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Pregnancy Results of Intracytoplasmic Sperm Injection in Infertile Males with Non-obstructive Azoospermia: A Retrospective Study

Non-obstrüktif Azospermili İnfertil Erkeklerde İntrasitoplazmik Sperm Enjeksiyonunun Gebelik Sonuçları: Retrospektif Bir Çalışma

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Abstract

Objective: This study investigated the number of live births in men with non-obstructive azoospermia (NOA) using a combination micro-testicular sperm extraction and intracytoplasmic sperm injection.

Methods: A total of 434 patients who underwent micro-testicular sperm extraction because of NOA were included in the study. Data such as date of birth, duration of infertility (in years), number of mature oocytes obtained from the spouse, number of embryos transferred, day of transfer, medical histories of the spouses, physical examination findings, and comorbidities were recorded.

Results: Ultimately, 19 live births were achieved through successful implantation.

Conclusion: The combination of micro-testicular sperm extraction and intracytoplasmic sperm injection in NOA cases continues to be the most ideal and current treatment method for couples who want to have children.

Keywords: Azoospermia, male infertility, micro-testicular sperm extraction

Öz

Amaç: Bu çalışmanın temel amacı non-obstrüktif azospermisi (NOA) olan erkeklerde mikro-testiküler sperm ekstraksiyonu ve intrasitoplazmik sperm enjeksiyonu kombinasyonu ile gerçekleşen canlı doğum sayılarını araştırmaktır.

Yöntem: NOA nedeniyle mikro-testiküler sperm ekstraksiyonu yapılan toplam 434 hasta çalışmaya dahil edildi. Kendisi ve eşine ait doğum tarihleri, infertilite süresi (yıl olarak), eşten elde edilen matür oosit sayısı, transfer edilen embriyo sayısı, transfer edilen gün, eşlere ait tıbbi öyküler, fizik muayene bulguları ve komorbiditeleri gibi veriler kaydedilmiştir.

Bulgular: Neticede implantasyon sonucunda 19 tane canlı doğum olmuştur.

Sonuç: NOA olgularda mikro-testiküler sperm ekstraksiyonu ve intrasitoplazmik sperm enjeksiyonu kombinasyonu çocuk sahibi olmak isteyen çiftler için en ideal ve güncel tedavi yöntemi olmaya devam etmektedir.

Anahtar Kelimeler: Azospermi, erkek infertilitesi, mikro-testiküler sperm ekstraksiyonu

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Introduction

Infertility is defined as the inability to achieve pregnancy in couples with normal sexual lives who have not used contraception for a period of one year[1]. Infertility affects approximately 20% of couples[2]. The prevalence of male factor infertility among infertile couples ranges from 30% to 50%[3,4]. Azoospermia, which is defined as the absence of sperm in the ejaculate, accounts for 7-15% of male infertility cases[4,5]. Approximately 40% of infertile men with azoospermia have obstructive azoospermia (OA) and 60% have non-OA (NOA)[5]. The prevalence of NOA is 1% among all men and 10% among infertile men[3]. The main difference between OA and NOA is that while spermatogenesis is normal in OA, it is either absent or severely impaired in NOA, which significantly reduces fertility rates compared with OA[4,6]. Detailed anamnesis and physical examination, along with laboratory investigations focusing on etiology and, if necessary, genetic testing, play a crucial role in elucidating the etiology of azoospermia[5]. In NOA etiology, besides small testes, there are conditions such as primary testicular failure characterized by high luteinizing hormone (LH) and follicle-stimulating hormone (FSH), secondary testicular failure characterized by low LH and FSH[7], previous exposure to radiation and chemotherapy, cryptorchidism, and varicocele[5]. Generally, NOA is characterized by the absence of sperm in the semen[6]. In the early and mid-1990s, it was extremely challenging for men diagnosed with NOA to father children[8]. However, by the mid-1990s, the introduction and subsequent development of testicular sperm aspiration, conventional testicular sperm extraction (TESE), and microdissection-TESE (micro-TESE) techniques increased the chances of achieving pregnancy for azoospermic infertile couples[8]. TESE-intracytoplasmic sperm injection (ICSI) has become a widely used procedure in assisted reproductive techniques[9,10].

Materials and Methods

Participant Cohort and Data Collection

This retrospective study included 511 cases diagnosed with azoospermia who applied to the Assisted Reproduction Center of the Department of Obstetrics and Gynecology at University of Health Sciences Turkey, İzmir Tepecik Education and Research Hospital, between 2009 and 2020. Ethical approval was obtained from the Non-Interventional Research Ethics Committee of the University of Health Sciences Turkey, İzmir Tepecik Education and Research Hospital (decision no: 2023/03-42, date: 05.04.2023). The diagnosis of azoospermia in all cases was confirmed through detailed history-taking, physical examination, three consecutive semen analyzes and measurements of testosterone and FSH levels. Semen samples were obtained through masturbation with visual stimulation, following the criteria set by the World Health Organization, in the andrology laboratory. Data recorded included the birth dates of the patients and their partners, duration of infertility (in years), number of mature oocytes obtained from the partner, number of embryos transferred, day of transfer, medical history, physical examination findings, and comorbidities of the couples.

Statistical Analysis

Statistical computations were performed using SPSS for Windows version 23.0 (SPSS, Chicago, USA). Results are presented in percentiles.

Results

The pregnancy outcomes of the 511 cases diagnosed with azoospermia are presented in Table 1 with numerical data and in Table 2 with percentage data.

Table 1. Numerical data on pregnancy outcomes in patients with azoospermia

Azospermia		NOA		Fertilization		Transfer		Implantation		Birth	
OA	NOA	Sperm (+)	Sperm (-)	Yes	No	Yes	No	Yes	No	Yes	No
77	434	235	199	201	34	191	10	64	127	19	45

OA: Obstructive azoospermia, NOA: Non-OA

Table 2. Numerical data on pregnancy outcomes in patients with azoospermia (as a percentage)

Azospermia		NOA		Fertilization		Transfer		Implantation		Birth	
OA %	NOA %	Sperm (+) %	Sperm (-) %	Yes %	No %	Yes %	No %	Yes %	No %	Yes %	No %
15.06	84.94	54.14	45.86	85.47	14.5	95.02	4.98	33.5	66.5	29.68	70.32

OA: Obstructive azoospermia, NOA: Non-OA

Of the 511 cases of azoospermia, 434 were diagnosed with NOA. Among these 434 cases, sperm was detected in the semen samples of 235 individuals, whereas no sperm was found in 199 individuals. In the cases where sperm was detected, fertilization occurred in 201 cases, while in 34 cases, fertilization did not occur. Of the fertilized oocytes, 191 were transferred, and of the transferred fertilized oocytes, implantation occurred in 64 cases. There were 19 live births following implantation.

Of the azoospermic cases, 84.94% were diagnosed with NOA, whereas 15.06% had OA. Among the NOA cases, sperm was detected in 54.14% of individuals, and 85.47% of these cases achieved fertilization following ICSI. Of the fertilized oocytes, 95.02% were transferred, and implantation was observed in 33.5% of these transfers. As a result, the live birth rate following implantation was 29.68%. In general, out of the total 511 azoospermic cases, 3.71% resulted in live births, whereas among the 434 NOA cases, 4.37% resulted in live births.

Discussion

Azoospermia is a significant public health problem and a serious cause of infertility in men, which can be attributed to both congenital and genetic factors, such as Klinefelter syndrome, microdeletions, and cryptorchidism, as well as acquired factors, such as surgical procedures, various medications, and exposure to air pollution[11]. Among patients diagnosed with azoospermia, 60% are classified as having NOA, whereas the remaining 40% have OA[12]. In our retrospective study, out of the 511 included azoospermic cases, 77 individuals (15%) were diagnosed with OA, whereas 434 individuals (85%) were diagnosed with NOA. In NOA cases, the age of the patient, testicular volume and size, and testosterone, prolactin, FSH, LH, and estrogen levels are crucial factors in obtaining sperm[13,14]. The rate of sperm retrieval in NOA cases ranges from 40% to 70%[15,16]. Different studies have shown that the rate of sperm retrieval with micro-TESE ranges from 20% to 70%, with an average of 46%[17,18]. In our study, out of the 434 NOA cases diagnosed in our center, sperm retrieval was achieved in 235 cases (54.14%) through micro-TESE. Numerous studies have demonstrated that the success of fertilization through ICSI is higher in OA than in NOA[4,18-22]. Furthermore, factors such as FSH levels determined before testicular biopsy, testicular volume and size, presence of spermatogenic defects, previous testicular biopsy attempts, laboratory methods used for sperm preparation, ovarian stimulation protocols for female factors, and the expertize of the personnel performing the procedures play an important role in fertilization success[8,21,23]. In one study, live birth rates were found to be lower in the NOA group than in the OA group[24], whereas another study did not find a significant difference in implantation and clinical pregnancy rates between the NOA and OA groups[15]. Yet another study reported higher rates of fertilization and biochemically confirmed pregnancies in the OA group than in the NOA group, but there was no significant difference in clinical pregnancy and miscarriage rates between the two groups[24]. In another study, fertilization rates were found to be lower in the NOA group than in the OA group[25]. In our study, out of the 235 NOA cases with sperm retrieval, fertilization was achieved in 201 cases (85%), while in 34 cases (15%), fertilization did not occur. Both our study findings and the existing literature suggest that the higher fertilization rate in OA cases compared with that in NOA cases can be explained by more normal spermatogenesis. In a previous study, the implantation rates in fertilized and transferred embryos were similar in the NOA and OA groups, but ongoing clinical pregnancy rates were higher in the OA group[25]. In our study, out of the 201 fertilized embryos, 191 (95%) were transferred, whereas 10 (5%) could not be transferred. Of the 191 transferred embryos, 64 (34%) resulted in implantation, and 19 live births were achieved. In another study, a combination of micro-TESE and ICSI resulted in a clinical pregnancy rate of 45.45% and a live birth rate of 20.83%[26].

Study Limitations

The main limitation in the present study that can be addressed and overcome in future research is the relatively limited sample size.

Conclusion

Based on our study and previous research, the combination of micro-TESE and ICSI continues to be the most ideal and up-to-date treatment method for couples seeking to have children with NOA.

Ethics

Ethics Committee Approval: The study was approved by the University of Health Sciences Turkey, İzmir Tepecik Education and Research Hospital's Non-Interventional Research Ethics Committee (decision no: 2023/03-42, date: 05.04.2023).

Informed Consent: Retrospective study.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Surgical and Medical Practices: M.Z.K., Concept: C.K., Design: C.K., M.Z.K., Data Collection or Processing: C.K., M.Z.K., Analysis or Interpretation: C.K., M.Z.K., Literature Search: C.K., Writing: C.K.

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