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Original Article

Effects of Sperm Parameters to Fertility for Intrauterine Insemination Patients According to WHO 2010 Criteria

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ABSTRACT

To evaluate sperm parameters as morphology of sperms in conjunction with number of motile sperms, according to 2010 World Health Organization (WHO) criteria's and to obtain optimal sperm parameters. We have examined prospectively 50 Intrauterine Insemination (IUI) cases for sperm parameters (morphology, TPMSC) and effects of some variables (woman age, infertility duration, FSH level, primary and secondary infertility) to pregnancy rate. First we divided cases in to 2 groups according to TPMSC (Total Progressive Motile Sperm Count) less than 1 million-greater than 1million- and compared number of progressively motile sperms and fertility rate. There was no statistically significant difference between pregnancy rate and sperm morphology (p>0.05) The pregnancy rate for the patient population with TPMSC >1million was more than another and this was statistically significant (p<0.05). There was no significant fertility difference among subgroups for Morphology and TPMSC as these 2 parameters are evaluated together (p>0.05). There was no significant difference according to age related pregnancy rate (p>0.05). There was no significant statistical differences among groups and subgroups in infertility duration, FSH level and woman age (p>0.05). Our study shows that pregnancy rate has no correlation with sperm morphology -as sperm parameter- for patients that IUI was applied. For the group with TPMSC >1 million, fertility rate was higher and this was statistically significant. Sperm parameters especially TPMSS that are important in determining the treatment plans of infertile patients but the effectiveness of morphology should be discussed.

Key words: *Intrauterine insemination, sperm parameters, pregnancy rate.*

İntrauterin İnseminasyon Uygulanan Hastalarda, 2010 DSÖ Kriterleri'ne Göre, Sperm Parametrelerinin Gebelik Oranlarına Etkileri

ÖZET

Çalışmamızda sperm parametrelerinden morfoloji ve hareketli sperm sayısının birlikte ele alınarak 2010 WHO (Dünya Sağlık Örgütü) kriterleri'ne göre değerlendirip gebelik oranlarına etkilerini tespit ve optimal sperm parametrelerini elde etmeyi amaçladık. IUI uygulanan 50 hastada sperm parametrelerinin (morfoloji, TPMSS) ve bazı değişekenlerin (kadın yaşı, infertilite süresi, FSH değeri, primer ve sekonder infertilite) gebelik oranlarına etkilerini prospektif olarak inceledik. Çalışmamızda IUI siklusların ilk önce hastaları TPMSS'na göre <1milyon ve >=1milyon olarak iki gruba ayırıp gebelik oranlarını karşılaştırdık. Sperm morfolojisine göre de <%4 ve >=%4 olmak üzere 2 ayrı grup oluşturuldu ve gebelik oranları karşılaştırıldı. Sperm morfolojisi ile gebelik oranları arasında anlamlı istatistiksel fark izlenmedi(p>0.05). TPMSS>1 milyon olan hasta populasyonunda, gebelik oranları %45 olup TPMSS <1 milyon olan gruba göre (%10) istatistiksel olarak anlamlı oranda daha yüksek bulunmuştur (p<0.05). Çalışmamızda IUI uygulanan siklusları TPMSS <1milyon ve >=1milyon ve normal morfoloji <%4 ve >=%4 olarak birlikte değerlendirdiğimizde oluşan dört adet alt grub arasında kadın yaşı, infertilite süresi ve FSH değerleri ortalamaları arasındaki farklar istatistiksel olarak anlamlı değildi (p>0.05). Morfoloji ve TPMSS birlikte ele alındığında alt gruplar arasında gebelik oranları bakımından anlamlı istatistiksel fark izlenmedi (p>0.05). Yaşa bağlı gebelik oranlarında anlamlı istatistiksel fark izlenmedi (p>0.05). Yaş, infertilite süresi ve FSH değerleri açısından değerlendirildiğinde, gruplar ve alt gruplar arasında anlamlı istatistiksel fark izlenmedi. Çalışmada IUI uygulanan hastalarda gebelik oranlarının sperm parametrelerinden morfolojiyle korelasyon göstermediği ancak TPMSS >1 milyon olan grupta istatistiksel olarak anlamlı oranda daha yüksek gebelik oranları elde edildiğini gözlemledik. İnfertil hastaların tedavi planlarının belirlenmesinde önemli olan sperm parametrelerinden TPMSS sayısının önemliliğini yinelerken, morfolojinin etkinliğinin tartışılması gerekmektedir.

Anahtar Kelimeler: *İntrauterin inseminasyon, sperm parametreleri, gebelik oranları*

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INTRODUCTION

Intrauterine insemination is much more preferred a technique in compare to other assisted reproduction techniques in infertility clinics; because it is easy to perform, cost effective and has a lower rate of morbidity in compare to other techniques. In previous studies different and conflicting results have been reported. According to our knowledge; discrepancy in these studies emerge from; variation in patient selection criteria, ovarian stimulation methods and number of cycles. In some of them; during evaluation of pregnancy rate, motile sperm counts have been ignored and that may also cause conflicting results.

In this study we aimed to evaluate sperm parameters as morphology of sperms in conjunction with number of motile sperms, according to 2010 World Health Organization (WHO) criteria and to obtain optimal sperm parameters. So we aimed to prevent unnecessary application of in vitro fertilization (IVF) and intracellular sperm injection (ICSI), which are more expensive and have a high morbidity rate in compare to IUI. We also aimed to prevent unnecessary application of intrauterine insemination in patients who have a low chance of fertility with insemination so decrease time consumption and morbidity risk in these patients.

MATERIAL AND METHODS

Fifty patients who are admitted to Necmettin Erbakan University, Infertility Unit between 01.08.2012-01.02.2013 and received to KOH program due to intrauterine insemination indication were included in this study. Our study is designed as prospective and approved by ethical committee of our hospital. Inclusion criteria were: (i) Patient has IUI treatment indication; (ii) patients aged 19-39; (iii) body mass index between 19 and 27 kg/m2; (iv) baseline FSH ≤10 IU/l; (v) Patient with patent fallopian tube (confirmed with hysterosalphingiography or laparascopy; (vi) Primary or secondary infertility; (vii) Patient has regular menstrual cycles (25-32 days). Patients were excluded if they met any of the following criteria: (i) Patients with a known diagnosis of clinically significant systemic or endocrinological diseases; (ii) Patient has a space-occupying lesion in uterus, such as; polyp, sub-mucous fibroids, uterine septum (confirmed with hysterosalpingography or office hyserescopy); (iii) Seriously impaired male infertility (sperm count < 1 million/ml).

These couples were candidates for IUI because of mild male factor infertility or unexplained infertility. Men with mild male factor infertility had semen analysis where only one of the sperm parameters was below the normal range (WHO 2010). Normal semen analyses were defined by the threshold values of the WHO (2010) (volume ≥1.5 ml, total count ≥15 × 106, progressive motility ≥32%, typical morphology ≥4%). The threshold values of sperm parameters according to WHO (1999) (total count ≥20 × 106, progressive motility ≥50%, typical morphology ≥14%).

Stimulation Protocol

On the third day of menstruation; all patients underwent transvaginal ultrasonography and ovulation induction protocol with recombinant FSH (Gonal F, Puregon) were started to all patients. The treatment protocol was determined in consideration of ovarian reserve, body mass index, age and previous induction dose. In necessary situations, bromocriptine or metformin was added to the protocol. Ovary and endometrium of patients were monitored with transvaginal ultrasound (folliculometry). When at least one follicle reached a diameter of 18 mm, if there were no ovarian hyperstimulation or multiple pregnancy risk; 10,000 IU beta hCG (Pregnyl N.V. Organon, Holland) were administered to all patients. Thirty-six hours after injection, IUI was performed through the insemination catheter. On the fourteenth day of insemination, beta-HCG level was determined and a value of ≥10 IU/ml accepted as pregnancy. Motility and count of sperms are determined for each ejaculate following washing. We have used Total Progressive Motile Sperm Count (TPMSC) which is also known as 'a motile' and that indicates sperms showing progressive motility. Post wash TPMSC calculated with volume (ml) x concentration (million/ml) x % of 'a motile' sperm formula. In our clinic, we have not evaluated post-wash sperm morphology so we use percentage of morphological normal sperm on basal spermiogram for all IUI cycles. We used swim up method for sperm preparation.

First we divided cases in to 2 groups according to TPMSC - less than 1 million-greater than 1million- and compared number of progressively motile sperms and fertility rates. Then we constituted two groups, according to morphology (Kruger strict criteria) as less than 4% and greater than 4%. We compared morphology and fertility rates. Finally we evaluated two parameter together and divided cycles to four subgroups and compared fertility rates. WHO 1999 and 2010 semen parameters are summarized in Table 1.

Table 1. WHO 1999 and 2010 semen parameters.

Semen Parameters	WHO 1999	WHO 2010
Volume (Ml)	≥2.0	≥1.5
Count ($X10^6$/Ml)	≥20	≥15
Motility(%)	≥50 (A+B)	≥32 (A+B)
Vitality(%)	≥75	≥58
Morphology(%)	≥(14)	≥(4)
Leucocytes($X10^6$/Ml)	≤1	≤1.0
Total Sperm Number Per Ejeculate($X10^6$)	≥40	≥39

Cycle cancelation criteria

Possibility of multiple pregnancies: Detection of more than four follicles greater than 15 mm (On the day of human corionic gondatropin (hCG) administration).

Statically Analysis

All statistical analyses were performed with Statistical Package for Social Sciences version 16.0 (SPSS, USA). Data were expressed as the mean ± SD. The chi-squared test and Fisher's exact test were used to compare clinical outcome between the groups. Results were considered significant at the 5% level ($p<0.05$).

RESULTS

There were no significant statistical differences among groups and subgroups in infertility durations, FSH levels and women's ages ($p>0.05$). Baseline characteristics of the groups are summarized in Table 2. There was no statistically significant difference between pregnancy rates and sperm morphology ($p>0.05$). The pregnancy rates for the patient population with TPMSC >1million was more than in compare to patient population with TPMSC <1 million and this difference was statistically significant ($p<0.05$). Pregnancy rates for groups of TPMSC>1 milion and < 1 milion and subgroups of normal morphology ≥ %4 and <%4 are summarized in Table 3. There were four subgroups and these were TPMSC >1million, TPMSC <1 million, sperm with normal morphology <%4 and sperm with normal morphology ≥%4. There were no significant fertility differences among subgroups in women's ages, infertility durations and average FSH levels ($p>0.05$). There were no significant fertility differences among subgroups in morphology and TPMSC as these 2 parameters studied together ($p>0.05$). There was no significant difference in age related pregnancy rate ($p>0.05$).

DISCUSSION

It is difficult to make a clear assessment about intrauterine insemination results. Because there are some differences in between previously conducted studies such as age, patient selection criteria, types of sperm, cause of infertility, insemination methods and inducing ovulation in conjunction with IUI. The most important factors affecting treatment outcome is patient selection. The good results are received among the patient with coitical and anotimical disorders. Because usually there is not any important pathological factor in this couples.

In a study, age factor is emphasized and average pregnancy rate per patient and per cycle was 31.5% and 12.5 % respectively. However, in patients older than 36 years these rates have fallen by half (1). Badawy et al. reported that intrauterine insemination used for treating male factor infertility has little chance of success when the woman is older than 35 years, the number of motile spermatozoa inseminated is <5 x 10(6), or normal sperm morphology is <30% (2).There was no statically significant difference in age related pregnancy rate in our study ($p>0.05$). In some studies it is reported that pre-wash TPMSC should be at least 5 million for IUI (3, 4) and in other studies, it is reported that post-wash TPMSC should be at least 1 million (5, 6, 7, 8), otherwise patients should be directed to IVF. Recent studies it is reported that TPMSC which has been found to be a predictor of pregnancy when evaluated in isolation, may be due to a confounding ef-

Table 2. Baseline characteristics of the groups.

Morphology* TPMSC	≥4% ≥ 1 million (n:36)	≥4% <1 million (n:5)	<4% ≥1 million (n:4)	< 4% <1 million (n:5)	p value
FSH	4.97±1.50	4.40±1.67	6.25±2.21	5.20±0.44	>0.05
Infertility Duration (years)	4.33±2.48	3.60±2.07	3.50±1.29	3.60±2.50	>0.05
Age	29.56±4,16	28.60±3.91	22.00±15.34	29.60±4.72	>0.05

**According to Kruger strict criteria, TPMSC = Total Progressive Motile Sperm Count.*

***Table 3**. Pregnancy rates for groups of TPMSC>1 milion and < 1 milion and subgroups of normal morphology ≥ %4 and <%4*

	TPMSC		P value	Morphology*		p value
	≥1 million (n=40)	<1 million (n=10)		≥ 4% (n:42)	< 4% (n:8)	
Pregnancy Rate (n/%)	18 (45)	1 (10)	<0.05	17 (40.5)	2 (25)	>0.05

**According to Kruger strict criteria, TPMSC = Total Progressive Motile Sperm Count*
The pregnancy rate higher in population with TPMSC ≥1million and this was statistically significant (p<0.05).

fect (9). Nikbakht R et al. reported that the most of IUI success when the range of total motile count was 5×106 to <10×106. Also, the findings of that study showed that TMC<1×106 was not justified for IUI treatment (10). In our study pregnancy rate was higher in TMPSC > 1 million group in compare to TMPSC < 1 million group and that finding was statically significant (p<0.05).

Some researchers concluded that sperm morphology has positive predictive effect of on pregnancy rate (11, 12). In a study, Burr et al. divided patient into to two groups as -percentage of sperm with normal morphology <10 and ≥ 10 - according to WHO (1992) criteria and obtained pregnancy rates per cycle was 4.3% and 18.2% respectively and they have reported that difference was statistically significant (11). In that study, pregnancy rates were higher because, patients were divided to two groups according to WHO (1992). But in our study, we divided to groups as -percentage of sperm with normal morphology <4 and ≥ 4 according to WHO (2010). So we found that there was no significant difference pregnancy rates between subgroups (p>0.05).

However many studies concluded that sperm morphology has no predictive effect on pregnancy rate (13, 14). In one of these studies, Karabinus et al. observed no statistically significant difference between pregnant and non-pregnant patients (15). In another study Check et al. divided patients into the three groups as sperm with normal morphology ratio <4%, 4-15% and >15% and obtained pregnancy rates as 30%, 26% and 20% respectively and they concluded that there was no positive correlation between pregnancy rate and morphological normal sperm ratio (13). Deveneau et al. reported that there is no statistically significant difference in per cycle pregnancy rates when comparing patients with a strict sperm morphology of ≤4% versus >4% who undergo IUI (16). In our study we also observed that morphology alone does not result significant difference on pregnancy rate. There was also no significant difference in pregnancy rate when a combination of both parameters taken into consideration (p>0.05). In our clinic, IUI applications result 19 pregnancies among 50 patients (36%) and we obtained a higher rate of pregnancy in compare to many other studies. Burr et al, Miller et al. and Wainer et al. reported 16%, 10% and 12% of pregnancy rates respectively (11, 17, 18).

In conclusion; as shown in all these studies in the literature; variation in ovulation induction protocol and heterogeneity in selected groups cause different rate of pregnancy in IUI. Maybe in the near future, if optimal sperm count and threshold level determined, patients will have more chance of getting pregnant with IUI so that protect patients from unnecessary application of IVF and ICSI which are more expansive and invasive. The determination of optimal sperm count and threshold will also provide time saving for patient who has a low possibility of getting pregnant with IUI so these patients will be directed alternative treatment options.

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