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Intrauterine Insemination: Relationship of Postwash Total Motile Sperm Count to Pregnancy Rates per Cycle in Siriraj Hospital

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ABSTRACT

Objective: To evaluate the effect of postwash total motile sperm count (TMSC) of <10 million and ≥10 million to pregnancy rates per cycle after intrauterine insemination (IUI) with husband's spermatozoa in Siriraj Hospital.

Study design: Retrospective cohort study.

Materials and Methods: A retrospective study of 900 IUI treatment cycles from July 2006 to July 2009 at Siriraj Hospital. Two groups were selected, 300 cycles in postwash TMSC <10 million group and 600 cycles in postwash TMSC ≥10 million group. The patients might stimulate ovarian follicles by several protocols. Bilateral tubal occlusions were excluded from this study. Sperm parameters before and after preparation for IUI were evaluated and correlated with pregnancy rate.

Results: The overall pregnancy rate was 5.7% per cycle. Pregnancy rates per cycle in couples with postwash TMSC of <10 million and ≥10 million were 1.7% and 7.7%, these differences were significant. The couples with postwash TMSC of ≥10 million were 4.60 times higher pregnancy rate than group of <10 million (95% CI 1.85 – 11.46). Moreover, the pregnancy rate was significantly lower for couples with <20 million/ml of prewash sperm concentration and <10 million of prewash TMSC.

Conclusion: Postwash TMSC significantly affected the pregnancy rate after IUI. Cycles with <10 million postwash TMSC are significantly less likely to result in a pregnancy.

Keywords: intrauterine insemination; postwash total motile sperm count; pregnancy rate; prewash total motile sperm count

Introduction

Intrauterine insemination (IUI) with husband's spermatozoa is commonly used to treat infertile couples because of its relatively low cost and simplicity compared with in vitro fertilization (IVF) or intracytoplasmic sperm injection (ICSI). The indications for IUI with husband's spermatozoa are ejaculatory failure, impaired semen quality, unexplained infertility, cervical hostility, immunological factor, endometriosis, ovulatory dysfunction, and combined non-tubal infertility factors. IUI has a higher pregnancy rate than natural conception because the washed and concentrated motile

spermatozoa would be directly injected into the uterine cavity near the ovulating time.

The pregnancy rates per cycle for IUI varied from 5.6% to 16.1%.[1] In literatures, many factors which would influencing pregnancy rate after IUI, have been reported: women's age[2-4], gravidity[4], duration of infertility[4], the prewash[3-4] and postwash[2] total motile sperm count, type of infertility[3-4], type of catheter[3], numbers of mature follicles[3] and E2 concentration on the day of hCG administration.[3] Several studies suggested that an optimal postwash total motile sperm count could be used as an indicator of a successful IUI.[5-7] However, the thresholds of postwash total motile sperm count were varying. There was no report which could clarify that the postwash total motile sperm count had a correlation with a success rate in IUI. In Siriraj Hospital, the recommended postwash total motile sperm count threshold for IUI is 10 million. No study in Thailand has mentioned the relationship between the postwash total motile sperm count and the success of IUI treatment cycles. There is no information, about the correlation of pregnancy rate with varying levels of postwash total motile sperm count in Siriraj Hospital, to counsel candidate couples for IUI.

The aim of this study was to evaluate the effect of postwash total motile sperm count of < 10 million and ≥ 10 million to pregnancy rates per cycle after intrauterine insemination with husband's spermatozoa in Siriraj Hospital.

Materials and Methods

Patient Population

This retrospective cohort study was performed at Siriraj Hospital, after an institutional ethical board approval was obtained. Data were collected from medical records of IUI cycles between July 2006 and July 2009, which only data with fresh husband's semen specimens were included in the study. From the total of 1054 IUI cycles, 900 IUI cycles were randomly selected, using SPSS software for windows. The data were divided into two groups: total motile sperm count < 10 million and total motile sperm count ≥ 10 million, at ratio of 1:2 respectively. All of these patients' charts were reviewed retrospectively for age, gravida, duration of infertility, semen parameters, number of mature follicles, and outcome of treatment. For categorizing type of infertility, patients with no gravida were defined as primary infertility and patients with 1 or more gravida were defined as secondary infertility. In Siriraj Hospital, patients who had risk of tubal occlusion such as dysmenorrhea, chronic pelvic pain, history of pelvic inflammatory disease or endometriosis would have tubal patency evaluated by hysterosalpingography or diagnostic laparoscopy before treatment. However in some cases that had low risk for tubal occlusion, trial of 1 or 2 cycles of intrauterine insemination might be considered after counseling with couples. The patients who had a documented bilateral tubal occlusion were excluded from this study. Frozen semen specimens might affect to pregnancy outcome, and then we also excluded frozen-thaw semen from husband's and donor's specimens.

Ovulation monitoring

There were many ovarian stimulation protocols depended on physician's decision: clomiphene citrate with or without gonadotropin, aromatase inhibitor with or without gonadotropin and gonadotropin only ovulatory cycles. Some patients had natural cycles IUI without ovarian stimulation. Transvaginal ultrasonography was performed to monitor the development of dominant follicles. When one or more follicles 16-18 mm in diameter were presented, human chorionic gonadotropin was administered for initiation of ovulation.

Semen preparation and insemination

Semen specimens were obtained by masturbation into a sterile cup after 3-5 days of abstinence and were examined after liquefaction. Sperm processing was performed using simple wash and resuspension, swim-up, or density gradient centrifugation. After processing, the sperm parameters were recorded.

Insemination was performed 36-48 hour after hCG administration. For insemination, the processed sperm was injected into the uterine cavity with soft catheter. If soft catheter couldn't pass into the uterine cavity, the hard catheter was used. A urinary pregnancy test was performed if menses were delayed for 1 week. If positive, transvaginal ultrasonography was performed to detect the gestational sac. Pregnancy was

defined as those with the intrauterine gestational sac on ultrasound.

Statistical analysis

Statistical analysis was performed by SPSS for windows, version 14. The results were reported as mean and standard deviation. Categorical variables were compared using a Chi square test, and continuous variables were analyzed using unpaired student's t-test. Statistical significance was considered if P value < 0.05.

Results

A total of 900 IUI cycles were included in the study. Two groups were selected, 300 cycles in postwash total motile sperm count < 10 million group and 600 cycles in postwash total motile sperm count ≥ 10 million group.

The overall pregnancy rate was 5.7% per cycle. Patient and semen characteristics in postwash total motile sperm count < 10 million versus ≥ 10 million group are shown in Table1. There were statistically significant difference between groups in age (34.48 ± 4.41 versus 33.69 ± 4.53) and duration of infertility (4.55 ± 3.64 versus 4.03 ± 3.10). Percentage of primary infertility (75.0% versus 75.7%), documented tubal patency (62.3% versus 60.3%) and number of mature follicles (1.64 ± 1.00 versus 1.59 ± 0.92) were not statistically significant difference.

Pregnancy rates per cycle in relation to total motile sperm count are shown in Table 2. Pregnancy rates per cycle in couples with postwash total motile sperm count of < 10 million and ≥ 10 million were 1.7% and 7.7% respectively. These differences were statistically significant. The couples with postwash total motile sperm count of ≥ 10 million were 4.60 times higher pregnancy rate per cycle than group of < 10 million (95% CI 1.85 – 11.46). The pregnancy rates per cycle according to 4 subgroups of postwash total motile sperm count are shown in Fig. 1. The postwash total motile sperm count < 5 million group and 5-<10 million group had significantly lower pregnancy rates per cycle than 10-<20 million group. Pregnancy rates per cycle in 10-<20 million group and >20 million group were not statistically significant difference.

In clinical practice, postwash total motile sperm count needs time for processing and it was done after decision of IUI treatment. But the couples should be counseled about chance of success with IUI before the treatment. Therefore, our study also demonstrates the relationships between prewash sperm parameter and pregnancy rates per cycle (Table 3). Couples with lesser than 20 million/ml prewash sperm concentration were significantly less likely to achieve a pregnancy. The pregnancy rates were significantly lower in less than 10 million prewash total motile sperm count.

Table 1. Patient and semen characteristics in postwash total motile sperm count (TMSC) < 10 million versus ≥ 10 million group

	Postwash TMSC < 10 million	Postwash TMSC ≥10 million	P-value
Age (year)	34.48 ± 4.41	33.69 ± 4.53	0.014*
Infertility (year)	4.55 ± 3.64	4.03 ± 3.10	0.029*
Primary infertility (%)	75.0	75.7	0.870
Documented tubal patency (%)	62.3	60.3	0.306
Number of follicle > 16 mm at hCG administration	1.64 ± 1.00	1.59 ± 0.92	0.461
Volume (ml)	1.84 ± 0.92	2.03 ± 0.73	0.001*
Prewash motility (%)	36.79 ± 9.68	44.41 ± 6.35	0.001*
Prewash concentration (million/ml)	14.34 ± 9.34	34.33 ± 12.14	0.001*

*P < 0.05 significant

Table 2. Pregnancy rates per cycle in relation to postwash total motile sperm count

	No. of cycles	No. of pregnancies	Pregnancy rate per cycle (%)	P-value
Postwash total motile sperm count				
< 10 million	300	5	1.7	0.001*
≥ 10 million	600	46	7.7	
Total	900	51	5.7	

*P < 0.05 significant

Relative risk 4.60, 95% CI 1.85-11.46

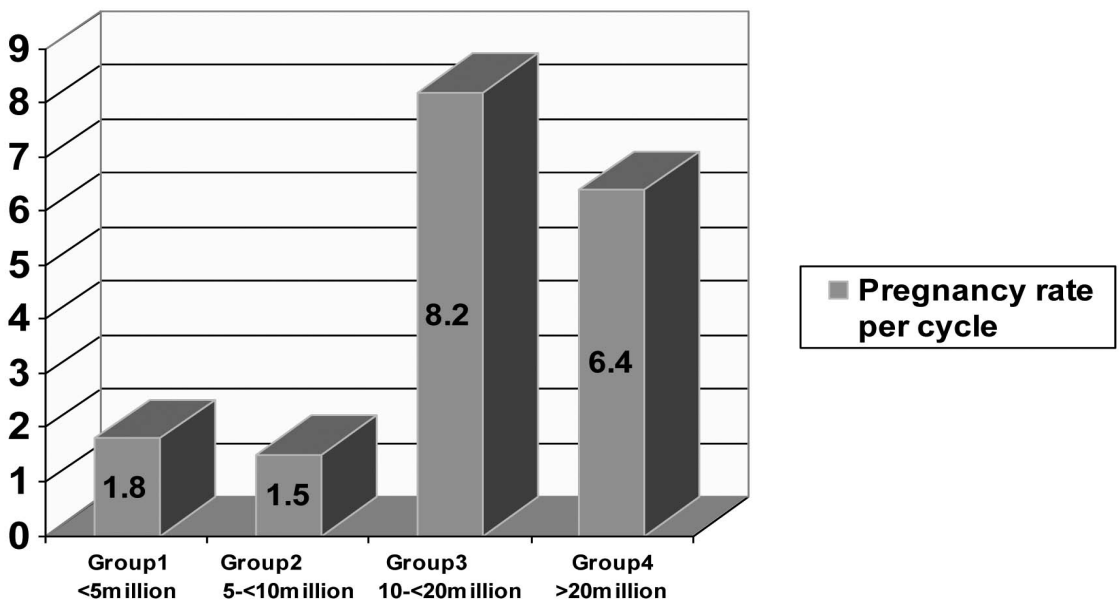


Fig. 1. Pregnancy rates per cycle in relation to postwash total motile sperm count

Table 3. Pregnancy rates per cycle in relation to prewash sperm parameter

	No. of cycles	No. of pregnancies	Pregnancy rate Per cycle (%)	P-value
Prewash volume				
< 2 ml	362	21	5.8	0.498
≥ 2 ml	538	30	5.6	
Prewash motility				
< 50%	774	42	5.4	0.276
≥ 50%	126	9	7.1	
Prewash concentration				
< 20 million/ml	249	7	2.8	0.013*
≥ 20 million/ml	651	44	6.8	
Prewash total motile sperm count				
< 10 million	203	4	2	0.004*
≥ 10 million	697	47	6.7	

*P < 0.05 significant

Discussion

From the results of our study, the overall pregnancy rate was 5.7% per cycle. The pregnancy rates found in this study are quite lower than those found in other studies: overall pregnancy rates of 6.9% and 10.8% per cycle were reported by Van der westerlaken et al.[5] and Miller et al.[6] The documented tubal patency may be responsible for difference. In our study, about 60% of the patients had documented by hysterosalpingography or laparoscopy. But in other studies, all of the patients had evaluated tubal patency before treatment.

The couples with postwash total motile sperm count of ≥ 10 million were 4.60 times higher pregnancy rate than group of < 10 million. Pregnancy rates per cycle in couples with postwash total motile sperm count of < 10 million and ≥ 10 million were 1.7% and 7.7%, respectively. These differences were statistically significant. Several studies have reported on the influence of postwash total motile sperm count on pregnancy rate. Van der westerlaken et.al[5] noted when the total motile sperm count were above 10 million, the pregnancy rate increased. Mehrafza et.al.[8] showed number of inseminated motile sperm of over 10 million significantly increased the pregnancy rate. Miller et.al.[6] reported a pregnancy rate per cycle of 12.4% when the processed total motile sperm count is over 20 million, compared with 1% when it is under 10 million. He suggested steering the couple towards IVF when the processed semen sample has less than 10 million motile sperm. According to other investigator, Huang et al[7] reported the success rate of IUI was significantly improved when the postwash total motile sperm count > 5 million. In Siriraj Hospital, couples with postwash total motile sperm count less than 10 million are counseling for IVF. Our result was similar to that of Van der westerlaken et.al, Mehrafza et.al, Miller et.al, we demonstrated significantly improved pregnancy rates with postwash total motile sperm count ≥ 10 million. The patient's characteristics in Table 1 show that there may be some bias in this study due to statistically significant differences for age and duration of infertility, by the younger age and shorter of duration of infertility of postwash total motile sperm count ≥ 10 million group. Although there may be no clinically significance (34.48 ± 4.41 versus 33.69 ± 4.53 and 4.55 ± 3.64 versus 4.03 ± 3.10) but these differences may be the cause of higher pregnancy rate.

Moreover, our study showed that prewash sperm concentration was significantly higher in specimens which prewash sperm concentration of < 20 million/ml than prewash sperm concentration of ≥ 20 million/ml. Zhao et.al.[9] reported that initial sperm concentration was not associated with successful IUI outcome, but this study divided into three groups; <50 million/ml group, 51-100 million/ml group and > 100 million/ml group. Division in these two studies may be responsible for the difference. We also found that couples with prewash total motile sperm count of less than 10 million had significantly lower pregnancy rate than the couples with prewash total motile sperm count of ≥ 10 million. Our result was similar to that of Von Voorhis et.al.[4], he reported that the total motile sperm count in the ejaculate was an important factors, with a threshold value of 10 million. In contrast, Zhao et.al.[9] reported that prewash total motile sperm count did not correlate with IUI outcome. The differences may be reflected to patient population and/or analysis methodology.

Our study has several limitations. Due to the retrospective method, there are many limits of data collection in the study, for example, there are diversity of ovarian stimulation protocols which were depended on the physician's decision (the best protocol has not been established in Siriraj Hospital), about 40% of undocumented tubal potency which female factor cannot be excluded, and the diversity of sperm preparation which also affects pregnancy rate. In the future, prospective study should be performed for further analysis of these confounding factors.

Conclusion: Sperm parameters such as prewash sperm concentration, prewash total motile sperm count and postwash total motile sperm count significantly affected the pregnancy rate after intrauterine insemination. Cycles with less than 10 million postwash total motile sperm are significantly less likely to result in a pregnancy.

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ความสัมพันธ์ระหว่างจำนวนอสุจิที่เคลื่อนไหวทั้งหมดหลังการเตรียมอสุจิและอัตราการตั้งครรภ์ต่อรอบที่ฉีดน้ำอสุจิในผู้ป่วยที่มารับการรักษาภาวะมีบุตรยากด้วยวิธีการฉีดน้ำอสุจิเข้าในโพรงมดลูกในโรงพยาบาลศิริราช

ชุติมน อสัมภินวงศ์, จปรัฐ ปรีชาพานิช

วัตถุประสงค์ *: เพื่อศึกษาผลของจำนวนอสุจิที่เคลื่อนไหวทั้งหมดหลังการเตรียมอสุจิที่น้อยกว่า 10 ล้านตัวกับ ตั้งแต่ 10 ล้านตัวขึ้นไปต่ออัตราการตั้งครรภ์ต่อรอบในผู้ป่วยที่มารับการรักษาภาวะมีบุตรยากด้วยวิธีการฉีดน้ำอสุจิของสามีเข้าในโพรงมดลูกที่หน่วยรักษาผู้มีบุตรยาก คณะแพทยศาสตร์ศิริราชพยาบาล*

วิธีการศึกษา *: การศึกษาแบบย้อนหลัง*

วัสดุและวิธีการ *: ทำการศึกษาแบบย้อนหลังในผู้ป่วยที่มารับการรักษาภาวะมีบุตรยากด้วยวิธีการฉีดน้ำอสุจิของสามีเข้าในโพรงมดลูกที่หน่วยรักษาผู้มีบุตรยาก คณะแพทยศาสตร์ศิริราชพยาบาล จำนวน 900 รอบ ในช่วงเดือนกรกฎาคม พ.ศ. 2549 ถึงเดือนกรกฎาคม พ.ศ. 2552 โดยแบ่งเป็น 2 กลุ่ม คือ ในผู้ป่วยที่มีจำนวนอสุจิที่เคลื่อนไหวทั้งหมดหลังการเตรียมอสุจิที่น้อยกว่า 10 ล้านตัวจำนวน 300 รอบกับ ตั้งแต่ 10 ล้านตัวขึ้นไปจำนวน 600 รอบ โดยผู้ป่วยอาจได้รับยากระตุ้นไข่วิธีใดก็ได้ และในการศึกษานี้ได้คัดผู้ป่วยที่มีท่อนำไข่ทั้งสองข้างตันออกจากการศึกษา*

ผลการศึกษา *: ในผู้ป่วยที่มารับการรักษาภาวะมีบุตรยากด้วยวิธีการฉีดน้ำอสุจิของสามีเข้าในโพรงมดลูกที่หน่วยรักษาผู้มีบุตรยาก คณะแพทยศาสตร์ศิริราชพยาบาล มีอัตราการตั้งครรภ์โดยรวม 5.7 % ต่อรอบ และเมื่อเปรียบเทียบอัตราการตั้งครรภ์เมื่อมีจำนวนอสุจิที่เคลื่อนไหวทั้งหมดหลังการเตรียมอสุจิที่น้อยกว่า 10 ล้านตัวกับ ตั้งแต่ 10 ล้านตัวขึ้นไป พบว่ามีความแตกต่างกันอย่างมีนัยสำคัญทางสถิติ (1.7% และ 7.7% ต่อรอบ ตามลำดับ) โดยในคู่สมรสที่มีจำนวนอสุจิที่เคลื่อนไหวทั้งหมดหลังการเตรียมอสุจิตั้งแต่ 10 ล้านตัวจะมีอัตราการตั้งครรภ์สูงกว่ากลุ่มที่มีจำนวนอสุจิที่เคลื่อนไหวทั้งหมดหลังการเตรียมอสุจิน้อยกว่า 10 ล้านตัว 4.60 เท่า (95% CI 1.85 – 11.46) นอกจากนี้ยังพบว่าเมื่อเปรียบเทียบอัตราการตั้งครรภ์เมื่อความเข้มข้นของอสุจิก่อนเตรียมอสุจิน้อยกว่า 20 ล้านตัว/มล. กับตั้งแต่ 20 ล้านตัว/มล. และจำนวนอสุจิที่เคลื่อนไหวทั้งหมดก่อนการเตรียมอสุจิที่น้อยกว่า 10 ล้านตัวกับตั้งแต่ 10 ล้านตัวพบว่าอัตราการตั้งครรภ์ในกลุ่มแรกน้อยกว่าอย่างมีนัยสำคัญทางสถิติ*

สรุป *: ผลของจำนวนอสุจิที่เคลื่อนไหวทั้งหมดหลังการเตรียมอสุจิในผู้ป่วยที่มารับการรักษาภาวะมีบุตรยากด้วยวิธีการฉีดน้ำอสุจิของสามีเข้าในโพรงมดลูกมีผลกับอัตราการตั้งครรภ์ต่อรอบ โดยอัตราการตั้งครรภ์จะน้อยกว่าเมื่อมีจำนวนอสุจิหลังการเตรียมที่น้อยกว่า 10 ล้านตัว*