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ICSI outcome in severely oligoasthenozoospermic patients and its relationship to prewash progressive sperm motility*

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Aim: To investigate the association between prewash progressive sperm motility and pregnancy rate in cases of severely oligoasthenozoospermic patients in intracytoplasmic sperm injection (ICSI) cycles.

Materials and methods: The study included 80 infertile couples who were treated by ICSI due to severe oligoasthenozoospermia (<106). Results were obtained by retrospective analysis of data that are regularly entered into SPSS in our In Vitro Fertilization Unit. Female patients older than 35 years were excluded. The patients were divided into 2 groups according to prewash progressive sperm motility. Group I had progressive sperm motility below 10% (n = 40), and group II had progressive sperm motility equal to or greater than 10% (n = 40). The main outcome measure was the clinical pregnancy rate.

Results: The patient characteristics were similar in both groups. There were no significant differences between the 2 groups in terms of total number of oocytes retrieved, number of mature oocytes, fertilization rate, or the number of transferred embryos. A total of 38 (47.5%) clinical pregnancies were obtained in 80 ICSI treatment cycles. The clinical pregnancy rate was significantly higher in group II (62.5% [25/40] than in group I (32.5% [13/40]), with P = 0.014.

Conclusion: Severe sperm motility impairment results in human infertility, which can be overcome by ICSI. The data from this study demonstrated that severe progressive motility defects in cases of severe oligoasthenozoospermia do not prevent fertilization or normal embryo production in ICSI cycles; however, the rate of ICSI success may be influenced by progressive sperm motility. Our results show that oligoasthenozoospermic patients with progressive sperm motility above 10% have better clinical pregnancy results.

Key words: Intracytoplasmic sperm injection, oligoasthenozoospermia, pregnancy

Yıkama öncesi progresif sperm motilitesinin ciddi oligoastenozoospermisi olan hastalarda İCSİ sonuçları üzerine etkisi

Amaç: İCSİ yapılan ciddi oligoastenozoospermik hastalarda yıkama öncesi progresif sperm motilitesi ile gebelik oranı arasındaki ilişkiyi araştırmak.

Yöntem ve gereç: Ciddi oligoastenozoospermi (<106) nedeni ile İCSİ ile tedavi edilen 80 infertil çift çalışmaya dahil edildi. Sonuçlar IVF ünitemizde düzenli olarak SPSS istatistik programına kaydedilen verilerin retrospektif analizi ile değerlendirildi. 35 yaşından büyük kadın hastalar çalışmaya dahil edilmedi. Hastalar yıkama öncesi progresif sperm motilitesine göre iki gruba bölündü. Grup 1, progresif sperm motilitesi <% 10 (n = 40), grup 2 progresif sperm motilitesi >% 10 (n = 40). Sonuç klinik gebelik oranı ile değerlendirildi.

Bulgular: Hasta karakteristikleri her iki grupta benzerdi. Her iki grup arasında, toplanan toplam yumurta sayısı, matür oosit sayısı, fertilizasyon oranı ve transfer edilen embriyoların sayısı ile ilgili olarak önemi farklılıklar yoktu. 80 İCSİ

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tedavi siklusunda toplam 38 (% 47,5) klinik gebelik elde edildi. Klinik gebelik oranı grup 2'de (% 62,5), grup 1'e (% 32,5) göre belirgin olarak daha yüksekti, P = 0.014.

Sonuç: Ciddi sperm motilite bozuklukları İCSİ ile tedavi edilebilen insan infertilitesi ile sonuçlanmaktadır. Bu çalışmadan elde edilen veriler ciddi oligoastenozoospermisi olan olgulardaki progresif sperm motilite defektlerinin İCSİ sikluslarında normal fertilizasyon ve normal embryo gelişimini engellemediğini göstermektedir, fakat, İCSİ başarı oranı progresif sperm motilitesinden etkilenebilir. Bizim sonuçlarımız % 10'un üzerinde progresif sperm motilitesi olan oligoastenozoospermik hastaların klinik gebelik sonuçlarının daha iyi olduğunu göstermiştir.

Anahtar sözcükler: İCSİ, oligoastenozoospermi, gebelik

Introduction

The technique of in vitro fertilization (IVF) was successfully applied for the first time in 1978 to bypass complete occlusion of the fallopian tubes (1). Since then, the indications for IVF have expanded internationally to include other infertility conditions such as male infertility, endometriosis-associated infertility, immunological infertility, and unexplained infertility, or as the last option for couples with infertility who have tried and failed to conceive using standard therapies (2,3).

The management of male infertility totally changed after the introduction of intracytoplasmic sperm injection (ICSI). This technique was rapidly integrated into the routine clinical practice of fertility clinics offering assisted reproductive technology (ART) throughout the world as a potential treatment for severe male infertility (oligoasthenoteratospermia), and high rates of fertilization and pregnancy have been reported (4,5). During recent years, ICSI has become the most frequently used method for fertilization, and, in 2004, ICSI was used in nearly 60% of all reported ART cycles in Australia and New Zealand, Europe, and the USA (6-8). In a recent publication of trends in the use of ICSI in the USA, it was shown that from 1995 to 2004, the proportion of cycles in which ICSI was used increased from 11% to 57.5% (9). Several studies have indicated that there has been a global decrease in sperm concentration during the past 5 to 6 decades (10-14), with wide regional differences (12,15). A real decline in semen quality and a higher proportion of subfertile men could be a contributing factor to the rise in the use of ICSI. It could also be speculated that an increase in subtle changes in semen quality, which may not always be recorded as male infertility, has occurred.

The total number of motile sperm after sperm preparation has been shown to predict the outcome after IVF (16) and a count of 500,000 has been suggested as a cut-off value for IVF (17), although others recommend a number of $>10^6$ progressive motile sperm (16). However, a metaanalysis of sibling oocytes studied in patients with moderate oligoasthenoteratozoospermia (OAT) revealed that the odds of fertilization after ICSI were 3.9-fold greater than with IVF. The number needed to treat (NNT) in order to prevent 1 complete fertilization failure after IVF could be 3, indicating that 3 ICSI procedures would have to be performed instead of conventional IVF in couples with moderate OAT in order to prevent 1 complete fertilization failure (18). There are fewer unexpected fertilization failures in the ICSI group, but if embryos are obtained, ICSI embryos generate a similar percentage of pregnancies as do IVF embryos (19). It has been suggested that ICSI should be the treatment of choice in all assisted reproduction cycles.

Our aim was to investigate the association between progressive sperm motility and pregnancy rate in cases of severely oligoasthenozoospermic patients treated with ICSI cycles in couples where the woman's age was 35 or younger.

Materials and methods

The study included 80 infertile couples who were treated with ICSI due to severe oligoasthenozoospermia ($<10^6$) at the Fatih University School of Medicine Reproductive Endocrinology and IVF Unit between August 2005 and July 2009. Results were obtained by retrospective analysis of data that are regularly entered into SPSS.

The patients had a comprehensive history taken followed by physical examination, including gynecologic examination. Patients were excluded from this analysis if the female's age was older than 35. Hormone levels, including day 3 follicle-stimulating hormone (FSH) and estradiol (E2), were evaluated in all women, and transvaginal ultrasonography was performed to evaluate endometrial thickness.

The patients were divided into 2 groups according to prewash progressive sperm motility. Group I had progressive sperm motility below 10% (n = 40), and group II had progressive sperm motility equal to or greater than 10% (n = 40).

Ovarian stimulation was performed using a long protocol of the standard technique of gonadotropin-releasing hormone agonist downregulation and controlled stimulation with a recombinant FSH. Cycles were monitored by ultrasonography and serial monitoring of E2 levels. Once the follicular sizes exceeded 17 mm, ovum pick-up (OPU) was performed under general anesthesia. On the OPU day, sperm retrieval was also performed and ICSI was performed on mature eggs. Fertilization was confirmed 24 h later and embryo transfer was performed on day 3 after OPU. The main outcome measure was the clinical pregnancy rate.

Results

The clinical characteristics of women in group I and group II are presented in Table 1. None of the evaluated parameters demonstrated significant differences. There were no significant differences noted between the 2 groups in terms of the total number of oocytes retrieved, number of mature oocytes, number of transferred embryos, or fertilization rate (Table 2). A total of 38 (47.5%) clinical pregnancies were obtained in 80 ICSI treatment cycles. The clinical pregnancy rate was significantly higher in group II (62.5% [25/40]) than in group I (32.5% [13/40]), with P = 0.014.

Conclusion

Severe sperm motility impairment results in human infertility, which can be overcome by ICSI. The report of the first pregnancy with the intracytoplasmic injection of sperm and the high fertilization rate reported by Van Steirteghem et al. brought new hope for couples with severe male-factor infertility (5). The approach to patients with various sperm defects like oligoasthenoteratospermia has changed significantly with the introduction of sperm retrieval techniques and assisted reproduction, especially with ICSI. In addition to improving pregnancy rates using sperm from ejaculated semen, ICSI has opened new possibilities for achieving pregnancy with sperm retrieved from the epididymis or testes, approaches which have been performed for more than 10 years. Satisfactory results have been achieved in various studies using these techniques (4).

ICSI results were shown to be the same with various sperm defects such as severe oligospermia, oligoasthenoteratospermia, and asthenoteratospermia (20,21). Nevertheless, it is well known that the outcomes of ICSI are much better

Table 1. Clinical characteristics of the patients.

	Group I (n = 40)	Group II (n = 40)	P-value
Age (female)	28.97 ± 3.66	28.82 ± 4.00	>0.05
Age (male)	33.05 ± 5.32	32.55 ± 4.66	>0.05
Duration of infertility (years)	5.21 ± 3.55	4.68 ± 2.86	>0.05
Day 3 FSH (mIU/ mL)	7.25 ± 2.19	7.14 ± 2.51	>0.05
Day 3 E2 (pg/mL)	40.11 ± 21.15	33.27 ± 28.33	>0.05
Endometrial thickness	9.32 ± 1.85	9.62 ± 1.88	>0.05

Table 2. Outcome measures of the patients.

	Group I (n = 40)	Group II (n = 40)	P-value
Number of oocytes	12.00 ± 6.21	10.68 ± 4.26	>0.05
Number of mature oocytes	7.83 ± 4.04	8.55 ± 3.76	>0.05
Fertilization rate (%)	63.60 ± 27.30	69.20 ± 21.59	>0.05
Number of embryos transferred	2.34 ± 0.77	2.21 ± 0.69	>0.05
Clinical pregnancy (%)	32.5% (13/40)	62.5% (25/40)	0.014

when motile sperm can be selected (22,23), even though each spermatozoon is immobilized before injection. In the present study, asthenozoospermia is defined as a low proportion of progressive motile spermatozoa (+4 and +3) of less than 10% in a fresh semen sample. Different conditions may impair sperm motility, but the etiology of asthenozoospermia often remains unknown. Motile spermatozoa should be selected for ICSI not because of their movements but with a view to their vitality. Progressive motility may be an indicator of adequate metabolic activity of the spermatozoon. This may explain why when viable but immotile spermatozoa were used for ICSI, the resulting embryos were of diminished quality and had poor developmental potential (24).

The data from this study demonstrate that severe progressive motility defects in cases of severely oligoasthenozoospermic patients do not prevent fertilization or normal embryo production when ICSI is used. However, the rate of ICSI success may be influenced by progressive sperm motility. Our results show that oligoasthenozoospermic patients with progressive sperm motility above 10% give better clinical pregnancy results.

We conclude that progressive sperm motility is an important and powerful factor in determining the chance of pregnancy in oligoasthenozoospermic patients.

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