Sperm Quality as a Prognosticator in Intrauterine Insemination-treated Sub-fertile Saudi Patients

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ABSTRACT

Background: Intrauterine insemination (IUI) is recognized as the most feasible infertility treatment, yet its success indications need further refinement.

Objective: This study aims to determine the most effective sperm parameters that help in prescribing IUI for infertility treatment within a Saudi population sample.

Method: We prospectively studied the inseminated post-wash total motile sperms count (TMSC), and the percentages of the fast(A)-plus-moderate(B)sperm progression of the specimens used for the IUI-treated infertility patients compared with the pregnancy rates (PR) corresponding to those parameters among a Saudi group of infertile patients.

Results: Our results showed clearly that over ten million TMSC would significantly make a better chance for conception after IUI treatment ($\rho = 0.034$). However, when the TMSC was sixty million or more, the chances for conception became significantly higher ($\rho = 0.007$). The A+B progression percentage did not significantly affect the PR ($\rho = 0.295$). The minimal post-wash TMSC that resulted in conception was 0.5 million sperms, with A+B of 55%, while the minimal post-wash A+B progression percentage that resulted in conception was 25%, with TMSC of eight million.

Conclusions: Although the semen quality of the studied population is declining, the TMSC is still the eligibility determining factor for IUI treated sub-fertile couples. A TMSC of at least ten million is still the recommended number for IUI suitability, although as few as 0.5 million still maintains the conception possibilities if the progression and morphology are normal.

Keywords: Infertility, insemination, pregnancy rate, sperm count

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INTRODUCTION

The benefits of intrauterine insemination (IUI) were acknowledged early for infertility treatment with mild male factor, cervical factor, immunological factor, or unexplained reasons (1). Intrauterine insemination was also shown to be an expensive and less invasive procedure in comparison with the *in vitro* fertilization (IVF) procedure (2). Pregnancy rate (PR) difference after IUI is wide ranging because of the variations between the patient groups, and the variation of the studied parameters (3–7). However, results from some other studies indicate a degree of consistency (1).

The objective of this study is to evaluate the clinical results of IUI in infertile couples treated in our centre that belongs to a public hospital in Saudi Arabia. We wanted to determine which sperm parameters underly the success of IUI treatment in a local infertile population in comparison with other patient populations worldwide. We studied the relationship between the post-wash total motile sperms count, as well as the post-wash sum of fast-forward (A) and moderate-forward (B) sperm progression percentages and the corresponding PR of each as prognostic factors.

SUBJECTS AND METHODS

In this prospective cohort study of local sub-fertile patients who were eligible for IUI treatment, and over a period of twenty months (January 2010 to August 2011), we analyzed the cases and the outcome in terms of pregnancy rate, and compared that with results from previous studies around the world.

For the purpose of accomplishing the goals of this study, cases with at least two million of initial TMSC and with 10% of A+B progression were included, while cases with 100% of abnormal morphology were excluded. Also, couples with wives of 43 years or older (unless IUI treatment was their only option for personal reasons), or with blocked fallopian tubes were excluded.

After evaluating the infertility cases, those who approved their participation in the study signed informed consent. For those cases, two semen analyses were done; one semen specimen was washed to get an idea of the TMSC and the progression profile before the IUI procedure. Further tests for the male partners included serum levels of follicular stimulating hormone (FSH) and testosterone. For the female patients, the baseline hormonal levels of FSH, luteinizing hormone (LH), thyroid stimulating hormone (TSH), and prolactin were tested. Intrauterine insemination was then prescribed to those who were eligible and a gonadotropin stimulation protocol was assigned and patients were monitored by ultrasound for the proper timing of insemination. When the one/two leading follicle(s) reached at least 15 mm in diameter, instructions were given to inject 5000 IU of human chorionic gonadotropin hormone (HCH) 36 hours before the IUI time.

Semen specimens were centrifuged through density gradient (PureSperm 40/80 from Nidacon International, Sweden; Catalogue No. PSK-020) for 20 minutes, at 18000 rpm. The sperm pellet was then washed twice with HEPES-buffered media (Quinn's Advantage Medium, with HEPES, from SAGE Company; Cat. # 1023), supplemented with serum (Quinn's Advantage Serum Protein Substitute SPS from SAGE Company; Cat. # 3010). Final sperm pellet was constituted within 0.5 mL of the same media while all results were recorded, and data were analysed.

Statistical analysis

SPSS software (Statistical Package for the Social Sciences, version 16.0, SPSS Inc., Chicago, Illinois, USA) was used for analysing the data. We used Chi-squared test to compare between pregnant and non-pregnant groups with respect to all variables. We assumed there was a significant difference when $\rho < 0.05$.

Ethical considerations

The Institutional Review Board approved the above project under research project No. E-12-647. Complete informed written consents were obtained from all study participants ahead of all procedures. None of the authors has any kind of conflict of interest with any party related to any material used for this study.

RESULTS

Post-wash total motile sperm count (TMSC) and pregnancy rate in IUI-treated patients

Of the patients, 20.79% had TMSC of 5 million or less and this group had PR of 4.76% which was the lowest success rate amongst all groups (Table 1); 17.82% of the patients had > 5–10 million, and resulted in a PR of 7.4%. In total, 38.61% of the patients had ten millions/mL or less of TMSC and they had an average PR of 5.98%, which is significantly less compared to the rest of all the groups (ρ=0.034).

Table 1: Post-wash total motile sperm count (TMSC) and corresponding success rates of intrauterine insemination (IUI)-treated patients

	Post-wash TMSC	Patients # n[1] (%)	Pregnancy rate	ρ-value
1	≤ 5 million	63 (20.79%)	3 (4.76%)	
2	> 5–10 million	54 (17.82%)	4 (7.4%)	0.034 (comparing PR of ≤10 m with > 10 m TMSC groups)
3	> 10–20 million	59 (19.47%)	9 (15.25%)	
4	> 20–30 million	55 (18.15%)	1 (1.82%)	
5	> 30–< 60 million	50 (16.5%)	6 (12%)	0.007 (comparing PR of ≥ 60 m with < 60 m TMSC groups)
6	≥ 60 million	22 (7.26%)	6 (27.27%)	

Then there were 19.47% of the patients who had > 10–20 million of TMSC, resulting in a relatively high success rate of 15.25%. There was an unexpected drop in the PR to 1.82% in the 18.15% of the patients with 21–30 million of TMSC. The PR increased to 12% with the following group of patients that constituted 16.5% of the total and who had > 30–59 million of TMSC. The last group, 7.26% of the patients with TMSC of sixty million or more, resulted in the highly significant PR of 27.27% (ρ=0.007 with the rest of all groups).

Post-wash sperm fast-plus-moderate forward-progression (A+B) percentages and its relation with the pregnancy rate in IUI-treated patients

Approximately 7 % (6.71%) of the total IUI-treated group had a sperm post-wash A+B% of 35% or less, and this group had a PR which was the lowest amongst all groups (Table 2). Additionally, 17.45% of patients had

Table 2: Post-wash fast forward and moderate forward progression and corresponding success rate of IUI-treated patients

	A+B Progression %	Patients # and %	Success Rate	P-value
1	≤35	20 (6.71%)	1 (5%)	
2	40-50	52 (17.45%)	5 (9.62%)	
3	55-65	61 (20.47%)	8 (13.11%)	0.295
4	70-80	98 (32.89%)	7 (7.14%)	
5	85-100	67 (22.48%)	8 (11.94%)	

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a post-wash sperm of 40–50% of A+B progression types, and this group resulted in a PR of 9.62%. One-fifth (20.47%) of the patients had A+B progression profile of 55–65%, with a PR of 13.11%, which was the highest amongst all the groups. One-third (32.89%) of the total treated group had 70–80 % of A+B progression types, resulting in a PR of 7.14%. The final group comprised 22.48% of the all patients, and this group had 80–100% of A+B progression and resulted in a PR of 11.94%. There was no significant difference amongst all the groups.

DISCUSSION

Our results proved that relatively low TMSC for IUI was still hopeful. A PR of 4.76% was obtained when the post-wash TMSC was five million or less. This finding is in contrast with those of Khalil *et al* (8), and Yang *et al* (9), who considered that TMSC of five million or more was the least to consider for IUI treatment. Wainer *et al* (10) also considered TMSC of five million as the critical number only when the normal sperm morphology was less than 30%. In fact, one of our cases that resulted in pregnancy had only 0.5 million motile sperms (with 55% A+B sperm progression and 19% normal morphology) and another successful case had only one million motile sperms though the A+B progression was only 25% and 12% normal morphology. These findings fine-tune the way we think about the minimal post-wash TMSC that would be good enough for IUI treatment, though the success rate is expectedly low. It was many years ago that Campana *et al* (11) and Ombelet *et al* (12) reported similar results to our findings. They stated that IUI success rate was significantly adversely affected at values only less than one million. Pasqualotto *et al* (13) also reported a reasonable 3.5% live birth rate at TMSC of 0.5 million.

In our study, the second group (17.82% of the patients) was inseminated with TMSC of ≥ 5–10 million, with PR of 7.4%, which is still encouraging, especially for cases that refuse regular IVF.

The third category comprised 19.47% of the patients, and was inseminated with >10–20 million, and had a PR of 15.25% which is significantly higher than the previous groups. We currently try processing two semen specimens for patients with low sperm count so that the final TMSC would fall into this category. The results are promising and more data are being collected.

The fourth group of 18.15% of the patients was inseminated with >20–30 million TMSC and had a PR of only 1.82%, which is very low compared to all the studied categories. It was found that a high percentage of the patients in this group were diagnosed with hormonal imbalance such as endometriosis, high FSH, and hyperprolactinaemia that caused their infertility and impacted the IUI treatment results. These findings are in line with Burwinkel *et al* (14), and Rajashekar *et al* (15).

The pregnancy rate rose again to 12% with the fifth group (16.5% of the patients) that was inseminated with TMSC of >30–59 million. These results are comparable with that of Demir *et al* (16). Also, Doripurev *et al* (17) concluded that the PR per cycle was significantly higher (8.2%) with TMSC of at least 10 million.

Pregnancy rate significantly improved as it reached 27.27% in the sixth group, when the TMSC was ≥ 60, $\rho=0.007$ compared with all other groups. This result is comparable to IVF results in some cases, which endorses that TMSC plays the most important role. The reason such good quality sperm did not result in natural pregnancy is indicated by Alkhayali *et al* (18) who noted that sperm chromatin integrity may be abnormal in men enrolled in IUI treatment cycles, despite the fact that most of these men look normozoospermic. There could also be other hidden reasons that affect the success rate.

This variation in results is contrary with what Pasqualotto *et al* (13) has reported. They stated that what mattered only was the post-wash sperm-motility percentage. On the other hand, Zadehmodarres *et al* (19) reported that the only determining factor for IUI success was that the final fast progressing sperm concentration after preparation was $\geq 1 \times 10^6$/mL. In the survey done by Rawal *et al* (20) on 150 reproductive centres in the United Kingdom, the TMSC factor was the number three factor after progression and morphology.

We also found that the cut-off percentage of A+B progression, below which the PR noticeably dropped, was 40% (Table 2). Pregnancy rate of 5% was the result when A+B progression ranged between 10% and 35%. The lowest percentage that resulted in pregnancy was 25%, with eight million TMSC. This could be around the value of 10% of fast progressive sperms described by Haim *et al* (21).

For the rest of the A+B progression ranges, (40–50%, 55–65%, 70–80%, and 85–100%) the PRs were 9.62%, 13.11%, 7.14%, and 11.94%, respectively, (ρ=0.295). Once the A+B progression rates are over 25%, the success expectations become higher. When Zhao *et al* (22) considered that A+B progression was detrimental for IUI success, they may have meant the critical minimal value of it. However, these findings are neither in complete agreement with Shulman *et al* (23) who indicated that good sperm progressive motility was the only sperm indicator for IUI success, nor do they agree with Zadehmodarres *et al* (19) who stated that the only determining factor for IUI success was that the post sperm preparation fast progression count had to be $\geq 1 \times 10^6$/mL.

In regards to the sperm morphology, no difference was detected between the group that resulted in pregnancy with normal morphology of 8–28%, and the unsuccessful group of normal morphology of 8–21%. That was probably because both ranges are higher than the 4% threshold value for successful pregnancy *in vivo* as stated by many authors and reported by Van Waart *et al*. (24), which nullified the morphology effect in this study.

The overall results of the study are important, especially since a higher percentage of sperm abnormalities was detected in males of infertile couples in Saudi Arabia compared with other regions in the world (25).

CONCLUSION

Although the semen quality of the studied population is declining, the TMSC is still the eligibility determining factor for IUI treated sub-fertile couples. A TMSC of at least ten million is still the recommended number for IUI suitability, although as few as 0.5 million still maintains the conception possibilities if the progression and morphology are normal

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