Influence of semen quality on the success of intrauterineinsemination result in a university teaching hospital infertility center

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Abstract

Introduction: Intrauterine insemination is effective for the treatment of male factor and unexplained infertility.The objective of the study was to understand whether one or more parameters of sperm quality i.e. morphology, motility and concentration have predictive value for the pregnancy outcome of the intrauterine insemination treatment for couple with primary infertility with male factor or unknown cause in the select defined population.

Methods: This is a hospital based prospective study of 776 IUI cycles. The study population was those couples between 19-35 years of age who had been trying unsuccessfully to conceive for a minimum of one year. They were randomly distributed into two groups; partner with sperm morphology, motility and concentration below 5th percentile constituted group A and group B comprised of those with above 5th percentile and their IUI outcome was evaluated.

Results: A total of 776 IUI cycles were studiedout of which 94 clinical pregnancies were obtained, for a pregnancy rate/cycle of 12.1%. The study shows that sperm morphology is positively associated with IUI results with statistically significant p value (p=0.034). Likewise, a higher total motility level is positively associated with IUI results. Moreover, incidence of positive IUI results were significantly more with post processing motility with excellent progression >90% with statistically significance p value (P=0.004).

Conclusion: Combination of superovulation and intrauterine insemination is an effective means of achieving pregnancy for unexplained and male factor infertility. The probability of pregnancy increases with higher normal morphology, total motile spermswith excellent progression and sperm concentration. If semen parameters are below the 5th percentile value, IVF-ICSI would be preferred.

Key words: Male infertility, primary infertility, sperm morphology, sperm motility,sperm concentration, Intrauterine Insemination (IUI)

Introduction

Infertility is defined as one year of unprotected intercourse without pregnancy. Infertility affects about 10% to15% of reproductive-age couples. The main causes of infertility include male factor, decrease ovarian reserve, ovulatory disorders (ovulatory factor), tubal injury, blockage or paratubal adhesions, uterine factors, systemic conditions (including infections or chronic diseases), cervical and immunological factors, and unexplained factors.

Intrauterine insemination (IUI) recognized to be an effective and inexpensive method managing the patients with unexplained and male factor infertility. It is generally attempted before proceeding to more

invasive assisted reproductive techniques such as in vitro fertilization (IVF) and intracytoplasmic sperm injection (ICSI). IUI is a widely utilized method for treating distinct types of infertility such as unexplained infertility, endometriosis, male infertility, anovulation and cervical antisperm antibody[1,2].

Predictive sperm parameters for successful IUI have been controversial[1,3-5]. Several semen parameters have been shown to correlate with IUI outcome such as number of motile sperm and normal morphology[3]. Although WHO reference values for semen analysis are often used to assess sperm quality, more often unsuccessful pregnancies with IUI have been achieved in sub fertile couples with sperm parameters below WHO reference values. The minimal recommended number of normal sperm morphology inseminated varies from 30% (previous WHO reference value) to 4% (recent WHO reference value) depending on some studies[1,2,6-10].

The aim of our study was to assess the likelihood of IUI outcomes based on sperm morphology in the case of unexplained and male factor infertility and to help clinicians predict IUI outcome.

The effectiveness of IUI is reported to 10-20% per patient, but the reported rates range from as low as 5% to as high as 70%. Based on the etiology of infertility, the highest rates were reported when IUI was used in patients with anovulation who were undergoing ovulation induction therapy at the time of IUI treatment, male factor infertility, and unexplained infertility. The number of mature follicles (17mm in diameter or more) is another prognostic factor in IUI success, where the presence of 3-4 mature follicles was associated with higher pregnancy rates and a lower incidence of higher-order multiple pregnancies. In cases of unexplained infertility, the pregnancy rate with IUI has been reported to be 9-20%.

Methods

The present clinical study was a hospital based prospectivestudy conducted in Manipal hospital a Kathmandu University teaching hospital, Bangalore India from April 2011 to December 2012. The subjects were grouped into two according to WHO semen analysis criteria of <5th or >5th percentile to understand the influence of semen quality in IUI success.

Inclusion criteria of female were: age <35 years, normal pelvis and uterine cavity documented by hysterosalphingograpgy, normal serum follicle-stimulating hormone, Luteinizing hormone, Anti-mullerian hormone, prolactin and thyrotropin values on days 1-5 of cycle, length of 2 of the 3 most recent cycles between 24 to 40 days, negative pregnancy test, history of infertility > 1 year. Likewise, for male Age < 50 years, presence of any motile sperm in screening semen analysis, negative serum antisperm antibody test with history of infertility > 1 year.

Exclusion criteriaof female were: previous use of in vitro fertilization or other assisted reproductive technology, previous intrauterine insemination with current partner, history of chronic disease, history of PCOS or clinical signs of chronic anovulation with clinical and biochemical signs of hyperandrogenemia and USG findings of > 5 micro cysts per imaging plane in each ovary measuring 0.5-0.8cm, history of chemotherapy or radiation to the abdomen or pelvis, history of tubal surgery, extensive tubal adhesions, endometriosis of any stage, history of myomectomy, ovarian cystectomy or unilateral, oophorectomy. Likewise, exclusion criteria for male were-previous use of in vitro fertilization or other assisted reproductive technology, previous intrauterine insemination, history of vericocele or vasovasostomy or history of pelvic node dissection.

All the women who were inducted in this study underwent ovulation induction and the study was limited to those who underwent only one cycle of IUI.

Results

A total of 776 subjects who underwent IUItreatment and who met the set criteria were enrolled for the study. The mean age of the husband and wife in the study population who underwent semen analysis and IUI treatment were 32.79 years and 29.62 years with standard deviation of +/- 3.36 and 2.97 respectively.

Table I: Age distribution of husband and wife studied in the sample

Age in years	Number of subjects	%	Mean ± SD
Husband age			
• 21-30	201	25.9	
• 31-40	555	71.5	32.79±3.36
• 41-50	20	2.6	
Wife age			
• 21-25	58	7.5	
• 26-30	456	58.8	
• 31-35	248	31.9	29.62±2.97
• 36-40	14	1.8	
Total	776	100.0	

Table 2: IUI results with only one cycle of IUI attempts

IUI result	Number of subjects	%
Negative	682	87.9
Positive	94	12.1
Total	776	100.0

Among the 776 subjects who met the criteria of this study,94(12.1%) had chemical pregnancy. This outcome is comparable with many other studies and infertility center's outcome.

Table 3: Correlation of postprocessedsperm parameters and IUI positive results

Sperm quality parameters (as per 2010 WHO manual 5th centile guideline)	Total number of patients (n=776)	% of patients	IUI positive results	% IUI Positive results	P value
Sperm concentration(15 mill/ml)					
• <5th centile	41	5.3	2	4.9	0.145
• >5th centile	735	94.7	92	12.5	
Motility(40 %)					
• <5th centile	524	67.5	57	10.8	0.128
• >5th centile	252	32.5	37	14.7	
Rapid progressivemotility (32%)					
• <5th centile	606	78.1	77	12.7	0.475
• >5th centile	160	20.6	17	10.6	
Morphology(4%) (n=220)					
• <5th centile	98	44.5	8	8.2	0.034*
• >5th centile	122	55.5	22	18.1	

Analysis of post processing sperm concentration showed 4.9 %positive IUI results with less than5th percentile value(n=41) where as 12.5 %positive result when the sperm concentration wasmore than 5th percentile value(n=735). Hence, post processing sperm concentration waspositively correlated with IUI results, however without statistically significant p value (P=0.145).likewise, there was 10.8% positive IUI result with total sperm motility less than 5th percentile (n=524),whereas with more than 5th percentile motile sperm (n=252), positive IUI cases was 14.7%. Although statistically insignificant (P value=0.128), higher motility levels are positively associated with IUI results.

Comparison of sperm with rapid progressive motility and positive IUI result showed that less

than 5th percentile value (n=606) had 12.7% positive IUI cases whereas rapid progressivemotility with more than 5th percentile value (n=170) had positive IUI results in 10.6%. Hencerapidprogressive motility has no significant correlation with IUI results (P value=0.475).

Sperm morphology was assessed in 220 cases only. With the 2010 WHO 5th percentile value of

4% as normal morphology, 98(44.5%) had less than 5th percentile and 122(55.5%) had more than 5th percentile normal morphology.Normal sperm morphology with 5th percentile value of 4% and its impact on positive IUI resultshowed 8.2% positive IUI result with less than 5th percentile value(n=98) and 18.1% positiveIUI result with more than 5th percentile morphology(n=122). Hence, sperm morphology ispositively associated with IUI results with statistically significant p value (P=0.034)

Table 4: Post processing motility and IUI outcome

Post Processing Motility (Excellent progression) %	Number of subjects	Positive IUI result	Percentage
<80%	265	18	6.8
90%	313	44	14.1
100%	198	32	16.2
Total	**776**	**94**	**12.1**
Inference	Incidence of positive IUI results are significantly more associated with post processing motility >90% with P=0.004**		

The impact of post processing sperm motility with excellent progression in IUI outcome was also

studiedto find out the best possible cutoff motility level. It showed that motility with less than 80% excellent progression (n=265) was associatedwith 6.8% positive IUI result whereas motility with 90% excellent progression (n=313) was associated with 14.1% positive IUI result and motility with 100% excellent progression (n=198)was associated with 16.2% positive IUI results. Hence, incidence of positive IUI results are significantly more with post processing motility >90% with significant p value(P=0.004).

Discussion

IUI is regarded less stressful, less invasive and very less expensive treatment for infertility in comparison to techniques such as in vitro fertilization [11]. Moreover, it is oftenoffered as the first-line treatment to patients with mild to moderate male factor infertility. There is a common practice of induction of ovulation and intrauterine insemination for many cases of unexplained infertility and female infertility with no evidence of blocked fallopian tubes. The present study was done among couples in which evaluation of the woman revealed no structural or biochemical abnormalities thus fulfilling the criteria of either unexplained infertility or male-factor infertility. In these couples, the combination of the induction of ovulation with follicle-stimulating hormone and intrauterine insemination was associated with a likelihood of pregnancy.

The objective of the study was to understand whether one or more parameters of sperm quality i.e. morphology, motility and concentration have predictive value for the pregnancy outcome of the intrauterine insemination treatment for couple with primary infertility with male factor or unexplained cause in the select defined population who visitedManipal Hospital Bangalore during April 2011 to December 2012.The study population was those couples between 19-35 years of age who had been trying unsuccessfully to conceive for a minimum of 1 year. They were randomly distributed into 2 groups on the basis of WHO 5th manual minimum threshold value of sperm morphology, motility and concentration2010. Male partner with sperm morphology, motility and concentration below 5th percentile constituted group A. Group B was comprised of those with morphology, motility and concentration above 5th percentile.

A total of 776 IUI cycles over a period of 21 months were studied who met the study criteria.The mean age of the female partner who underwent IUI treatment was 29.62 years. The clinical pregnancy rate was 12.1% (pregnancy rate / cycle). The IUI success rate was found to be within the range of previous reports of between 8 and16 percent in the literature and it seems that our result is acceptable. The present study showed that sperm morphology is positively associated with IUI results with statistically significant p value (p=0.034). This study was done based on the WHO new threshold value of sperm morphology i.e. 4% as 5th percentile value, 2010. All other studied in the literature are based on the previous normal morphology cutoff of 30%.

Preprocessing sperm concentration and the result of IUI in terms of positive chemical pregnancy was assessed. Preprocessing sperm concentration of less than 50 million had positive IUI of 27.7% whereas concentration more than 50 million had positive IUI result of 72.3%. Although statistically insignificant (P=0.107), present study showed that pre-processing higher concentration is positively associated with positive results of IUI.

The present study based on WHO new threshold value of 15 million/ml as 5th percentile value showed that post processing sperm concentration were positively correlated with IUI results, however with statistically insignificant p value (P=0.145). Higher total motility levels is positively associated with IUI results but without statistically significant p value p=0.128. Incidence of positive IUI results are significantly more associated with post processing motility with excellent progression >90% with statistical significance, P=0.004**

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Conclusion

IUI is a valuable treatment modality for male factor and unexplained infertility. We conclude that for infertile couples in which the woman has no identifiable infertility factor and the man has motile sperm, the combination of super ovulation and intrauterine insemination is an effective means of achieving pregnancy. The probability of pregnancy increases by the following factors: higher sperm concentration, higher normal morphology and higher total motile sperms with excellent progression in processed sample. Hence, insemination of higher number

of morphologically normal sperm and improvement in sperm processing methods that yields to increased sperm concentration and total motile sperm count with excellent progression, cause higher pregnancy rate with IUI. If above mentioned semen parameters are below the 5th percentile value, IVF-ICSI would be preferred method of ART.

Conflict of interest: None declared

References

1. Wainer R, Albert M, Dorion A, Bailly M, Berger M, Lombroso R, et al. Influence of the number of motile spermatozoa inseminated and of their morphology on the success of intrauterine insemination. Hum reprod2004; 19: 2060-2065.

2. Hendin BN, Falcone T, Hallak J, Nelson DR, Vemullapalli S, Goldberg J, et al. The effect of patient & semen characteristics on live birth rates following intrauterine insemination: A retrospective study. J of Assisted Reprod and Genetics 2000; 17: 245-252.

3. Badawy A, Elnashar A, Eltotongy M. Effect of sperm morphology and number on success of intrauterine insemination. Fertil Steril 2009; 91: 777-781.

4. Saucedo de la E, Moraga MR, BatizaResendiz V, Galache Vega P, Santos HR. influence of sperm morphology on results of intrauterine insemination. GynecolObstet Mex 2003; 71: 455-459.

5. Lee RK, Hou JW, Ho Hy, Hwu YM, Lin MH, Tsai YC. et al. Sperm morphology analysis using strict criteria as a prognostic factor in intrauterine insemination.Int J Androl 2002; 25: 277.

6. Van Voorhis BJ, Barnett M, Sparks AET, Syrop CH, Rosenthal G, Dawson J. Effect of the total motile sperm count on the efficacy and cost effectiveness of intrauterine insemination and in vitro fertilization. FertilSteril2001; 76:1086-1087.

7. Dickey RP, Pyrzak R, Lu PY, Taylor SN, Rye PH. Comparison of the sperm quality necessary for successful intrauterine insemination with WHO threshold values for normal sperm. FertilSteril 1999; 71: 684-689.

8. World Health Organization, labratory manual for the examination of human semen and sperm-cervical mucus interaction. Cambridge university press, Cambridge, 1992.

9. Zhao Y, Vlahos N, Wyncott D, Petrella C, Garcia J, Zacur H, et al. Impact of semen characteristics on the success of intrauterine insemination. J of Assisted Reprod and genetics 2004; 21:143-148.

10. Goverde AJ, MC Donnell J, Vermeiden JPW, Schats R., Rutten FFH, Schoemaker J. Intrauterine insemination or in-vitro fertilization in idiopathic subfertility and male subfertility: A randomized trial and cost effectiveness analysis. The lancet 2000; 355:13-18.

11. Berek and Novak's gynaecology, 14th edition, Jonathan S. Berek (Editor), Lippincott Williams Wilkins; Fourteenth edition 2006.