

学 位 論 文 の 要 旨

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学 位 論 文 名	Impact of Current and Previous Sperm Findings on Outcomes of Intrauterine Insemination
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論 文 内 容 の 要 旨

INTRODUCTION

Infertility affects millions of people of reproductive age. Among the various infertility treatments, intrauterine insemination (IUI) is widely recommended as the first-line treatment for couples with subfertility. Although IUI treatment is offered as a step-up treatment, given the many variables potentially impacting the success rate. In this study, we evaluated the pre- and post-wash semen parameters at the time of IUI and investigated the association of these parameters with the success of IUI.

MATERIALS AND METHODS

Patients and study design

This is a retrospective observation study of all IUI procedures performed between January 2019 and December 2021 at Shimane University Hospital. The main clinical outcome measure was clinical pregnancy rate per IUI cycle. Sperm quality parameters were assessed before insemination. Sperm morphology was rated according to the World Health Organization (WHO) criteria. This study protocol was approved the Research Ethics Committee of Shimane University.

Intrauterine insemination

We included cases of IUI completed in unstimulated natural cycles, those with oral administration of 50–150 mg/day clomiphene citrate (Clomid tablets; Fuji Pharma Co., Ltd. Tokyo, Japan), and/or those with gonadotropin-stimulated cycles. Clinical pregnancy was

confirmed by the presence of a gestational sac on ultrasonography 4–5 weeks after IUI.

Statistical analysis

Results are expressed as the mean $\pm$ standard deviation or percentage. Categorical data were compared using the Mann–Whitney *U* test, the Wilcoxon signed-rank test, or the chi-squared test according to the variables. Statistical significance was set at $p < 0.05$. Correlations between two metric variables were determined by Pearson's correlation coefficient. All analyses were performed using IBM SPSS statistics 26 (IBM Japan, Tokyo, Japan).

RESULTS AND DISCUSSION

Background of pregnant and non-pregnant couples

During the study period, 421 couples underwent a total of 1380 IUI cycles, using the partner's sperm. Clinical pregnancy was achieved in 87 IUI cycles of 81 women, giving pregnancy rates of 19.2% per patient and 6.3% per IUI cycle. The mean age of women at the time of the IUI procedure resulting in pregnancy was significantly lower compared with those who did not achieve pregnancy during their IUI cycles.

Pre-wash and post-wash semen findings in pregnant and non-pregnant couples

The pregnancy rate was significantly lower when the post-wash sperm concentration was below $16 \times 10^6/\text{mL}$ compared with when it was above $16 \times 10^6/\text{mL}$ (6.8% vs. 3.2%, $p = 0.042$). There were no cases of pregnancy when post-wash sperm motility was below 42%. Similarly, there were no cases of pregnancy when both concentration and motility were below the WHO standards in post-wash semen samples. The sperm motility in the original semen findings seems to be more sensitive to the success of IUI. When the post-wash sperm motility is less than 42%, IUI is unlikely to succeed.

Changes in the semen findings and outcome of IUI

In the majority of cases, pregnancy was achieved when the pre-wash sperm concentration was normal or when the post-wash concentration had improved to normal. In all cases where pregnancy was achieved, the post-wash sperm motility was above the WHO normal range of 42%. Pre- and post-wash sperm concentration is not a predictor of the success of IUI. In contrast, although the improvement in sperm motility by washing also varied in each case, all cases of pregnancy had a motility rate above 42%, which is the lower limit of the WHO standard.

Previous sperm findings and outcome of IUI

In 11 of the 13 women (84.6%) who became pregnant on their third attempt, the post-wash sperm concentration was normal ($>16 \times 10^6$) in both of the previous two unsuccessful cycles. There were no cases of pregnancy in which the sperm concentration did not normalize after washing in their two previous attempts. In the 13 women who achieved pregnancy on their third IUI attempt, the post-wash sperm motility was above 42% in both of the previous two

unsuccessful cycles. In the 14 women who became pregnant on their fourth IUI attempt, 6 (42.9%) had used semen with a sperm concentration above the WHO standard in their previous three unsuccessful cycles. There was one case of pregnancy in which the post-wash sperm concentration did not normalize in any of the previous three cycles. Meanwhile, 13 of the 14 women who became pregnant on their fourth IUI attempt (92.9%) had normal motility in the previous three unsuccessful IUI cycles, while the remaining woman had normal motility sperm in two of the three unsuccessful cycles. This information should be considered when deciding whether to perform another IUI cycle.

Women's age and IUI outcome and partners' age and post-wash sperm findings

In all cases, pregnancy rates were significantly higher in women under the age of 35 years compared with those over the age 35 years (8.3% vs. 4.7%, $p=0.008$). This trend was also observed when comparing IUI cycles in which post-wash semen concentrations were normal ($>16 \times 10^6$ / ml) (8.8% vs. 5.3%, $p=0.018$). In contrast, pregnancy rates did not significantly differ between these two age groups when post-wash sperm concentrations were below the normal range (4.9% vs. 2.2%, $p=0.271$). Sperm concentration, total sperm count, and total motile sperm counting were not correlated with partner's age; only the motility rate in pre-wash sperm showed a slight negative correlation with the male partner's age. Pregnancy rates did not significantly differ according to the women's age in IUI with sperm concentrations below the normal range of the WHO standard. These findings suggest that the higher oocyte quality in younger women does not compensate for low sperm concentrations in achieving pregnancy with IUI.

CONCLUSION

Pre- and post-wash sperm characteristics did not differ between IUI cycles that resulted in pregnancy and those that did not. When the motility of pre-wash sperm was below the normal range established by the WHO (i.e., $<42\%$), the pregnancy rate was significantly lower. In the IUI cycles in which post-wash sperm motility was below the WHO standard, pregnancy was not achieved. At the third IUI cycle, there were no cases of pregnancy unless the post-wash sperm motilities used in the previous two IUI procedures were above 42%. At the fourth IUI cycle, pregnancy was not achieved unless the post-wash sperm motility was normal in at least two of the three previous attempts. From these findings, sperm motility above the lower limit of the WHO criteria is thought to be an important factor in IUI outcomes.