

Editorial

Does The Time Interval Between Semen Collection, Processing & Insemination affect results of IUI?

Controlled ovarian hyperstimulation coupled with intrauterine insemination (IUI) is the first choice of treatment for infertility caused by a variety of factors¹, because it is cost-effective and a non-invasive ART. IUI involves processing a semen specimen by a “sperm washing” procedure to obtain progressively motile spermatozoa by separation from seminal plasma, debris, dead spermatozoa, abnormal spermatozoa, leukocytes, and other types of cells. The World Health Organization (WHO) recommends that, ideally, the male partner produce the semen specimen in a private room near the laboratory². The purpose of this recommendation is to better assess liquefaction of the ejaculate and prevent its exposure to extremes of temperature. However, patients occasionally request that they collect semen specimens for IUI at home rather than at the clinic. Reasons for this request include convenience for the patients, convenience for the clinic, and the male partner’s preference.

In accordance with WHO recommendations², patients who request to collect semen specimens at home are advised that semen specimens collected at home should be delivered to the laboratory within 1 hour of collection and should be protected from extremes of temperature (<20°C and >40°C). However, the time interval from semen specimen collection to its delivery to the laboratory and the temperature to which the semen specimen is exposed during its transportation are still at the discretion of the patients and are not totally controlled by the laboratory.

Although it is well known that sperm progressive motility of a freshly ejaculated semen specimen declines both over time³⁻⁵ and by exposure to extremes of temperature⁶, a freshly ejaculated semen specimen will maintain an acceptable sperm progressive motility for up to 12 hours⁵, and spermatozoa will survive up to 24–48 hours⁶, which hence obviously will not

compromise the “semen analysis” results within 1 hour of collection. Although the WHO 1-hour maximum limit of interval from semen collection to its delivery to the laboratory relates to “diagnostic semen analysis” only, many clinics mistakenly apply this to “therapeutic semen processing” for clinical procedures, such as IUI and IVF, as well. However, even if the semen specimen was protected from extremes of temperature during transportation, whether delaying semen processing for up to 1 hour will not compromise the pregnancy outcome from clinical procedures remains relatively a grey zone.

There are ongoing controversies whether the location of semen collection (home vs. clinic) for IUI (intra uterine insemination) affect pregnancy rates. Shimuzu et al⁷ published a study this year to assess the relationship between the time interval from semen collection to sperm wash and IUI outcome. 449 infertile couples who underwent 1054 IUI treatment cycles were analyzed. The time interval from semen collection to sperm wash was divided to group A (less than 3 hours), group B (3-5 hours), and group C (over 5 hours). Total IUI pregnancy rate was 14.0 % (148/1054). IUI pregnancy rate was not different between group A, B and C. IUI pregnancy rate after 3-7 days abstinence (15.1%) and over 8 days abstinence (14.3%) were better than that after less than 2 days abstinence (7.9%). The authors concluded that the time interval from semen collection to sperm wash has no influence to IUI outcome⁷. It seems that the location of semen collection (home vs. clinic) for IUI do not affect pregnancy rates⁷.

The objective of a recent study was to correlate pregnancy outcomes with the subject time intervals in CC-IUI cycles. Analysis of pregnancy outcomes of 210 CC-IUI cycles from January 2001 to December 2002 was done by Alexander et al⁸. Indications for treatment with CC-IUI were the following: anovulation, unexplained infertility, male factor infertility, increased reproductive

age and multifactorial infertility. Women received 50-150mg/day of CC on cycle days 5-9. Follicular development was monitored via trans-vaginal ultrasonography. Twenty-four hours after detection of a spontaneous LH surge or 36 hours after administration of hCG, when indicated, a single IUI using a Cook IUI catheter was performed by the physician. Semen specimens were collected at the departmental andrology laboratory. Sperm preparations were performed by a density gradient centrifugation. The collection times were recorded in the laboratory; the duration of semen processing was approximately 30 minutes. Patients were then required to transport the processed specimen to the clinic for the insemination procedure. The time of IUI was recorded by the physician performing the IUI. Time intervals from collection to sperm processing, from sperm processing to IUI and from collection time to IUI were calculated for each CC-IUI cycle. Mean intervals from collection to sperm processing, from sperm processing to IUI and from collection time to IUI were similar in pregnant and non-pregnant CC-treated women. These findings suggest differences in time intervals from semen collection to sperm processing and sperm processing to IUI do not influence pregnancy outcomes for CC-IUI cycles⁸.

Yavas et al⁹ set-up a study to determine if IUI outcome was affected by: 1) place of semen collection (home vs. clinic); and 2) intervals from semen collection to sperm wash (C-SW), from sperm wash to IUI time (SW-IUI), and from semen collection to IUI time (C-IUI). In 132 IUI cycles, women with infertility of various causes received either clomiphene citrate (CC) or human menopausal gonadotropin (hMG). Women stimulated with CC received 50–250 mg/day for 5 days starting on cycle day 3; and women stimulated with hMG were started on cycle day 3, if a baseline ultrasound revealed no ovarian cyst. When the largest follicle(s) reached a mean diameter of 19 mm, ovulation was induced with 10,000 IU hCG, and a single IUI was performed 36–38 hours later. Women underwent IUI using their respective partners' washed sperm obtained from ejaculates collected either at home (H), or at the clinic (F). Ejaculates were allowed at least 15 minutes for liquefaction before sperm wash by a gradient density method. In a sub-group of 70 women, the intervals of C-SW, SW-IUI, and C-IUI were compared by Student's t-test between: 1) collection places; and 2) pregnant and non-pregnant women within medication types. The authors concluded that CC and hMG result in similar pregnancy rates when semen is collected either at home or at clinic⁹. Semen collection at clinic results in higher

pregnancy rates than at home both in CC- and hMG-treated women⁹. Pregnancy is not affected by intervals of C-SW, SW-IUI, and C-IUI in CC-treated women, but is associated with shorter intervals in hMG-treated women⁹.

Yavas & Selub¹⁰ published a larger follow-up study in 2004 that found semen collection at clinic resulted in a higher pregnancy rate than collection at home in hMG-treated (44% vs. 18%; $P=.03$) but not in CC-treated women (9% vs. 9%; $P=.93$). Intervals of C-SW, SW-IUI, and C-IUI were shorter in pregnant than in non-pregnant hMG-treated women (27 vs. 41 minutes, 42 vs. 85 minutes, and 99 vs. 156 minutes, respectively; $P=.01$) but not in CC-treated women (28 vs. 38 minutes, 51 vs. 63 minutes, and 109 vs. 131 minutes, respectively; $P=.19$). Semen processed within 30 minutes after collection resulted in a higher pregnancy rate than that processed 31–60 minutes after collection in hMG-treated (48% vs. 18%; $P=.02$) but not in CC-treated women (10% vs. 8%; $P=.81$). Intrauterine insemination performed within 90 minutes of collection resulted in a higher pregnancy rate than IUI performed at 91–120 minutes or >120 minutes after collection in hMG-treated (99% vs. 22% and 7%, respectively; $P<.0001$) but not in CC-treated women (11%, 4%, and 10%, respectively; $P=.46$). They concluded that for IUI with hMG but not CC, semen collection at the clinic is more effective than, and should be chosen over, collection at home¹⁰. The results of this present study validate the previous recommendations by Mortimer¹¹ & Mortimer et al¹² that spermatozoa for clinical procedures such as IVF, GIFT, or IUI and for laboratory tests of sperm fertilizing ability, must be separated from the seminal environment as soon as possible after ejaculation.

Delaying semen processing from 30 minutes up to 1 hour and/or delaying IUI from 90 minutes up to 2 hours after collection compromises the pregnancy outcome in hMG-IUI cycles. Semen specimens should be processed as soon as just after liquefaction and within 30 minutes of collection, and IUI performed as soon as just after processing and within 90 minutes of collection.

One such factor that is likely to adversely affect the fertilizing ability of washed motile spermatozoa is exhaustion of energy sources in the sperm-washing medium by the motile spermatozoa during a prolonged SW-IUI interval. Because sperm motility requires energy sources, such as glucose and fructose¹³, washed motile spermatozoa deprived of energy sources during a

prolonged SW-IUI interval might not be able to reach the fertilization site in fallopian tubes after IUI. Another such factor could be premature (in vitro) capacitation of washed motile spermatozoa in the sperm-washing medium during a prolonged SW-IUI interval, because [a] seminal decapacitation factor(s) are removed along with seminal plasma during the sperm wash procedure, [b] capacitation occurs spontaneously in simple defined medium, implicating a potential role of autocrine induction¹⁴, and [c] washed spermatozoa undergo capacitation in response to human follicular fluid when incubated overnight at 37°C¹⁵. Thus, washed motile spermatozoa that have undergone in vitro capacitation, prematurely relative to fertilization time, during a prolonged SW-IUI interval might not be able to undergo subsequent changes in the female reproductive tract after IUI.

Conclusions

Thus, to maximize the IUI pregnancy outcomes, not only should semen specimens be collected at the clinic and processed as soon as just after liquefaction and within 30 minutes of collection, but also IUI should be performed as soon as within 90 minutes of semen collection. Whether delaying delivery of semen specimens to the laboratory for up to 1 hour after collection will compromise the pregnancy outcome of other clinical procedures, such as IVF or GIFT, warrants further study.

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