, we investigated whether abnormal findings at laparoscopy were correlated with sperm quality. We also tried to define the best cutoff value for the sperm predicting female pathology at laparoscopy.

Initially we reviewed the laparoscopic results of 207 women who were classified according to their partners' sperm characteristics by WHO criteria (11). The percentage of abnormal results at laparoscopy was not significantly different in the normal and abnormal sperm groups (7.6 versus 6.6%, respectively). This observation showed that sperm quality, when all sperm parameters were evaluated according to WHO criteria, could not discriminate between partners with and those without pathology in our series. In this group five abnormal findings at laparoscopy were described. Two of these five pathologies were tubal blockage without influence on ICSI treatment. One case showed severe endometriosis. The effect of endometriosis on IVF outcome is controversial (13,14). A low fertilization rate probably related to ovulatory disorders, an altered follicular response because of disruption of ovarian blood supply or mechanical pressure, an alteration of oocyte quality resulting in a reduced implantation rate, and, finally, a toxic effect of human serum have been considered responsible for a poor outcome in IVF cycles (13,15–18). In contrast, recent reports have concluded that, regardless of its stage, endometriosis does not affect the outcome of IVF treatment (14, 19–21). The third pathology was bilateral hydrosalpinx. In the literature there is a consensus that hydrosalpinx adversely affects the outcome of IVF. The suggestion is that toxic substances and inflammatory cellular elements coming from the dilated tube can adversely influence the implantation of the embryo (22–24). With these observations taken into account, it seems that laparoscopy may have been important for the ICSI treatment of 2 (2.6%) of 76 couples.

We therefore performed the same analysis in 135 patients in whom sperm morphology was assessed according to Kruger's strict criteria. The percentage revealing an abnormality at laparoscopy in group B1 was 1.8%. In group B2 two cases (8.3%) showed pathology at laparoscopy. In the normal male-factor group (B3) 16.7% of the patients had abnormalities at laparoscopy. The percentage of abnormal findings at laparoscopy for group B3 was significantly higher compared to that for group B1. Because of this finding we applied ROC curve analysis to assess the accuracy of sperm

parameters, to predict female pathology at laparoscopy, and to define the best cutoff value for the sperm parameters. But this analysis showed that the best cutoff value for TNMC is not accurate enough for clinical use. In the severe male-factor group (group B1), according to Kruger's strict criteria, 1 case (1.8%) of 57 showed cornual myoma with hampered patency. Probably this myoma does not interfere with infertility (25). In our second series, this finding led us to conclude that none of the performed laparoscopies ($n = 57$) showed any pathology hampering the outcome of an eventual ICSI treatment.

Finally, in male-factor infertility (groups A1 + B1 + B2) ($n = 157$), only two pathologies possibly interfering with ICSI outcome were observed by diagnostic laparoscopy (1.3%). When we evaluated the sperm morphology by more strict criteria and when we considered only patients who were candidates for an ICSI procedure because of the poor sperm quality, we did not find any pathology at laparoscopy with a possible risk for the procedure's outcome. Thus the role of routinely performed laparoscopy is questionable in couples who may benefit from ICSI treatment.

In conclusion, when standard methods such as anamnesis, endocrinologic examination, ultrasonography, and hysteroscopy are normal in patients requiring ICSI for severe male-factor infertility, there is no need for a preliminary diagnostic laparoscopy.

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