

MALE INFERTILITY IS INCREASING: EVALUATION OF INDICATIONS FOR IN VITRO FERTILIZATION IN A PUBLIC INSTITUTION IN TURKEY

ERKEK İNFERTİLİTESİNDE ARTIŞ: TÜRKİYE'DE KAMU KURUMUNDA İN VITRO FERTİLİZASYON İNDİKASYONLARININ DEĞERLENDİRİLMESİ

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Abstract

Aim: Male -factor infertility underlies approximately 30% of couples seeking infertility treatment, 10% of which is azoospermia. Recently, we observed an increase in male infertility and investigated the part of male infertility among the in vitro fertilization (IVF)/intracytoplasmic sperm injection (ICSI) cycles in a public institution in Ankara, Turkey.

Materials And Method: We reviewed the indications for IVF cycles between 2007 and 2011. Subgroups of male infertility and cases requiring surgical sperm extractions were determined for the last three years. Possible environmental factors related to male infertility are reviewed.

Results: A total of 6806 IVF cycles were evaluated. The percentage of couples undergoing IVF therapy due to male infertility was 42.4 %, 46.9 %, 40.6 %, 39.8 %, 36 %, 46.6 %, 51.9 % respectively for each year from 2005 through 2011. In the last three years, a total of 1349 cycles were done of which 597 (44.25 %) were treated for male infertility. We found that 416 (69.7 %) of the cases had severe oligospermia and 181 (30.3 %) mild. There were 170 cases of azoospermia, 27 obstructive and 163 non obstructive. Surgical retrieval of sperm was possible in 105 of the them by PESA, TESA, PESA or MD TESE.

Conclusion: Our data suggests a gradual increase in male infertility in recent years. Identification and elimination of environmental hazards should be the subject

of both gynecologists and Public Health Services. Elimination of preventable damages will reduce the cost of assisted reproduction.

Keywords: male infertility, in vitro fertilization, environmental hazards

Özet

Amaç: Infertilite tedavisi için başvuran çiftlerin yaklaşık %30'undan erkek faktörü sorumludur ve bu vakaların %10'u da azoospermiktir. Son yıllarda, hastanemizin IVF ünitesine erkek infertilitesi nedenli başvurularında bir artış izledik ve IVF-ICSI sikluslarında erkek infertilitesinin sıklığını araştırmayı amaçladık.

Gereçler ve Yöntem: Retrospektif olarak 2007-2011 yılları arasında yapılan IVF-ICSI sikluslarında endikasyonların dağılımı incelendi. Son üç yılda erkek faktörü nedeniyle tedaviye alınan hastalar ayrıca incelenerek, erkek infertilitesinin subgrupları ve cerrahi olarak sperm elde edilen hastalar araştırıldı. Erkek infertilitesindeki artışın olası sebepleri değerlendirildi.

Bulgular: Toplam 6806 IVF siklusu değerlendirmeye alındı. Erkek faktörü nedeniyle IVF-ICSI yapılan hastaların oranı 2005-2011 arasında her yıl için sırasıyla % 42.4, % 46.9, % 40.6, % 39.8, % 36, % 46.6, % 51.9 olarak bulundu. Son üç yılda ise 597 tanesi (% 44.25) erkek faktörü sebebiyle 1349 IVF-ICSI siklusu yapıldı. Bu vakaların 416 (69.7 %) tanesi şiddetli, 181 (%30.3) tanesi ise hafif erkek infertilitesi idi. Azoospermik vakaların sayısı, 27 obstruktif ve 163 tanesi non-obstrük-

tif olmak üzere toplam 170'ti. Bu hastaların 105 tanesinde PESA, TESA, PESA veya MD TESE ile sperm elde edildi.

Sonuç: Verilerimiz erkek infertilitesinde bir artış yaşandığını işaret etmektedir. Çevresel faktörlerin tespiti ve eliminasyonu Jinekoloji ve Halk Sağlığı Birimlerinin iş-

birliği yapmasını gerektiren bir konudur. Önlenebilir hastaların eliminasyonu Yardımcı Üreme Teknikleri nedeniyle maliyeti azaltmada da faydalı olacaktır.

Anahtar Kelimeler : erkek infertilitesi, in vitro fertilizasyon, çevresel etkenler

Introduction

Reproduction and childbirth is one of the central themes of life but infertility affects one in seven to one in eight of reproductive age couples (1). Male factor infertility underlies approximately 30 % of infertility in couples seeking treatment ; of which 10% is due to azoospermia (2).

There are reports indicating temporal downward trends in semen quality (3,4). Occurance of testicular cancer, cryptorchidism and hypospadias are also reported to be increased across some time periods in some populations past 50 years (5,6).

There is increasing concern about the potential risk of environmental chemicals to male reproductive health .Moreover, changing dietary habits and life style in the fast pace of modern lives is suggested to have detrimental effect on both male and female fertility (7).

Recently, evidence from several studies supports that cell phone usage may have a detrimental effect on sperm parameters leading to decreased male fertility (8).

The aim of this study is to investigate the the part of male factor infertility among the IVF/ICSI cycles in a public instution in Ankara, Turkey and review possible

environmental factors related to male infertility .

Materials And Method

We examined the medical records of Zekai Tahir Burak Kadın Sağlığı Education and Research Hospital IVF Unit retrospectively and reviewed the indications for IVF cycles between 2005 and 2011.

The cases in the last three years (2009-2011) were further analized for subgroups of male infertility (azoospermia, mild or severe oligospermia) . Surgical sperm extraction was performed for male factor infertility due to severely impaired spermatogenesis (non- obstructive azoospermia, NOA) or non reconstructable reproductive tract obstruction (obstructive azoospermia ,OA) . The types and numbers of surgical sperm extractions were documented. A histopathologic specimen was obtained during surgical sperm extraction. Cytogenetic analysis were done for all subjects with azoospermia.

Prevalance of smoking and cell phone usage was also investigated.

Written informed consent of the participants were obtained and the study was approved by the local ethic committee of the institution.

Table 1.Distribution of IVF indications through years 2007-2011

Year/ total cases (n)	Tubal + Peritoneal	Male	Unexplained	Other
2011 (418)	34 (8.13%)	217 (51.91%)	141 (33.69 %)	26 (6.22%)
2010 (418)	21 (5.02 %)	195 (46.60%)	195 (46.60%)	7 (1.67%)
2009 (513)	24 (4.67%)	185 (36.00 %)	277 (53.90 %)	27 (5.26%)
2008 (1192)	99 (8.30%)	475 (39.8 %)	497 (41.60%)	121 (10.15%)
2007 (1835)	144 (7.84%)	746 (40.6%)	805 (43.86 %)	140 (7.62%)
2006 (1730)	177 (10.23%)	812 (46.9%)	565 (32.60 %)	176 (10.17 %)
2005 (700)	65 (9.28%)	297 (42.40%)	294 (42.00%)	44 (6.28%)

Table 2.Distribution of cases with surgical sperm retrieval

Surgical procedure (n)	Sperm + n
TESE (56)	37
MD TESE (77)	33
PESA (31)	30
TESA (6)	5
Total (170)	105

Results

We observed a significant increase in the percentage of couples undergoing IVF cycles due to male infertility through years. A total of 6806 IVF cycles between 2005 - 2011 were evaluated. The number of cycles per year varied between 418 and 1835. The percentage of couples undergoing IVF-ICSI due to male infertility was 42.4 %,46.9 %,40.6 %,39.8 %, 36 % , 46.6 %, and 51.9 % respectively for each year from 2005 through 2011. Distribution of indications for infertility treatment are represented in Table 1. In the last three years , a total of 1349 cycles were done of which 597 (44.25 %) were treated for male infertility.

When we evaluated the severity of male infertility, we found that 416 (69.7 %) were severe and 181 (30.3 %) were mild . There were 170 cases of azoospermia, 27 obstructive and 163 non obstructive. Surgical retrieval of sperm was possible in 105 of them by PESA, TESA, PESA or MD TESE. Cases with surgical sperm retrieval are expressed in Table 2.

In histopathologic analysis; we identified 102 cases with Sertoly cell only syndrome, 27 spermatocytic arrest, 31 mixed type spermatogenetic disorders and 10 tubuler sclerosis. Congenital bilateral absence of vas deference was detected in 16 men. There were 8 cases with unilateral orchiectomy and contralateral orchiopexy. Cytogenetic analysis revieled 9 cases of Klinefelter syndrome (47; XXY) .

Smoking was documented in 43 % of the participants. Cell phone usage was very common, 99.3 % of the men included in the study were using cell phones regularly for 2 years or more.

Discussion

Present data indicates that male –factor infertility makes up approximately 36-51 % of couples seeking treatment for infertility in our institution. The prevalence of male infertility is far greater than previously reported by many investigators. It was stated that in 20-25 % of the cases the problem was due to male partner while in 30-40 % it was predominantly female, and in approximately 30 % of the cases abnormalities were found in both partners, and in 15 % no specific factor could be identified (9).

There are studies that report a genuine decline in semen quality over years. Carlssen et al.(3) showed a significant decline in mean sperm count and seminal volume from 1940 to 1990. As male infertility is to some extent correlated with sperm count these results may reflect an overall reduction in male fertility. The biological significance of these changes is emphasized by a concomitant increase in the incidence of genitourinary abnormalities

suggesting a growing impact of factors with serious effects on gonadal function .

Scientific and public concern about the potential risk of environmental chemicals to male reproductive health has been heightened by reports of temporal downward trends in semen quality , increased rates of developmental urogenital tract abnormalities like hypospadias and cryptorchidism and increased rate of testicular cancer (5,6). These observations , along with the documentation of human exposure to environmental chemicals, raise the possibility that environmental chemicals in part may be responsible for these adverse reproductive and developmental outcomes. In a review by Hauser R (10), polychlorinated biphenyls (PCB) and pesticides are reported to be related to alterations in semen quality. The data on the relationship between PCB and semen quality support an inverse association of PCBs with reduced semen quality, specifically reduced motility. Although it is limited, human data suggesting an association between contemporary use pesticide exposure and altered semen quality also exists.

Phthalate esters (PE) are man made chemicals with known estrogenic effects like the PCBs. In a study by Rozati, concentration of PEs was significantly higher in infertile men compared with controls and PCBs were detected in seminal plasma of infertile men but not in controls (11). They concluded that PCBs and PEs may be instrumental in the deterioration of semen quality in infertile men without an obvious etiology.

Air pollution is another jeopardy of modern and industrialized life. There are several studies addressing links between ambient air pollution and various semen characteristics like reduced percentage of sperm with normal morphology and proportionately more sperm with abnormal chromatin, and reduction of motility. Additional research to corroborate this association and to establish the causal agents is needed (12).

We observed that 99.3 % of the men in this study were cell phone users for at least two years. Cell phones that emit radiofrequency electromagnetic waves (RF-EMW) to nearby relay base stations or antennas have become a vital part of everyday life. Evidence from several studies supports a growing claim that cell phone usage may have a detrimental effect on sperm parameters leading to decreased male fertility (8).

In a retrospective study involving 371 men, the duration and possession of cell phones and the daily transmission time had a significant negative correlation with the rapid progressive motile sperm (13). In an other study, a relation between the frequency of cell phone usage and

decreased normal forward progressive motility of the sperm cells was noted (14).

Furthermore, in a prospective in vitro pilot study where 32 neat semen samples were exposed to EMW radiation, it was concluded that RF-EMW emitted from cell phones can lead to an increase in human spermatozoa yielding decreased motility and viability characteristics (8).

Smoking is one of the long recognized hazard to spermatozoa. Smoking is very common and age at men start smoking is decreased down to around 15 years. In our study, 43 % of the men are smokers. In Turkey, population based studies report the prevalence of smoking among men aged between 25-44 years around 53 % (15). In a recent study, it was suggested that smoking was associated with altered semen quality, in terms of sperm motility and morphology. Serum FSH, and LH levels were increased and testosterone was decreased in smokers compared to the non smokers. The number of androgen receptor CAG repeats were also increased in smokers with low testosterone (16). Gaur et al.(17) reported smoke-induced toxins primarily hamper semen motility and seminal fluid quantity. Alcohol abuse was found to alter sperm production and morphology. Progressive deterioration in semen quality was related to increasing quantity of alcohol intake and cigarettes smoked.

In a recent study smoking was not identified as a risk factor for poor semen quality (18). However, a study on sperm bioenergetics reported that rate of sperm respiration was significantly lower in smokers. This negative impact of cigarette smoking on sperm aerobic metabolism may, in part, explain the lower rate of fertility in smokers even with normal sperm parameters (19).

In the last decades, there has been an enormous changes in eating and social habits of the people all around the world. We can observe such a shift from somewhat traditional and organic food intake to fast food, preserved food with additives and high carbohydrate diet rich in saturated fat in Turkey, too. Besides, technological innovations made life easier in many aspects in the expense of a sedentary life and increasing body mass index (BMI) of the society. A relation between food intake and semen quality was documented. Frequent intake of lipophilic foods like meat products or milk may negatively affect semen quality in human, some fruits or vegetables may improve (20). There are studies emphasizing the relation of life style including eating and social behaviour on semen quality and ICSI outcomes. Braga et al, (7) reported that sperm concentration was negatively influenced by BMI and alcohol consumption and was positively influenced by cereal consumption and the number of meals per day. The sperm motility was also negatively influenced by BMI,

alcohol consumption, and smoking habit, whereas it was positively influenced by the consumption of fruits and cereals. The consumption of alcohol had a negative influence on the fertilization rate. The consumption of red meat as well as being on a weight loss diet had a negative impact on the implantation rate.

In conclusion; available data indicates that there is a significant deterioration of the semen quality in the last decades. The part of male infertility is increasing among the indications for couples undergoing ART. Environmental pollutants, use of cellular phones and other electromagnetic radiation sources and the change in the life style towards a sedentary life with increasing body mass indices have all been linked to reduced semen quality in many studies. Identification and elimination of environmental hazards should be the subject of both gynecologists and Public Health Services. Public education in order to encourage a healthier eating behaviour and social habits should be a major topic of preventive medicine. Elimination of preventable damages will reduce the cost of assisted reproduction.

Conflict of interest: Authors declare that they have no conflict of interest.

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