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Impact of Semen Characteristics on the Success of Intrauterine Insemination

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Abstract: Intrauterine Insemination (IUI) is one of the most prevalent therapeutic modalities of infertility in the world, but the effect of various semen parameters on its success is controversial. Our purpose was the study of factors that may influence success of IUI and better selection of women that might have pregnancy after this method of treatment. Eighty-eight couples put in 2 groups each consists of 44 patients who undergone IUI. One group became pregnant after IUI (Successful Group) and another did not become pregnant (Failed Group). The groups were compared with each other in variables including: Woman's age, duration of infertility, number and motility of sperm, drugs used in ovulation induction phase, type of infertility, supporting of luteal phase and IUI method. There was not any significant difference between two groups about patency of one or two tubes, duration of infertility, sperm count and motility before washing, type of infertility, number and size of follicles; however, there was significant difference between them about woman's age, number and motility of sperm after washing, doing IUI in two consequent days and doing IUI with pooled maneuver and use of HMG. Doing IUI in following situations increases pregnancy rate and success chance of IUI: In women with lower age, doing it with pooled maneuver, use of HMG for induction of ovulation and performing IUI in 2 cycles.

Key words: Insemination, semen parameters, infertility, pregnancy

INTRODUCTION

Intrauterine insemination (IUI) is defined as artificial implantation of washed sperms within the uterine cavity during ovulation, raising the number of sperms entering the Fallopian tube and causing the higher chance of conception (Copeland, 2000). IUI is a widely utilized method for treating distinct types of infertility. IUI is cheaper, simpler and less invasive than more sophisticated Assisted Reproductive Techniques (ART) of IVF, Intra-Cytoplasmic Sperm Injection (ICSI) and Gamete Intra-Fallopian Transfer (GIFT). For these reasons, it is often the first line of treatment offered to infertile couples with a male factor (Esfandiari *et al*., 2006; Achard *et al*., 2005; Jurema *et al*., 2005), hostile cervical mucus (Steures *et al*., 2004b), anti-sperm antibodies (Van Weert *et al*., 2005) or idiopathic infertility (Van Waart *et al*., 2001; Cohlen *et al*., 2000).

The outcome of IUI is dependent on various prognostic characteristics of the couple (Steures *et al*., 2004a). Several determinants of success have been identified for IUI. IUI outcome is improved by the use of injectable gonadotrophins for ovulation induction in both unexplained infertility and mild male infertility and by the use of clomiphene citrate for ovulation induction in only unexplained infertility. Similarly, woman's age and number of pre-ovulatory follicles have also been reported to impact on IUI outcome (Duran *et al*., 2002). The effect of several sperm parameters has also been investigated. Sperm motility (Montanaro *et al*., 2001), morphology (Van Waart *et al*., 2001) and post-preparation motility (Hendin *et al*., 2000b) have been shown to affect IUI outcome. Total Motile Count (TMC) inseminated is the marker most consistently shown to be a determinant of success (Khalil *et al*., 2001; Nicopoullos *et al*., 2004). Ovulatory Stimulation (OS) doubles IUI pregnancy rates among young patients without a prior pelvic surgery and with good post-wash semen quality. The benefit of OS for patients with risk factors for IUI failure is unclear. These patients should be counseled that their chances for success with IUI are limited, with or without OS (Hendin *et al*., 2000a).

Conversely, advanced female age, poor post-wash sperm motility and a history of corrective pelvic surgery are significant risk factors for poor IUI success rates. Poor post-wash sperm motility in combination with either of these other two risk factors resulted in no successful pregnancies (Hendin *et al*., 2000b).

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However, although Intrauterine Insemination (IUI) is one of the most common infertility treatment methods in the world, the relative influence of various semen characteristics on the likelihood of a successful outcome is controversial. The aim of our study was to assess the impact of semen parameters and technical methods on the results of intrauterine insemination.

MATERIALS AND METHODS

We performed a historical cohort study among 88 couples presenting to Infertility Ward of Tabriz Al-Zahra Hospital since 2000-2003. Fourty-four couples with successful IUI were selected randomly in order to their variables to be compared with those of 44 randomly selected couples with failed IUI. All persons gave their informed consent prior to their inclusion in the study.

All couples had been trying to conceive for at least 12 months and all had undergone a fertility work-up consisting of a medical history, evaluation of ovulation either by basal body temperature, ultrasound and/or mid-luteal serum progesterone, semen analysis and a post-coital test (for cervical factor subfertility). The women had been evaluated regarding tubal patency of both tubes, endometriosis or uterine anomalies by hysterosalpingo-graphy and/ laparoscopy.

Ovulation induction was performed by one of these methods:

- Clomiphene citrate (100 mg daily from second day of cycle for 5 days).
- Menogon (75 IU daily from third day of menstruation for 7 days) and then adjusting the dose by evaluation of follicles by vaginal ultrasound examination.
- Combination regimen with minimal stimulation at first 100 mg clomiphene citrate was given from third day of menstruation for 5 days and 75 IU HMG (menogon) was added from day 8 of cycle for 3-5 days. After reaching of dominant follicles of ovary to 18 mm or more, 5000 IU HCG was given for all the patients for certain ovulation.

Fresh semen samples were produced by masturbation and prepared <2 h prior to insemination. The semen was processed using a density gradient centrifugation (15 min at 750 g) and a washing step (7 min at 300 g) with 2 mL culture medium containing 1% HAS (CLB, Amsterdam, The Netherlands). Less than 15 min before insemination the spermatozoa suspension was centrifuged (7 min at 200 g) and the cell pellet resuspended in 200-250 μL culture medium. The patient was placed in lithotomy position and the vaginal orifice opened by speculum. Then, using a tuberculin syringe attached to a catheter, the prepared semen was injected to uterus above the internal os of cervix and below of fondues.

The compared variables were including:

- Tubal factor
- Wife age
- Count and motility of sperms before and after washing
- Duration of infertility
- Cause of infertility (belong to male or female and uterine/ovulatory/cervical)
- Type of infertility (primary/secondary)
- Number of performed IUI(s)
- IUI method
- Type of drug used for ovulation induction
- Type of support of luteal phase
- The day of IUI performing
- Estradiol level in the day before or the same day of hCG prescription.

All collected data were recorded on questionnaire and analyzed statistically. For comparison of two "Successful" and "Failed" groups we used from *Independent t-test* and *Dependent t-test* (for quantitative variables) and χ^2-test (*Chi-Square test*) and *Exact Fisher's-test* (for qualitative variables). Also, Phi-coefficient and Kramer-V-coefficient were used for determination of value of dependence between variables.

RESULTS

The 88 patients were studied in two "Successful" and "Failed" groups each containing 44 women. The average variables of each group have been compared in Table 1. In addition, our study showed the change in motility following sperm washing; so that, there was significant raise in sperm motility in both groups after washing and this raise was more significant in successful group (Table 1).

Table 1: The comparison of average variables of two groups

Variables	Successful group	Failed group	p	t
Average age	26.05	28.6	0.018	2.41
Average duration of infertility	5.66	5.63	0.979	0.026
Average sperm motility before washing	52%	53%	0.79	0.26
Average sperm motility after washing	76%	62%	0.003	
Average sperm count in 1CC semen before washing	61,136,363	61,931,818	0.87	0.154

Average sperm count after seminal washing was not significantly different between 2 groups. However, the raise of sperm count in successful group was significant ($p = 0.02$) but this raise in failed group was not significant ($p = 0.313$). Average sperm abnormality before washing was 0.56 in successful group and 0.55 in failed group with no significant difference between 2 groups ($p = 0.57$). In successful group, infertility was primary in 13.64% and secondary in 86.36%, these figures in failed group were 15.9 and 84.1%, with no significant difference between 2 groups ($p = 0.57$).

The cause of infertility was belonging to male in 38.7% of successful group and 55.25 of failed group. These figures for other causes were as following: 54.8 and 41.4% for ovulatory causes, 3.2 and 3.4% for uterine causes and 3.2 and 3.25% for cervical causes. These differences were not significant between two groups ($p = 0.49$). According to the diagram 1, the day of IUI performance was later in successful group, but this difference was not significant ($p<0.05$). Also, diagram 2 shows the number of performed IUI (s) in successful and failed groups but the difference between number of IUI(s) between two groups was not significant ($p = 0.67$).

This study showed that performing double IUI in one cycle was associated with higher success rate: IUI in successful group was performed *in one cycle* in 61.4% and as *double injection* in 38.6%; these figures in failed group were 95.2 and 4.8% ($p<0.05$). In 5.3% of women in successful group, IUI was performed by pooled maneuver but this maneuver did not used in failed group. It seems that the pooled maneuver is associated with more success.

The serum estradiol in a day before (or the same day of) administration of HCG was 0-300 pg mL^{-1} in 18.2%, 300-1000 pg mL^{-1}, in 63.6% and more than 1000 pg mL^{-1}, in 18.2% of women in successful group; these percents for failed group were 4.8, 69 and 26.2%, respectively. However, the difference of serum estradiol in a day before (or the same day of) administration of HCG was not significant between 2 groups ($p = 0.15$) (Fig. 1).

We used drug(s) for ovary induction, the drug(s) was/were clomiphene in 18.2% of successful group and 6.8% of failed group, HMG in 22.7% of successful group and 2.3% of failed group, "clomiphene+HMG" in 56.8% of successful group and 90.9% of failed group and metrodin in 2.3% of successful group and none of failed group. According to the χ^2-test, the use of HMG was higher significantly in successful group ($p = 0.003$). Also, "clomiphene+HMG" had better results than other drugs and the effect of HMG was higher than clomiphene (Fig. 2).

Figure 3 shows the number of follicles in both groups which detected sonographically. The number of follicles in both groups was not significantly different ($p = 0.15$).

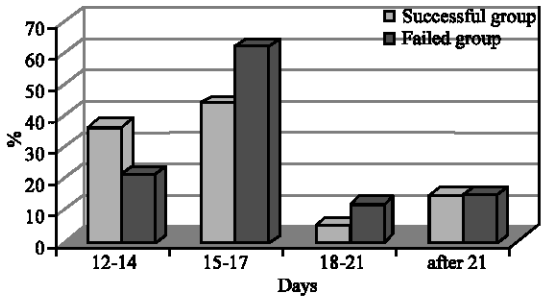

Fig. 1: Comparison of days of performing IUI in two groups

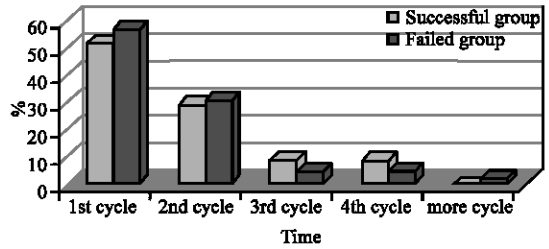

Fig. 2: The number of performed IUI (s) in successful and failed groups

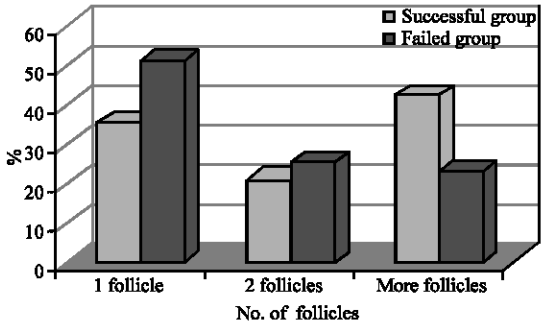

Fig. 3: The number of folicles in both groups which detected sonographically

Ultrasonography revealed that the size of the largest follicle was <20 mm in 36.4% of successful group and 44.1% of failed group, 20-25 mm in 59.1% of successful group and 55.8% of failed group and >25 mm in 4.5% of successful group and none of failed group. However, the size of the largest follicle in two groups was not statistically significant ($p = 0.313$).

Regarding the type of drug(s) used for luteal phase support, we used HCG in 86% of successful group and 81.8% of failed group, progesterone in 9.3% of successful group and 31.6% of failed group and "progesterone+ HCG" in 4.5% of successful group and 4.7% of failed group. However, the type of drug(s) used for luteal phase support was not significantly different in 2 groups ($p = 0.81$).

DISCUSSION

Our study showed that lower women age is associated with higher successful rate of IUI. Other studies also showed that advanced female age is a significant risk factor for poor IUI success rates (Hendin *et al*., 2000b; Sahakyan *et al*., 1999).

Intrauterine insemination can be performed with or without Controlled Ovarian Hyperstimulation (COH). Steures *et al.* conducted a study for evaluation of additional effect of COH on IUI in couples with cervical factor subfertility and found a 1.6 times higher ongoing pregnancy rate after IUI with COH compared with IUI without COH in the first four cycles. However, they suggest that although IUI with COH is more effective than IUI without COH, in clinical decision-making the risks of these two treatment policies should also be taken into account. In daily practice, COH carries the risks of multiple pregnancy and ovarian hyperstimulation syndrome (Steures *et al*., 2004b).

In our study, stimulation of single follicle was prevalent in failed group in comparison with more prevalence of multiple follicle growth in successful group. Prior studies showed that success rates of IUI increased linearly when more than one follicle could be induced with follicle stimulation. Controlled ovarian hyperstimulation thus always improves the outcome of infertility procedures (Van Waart *et al*., 2001; Montanaro *et al*., 2001).

Our study showed the higher pregnancy rate with HMG administration. Also, double IUI (18 hours and 36 h after HCG administration) was associated with more pregnancy rate than one-cycle IUI. Ragni *et al.* (1999) indicated that 2 IUIs performed 12 and 34 h after HCG administration is the most effective regimen for women undergoing COH cycles.

In our series, the HMG was more effective than clomiphene citrate in ovary stimulation but this result is in contrast with Ecochard *et al.* findings. They concluded that CC is an effective alternative to HMG in the population examined (Ecochard *et al*., 2000).

In our series, the difference of sperm morphology in two groups was not significant. A universal threshold level above which IUI can be performed with acceptable pregnancy rates has not been determined yet, although IUI success seems to be impaired with <5% normal spermatozoa and an Inseminating Motile Sperm Count (IMC) of $<1\times10^{(6)}$. Until now, no method of sperm preparation has been shown to be superior with regard to pregnancy rate after IUI (Ombelet *et al*., 2003; Van der Merwe *et al*., 2005; Wainer *et al*., 2004). However, our study showed the significant raise in sperm motility in both groups after washing and this raise was more significant in successful group. Tsai *et al.* (1998) showed that the postprepared sperm motility was the only parameter predicting the successful rate of intrauterine insemination. Seventy-five percent sperm motility can be used as a cut-off value for selecting patients (Tsai *et al*., 1998).

There is a trend toward an increasing percent of conception with increasing Total Motile Sperm (TMS) count, motility and percent of fast motile sperm. The TMS count, motility and percent of fast motile sperm independently predict success with IUI. Pregnancy rate increased 4 times with motility of =30% (Yalti *et al*., 2004). Sperm motility is an independent factor influencing IUI-related pregnancy. A forward progression score of 3-4 in a processed specimen is necessary for IUI success. The number of IUI attempts per patient should be individualized depending upon the needs of patients (Zhao *et al*., 2004). The Processed Total Motile Sperm (PTMS) count independently predicts success with IUI. Cycles with less than 10 million total motile sperm are significantly less likely to result in a pregnancy. If cause-specific therapy has failed, alternatives to IUI should be considered for couples when the PTMS count is less than 10 million (Miller *et al*., 2002).

The volume of insemination specimen did not influence the outcome. This finding is compatible with other studies (Van Waart *et al*., 2001; Tsai *et al*., 1998). Tsai *et al*. (1998) concluded that insemination with 1 mL of fluid was just as effective as insemination with 0.5 mL (Tsai *et al*., 1998).

REFERENCES

Achard, V., J. Perrin, J. Saias-Magnan, A. Noizet and J.M. Grillo *et al*., 2005. Optimization of artificial inseminations with donor semen: A four-year experience. Gynecol. Obstet. Fertil., 33: 877-883.

Cohlen, B.J., P. Vandekerckhove, E.R. te Velde and J.D. Habbema, 2000. Timed intercourse versus intra-uterine insemination with or without ovarian hyperstimulation for subfertility in men. Cochrane Database Sys. Rev., CD000360.

Copeland, L.J., 2000. Textbook of Gynecology. 2nd Edn. Saunders Company, Philadelphia, pp: 422-423.

Duran, H.E., M. Maorshedi, T. Kruger and S. Oehninger, 2002. Intrauterine insemination: A systematic review on determinants of success. Hum Reprod Update, 8: 373-384.

Ecochard, R., C. Mathieu, D. R oyere, G. Blache and M. Rabilloud *et al*., 2000. A randomized prospective study comparing pregnancy rates after clomiphene citrate and human menopausal gonadotropin before intrauterine insemination. Fertil. Steril., 73: 90-93.

Esfandiari, N., L. Gotlieb and R.F. Casper, 2006. Seminal hyperviscosity is associated with poor outcome of controlled ovarian stimulation and intrauterine insemination: A prospective study. Int. J. Fertil. Womens Med., 51: 21-27.

Jurema, M.W., A.D. Vieira, B. Bankowski, C. Petrella and Y. Zhao *et al*., 2005. Effect of ejaculatory abstinence period on the pregnancy rate after intrauterine insemination. Fertil. Steril., 84: 678-681.

Hendin, B.N., T. Falcone, J. Hallak, J. Goldberg and A.J. Thomas *et al*., 2000a. Effect of clinical and semen characteristics on efficacy of ovulatory stimulation in patients undergoing intrauterine insemination. J. Assist. Reprod. Genet., 17: 189-193.

Hendin, B.N., T. Falcone, J. Hallak, D.R. Nelson and S. Vemullapalli *et al*., 2000b. The effect of patient and semen characteristics on live birth rates following intrauterine insemination: A retrospective study. J. Assist. Reprod. Genet., 17: 245-252.

Khalil, Y., P.E. Rasmussen, K. Erb, S.B. Laursen and S. Rex *et al*., 2001. Homologous intrauterine insemination. An evaluation of prognostic factors based on a review of 2473 cycles. Acta. Obstet. Gynecol. Scand., 80: 74-81.

Miller, D.C., B.K. Hollenbeck, G.D. Smith, J.F. Randolph and G.M. Christman *et al*., 2002. Processed total motile sperm count correlates with pregnancy outcome after intrauterine insemination. Urology, 60: 497-501.

Montanaro, G.M., T.F. Kruger, K. Coetzee, K. Smith and J.P. Van de Merwe *et al*., 2001. Stepwise regression analysis to study male and female factors impacting on pregnancy rate in an intrauterine insemination programme. Andrologia, 33: 135-141.

Nicopoullos, J.D., P.A. Almeida, J.W. Ramsay and C. Gilling-Smith, 2004. The effect of human immunodeficiency virus on sperm parameters and the outcome of intrauterine insemination following sperm washing. Hum. Reprod., 19: 2289-2297.

Ombelet, W., K. Deblaere, E. Bosmans, A. Cox and P. Jacobs *et al*., 2003. Semen quality and intrauterine insemination. Reprod. Biomed. Online, 7: 485-492.

Ragni, G., P. Maggioni, E. Guermandi, A. Testa and E. Baroni *et al*., 1999. Efficacy of double intrauterine insemination in controlled ovarian hyperstimulation cycles. Fertil. Steril, 72: 619-622.

Sahakyan, M., B.L. Harlow and M.D. Hornstein, 1999. Influence of age, diagnosis and cycle number on pregnancy rates with gonadotropin-induced controlled ovarian hyperstimulation and intrauterine insemination. Fertil. Steril, 72: 500-504.

Steures, P., J.W. Van Der Steeg, B.W. Mol, M.J. Eijkemans and F. Van Der Veen *et al*., 2004a. Prediction of an ongoing pregnancy after intrauterine insemination. Fertil. Steril, 82: 45-51.

Steures, P., J.W. Van Der Steeg, H.R. Verhoeve, P.A. Van Dop and P.G. Hompes *et al*., 2004b. Does ovarian hyperstimulation in intrauterine insemination for cervical factor subfertility improve pregnancy rates? Hum. Reprod., 19: 2263-2266.

Tsai, M.Y., Y.C. Tsai, J.C. Chang, F.T. Kung and J.F. Wu *et al*., 1998. Effect of postprepared sperm parameters and insemination specimen volume on the outcome of intrauterine insemination. Changgeng Yi Xue Za Zhi., 21: 265-270.

Van Der Merwe, F.H., T.F. Kruger, S.C. Oehninger and C.J. Lombard, 2005. The use of semen parameters to identify the subfertile male in the general population. Gynecol. Obstet. Invest., 59: 86-91.

Van Waart, J., T.F. Kruger, C.J. Lombard and W. Ombelet, 2001. Predictive value of normal sperm morphology in Intrauterine Insemination (IUI): A structured literature review. Hum. Reprod. Update, 7: 495-500.

Van Weert, J.M., S. Repping, J.W. Van Der Steeg, P. Steures and F. Van Der Veen *et al*., 2005. IUI in male subfertility: Are we able to select the proper patients? Reprod. Biomed. Online, 11: 624-631.

Wainer, R., M. Albert, A. Dorion, M. Bailly and M. Bergere *et al*., 2004. Influence of the number of motile spermatozoa inseminated and of their morphology on the success of intrauterine insemination. Hum. Reprod., 19: 2060-2065.

Yalti, S., B. Gurbuz, H. Sezer and S. Celik, 2004. Effects of semen characteristics on IUI combined with mild ovarian stimulation. Arch. Androl., 50: 239-246.

Zhao, Y., N. Vlahos, D. Wyncott, C. Petrella and J. Garcia *et al*., 2004. Impact of semen characteristics on the success of intrauterine insemination. J. Assist. Reprod. Genet., 21: 143-148.