Male factors affect success of assisted reproductive technology

In this issue of *Fertility and Sterility*, Periyasamy et al. (1) present a retrospective study that examines the effect of male sexual abstinence on the results of assisted reproductive technology. They found that men with longer abstinence intervals contributed to in vitro fertilization (IVF) cycles with lower implantation, clinical pregnancy, and live birth rates. This study provides us with several interesting insights, but it should be interpreted with caution as well.

It is of particular interest that a sperm factor affects the results of (predominantly) intracytoplasmic sperm injection (ICSI) cycles reported in this article. The couples included in the analysis were those who had ICSI alone or a combination of ICSI and IVF used to initiate fertilization. Most experts have routinely rejected the possibility that sperm affect the results of ICSI, as long as viable sperm are present. This study provides strong evidence of male factors affecting ICSI results of implantation, clinical pregnancy, and live birth.

What is less clear is how the abstinence interval may have affected ICSI results. A number of studies, including those referenced in this article by Pons and Gosalves, and others such as Uppangala et al. (2), have documented a relationship between longer abstinence intervals and an increase in sperm DNA integrity. Meta-analytic reviews have also documented the relationship between abnormal sperm DNA integrity and IVF/ICSI results, with combined studies of IVF and ICSI showing a 2.37-fold decrease in clinical pregnancy rates when abnormal sperm DNA fragmentation is present in the neat sample of the man's ejaculate (3). This effect is not abrogated by sperm selection from the sample (although the processed sperm has lower sperm DNA fragmentation, these visually "undamaged" sperm adversely affect the success of assisted reproduction cycles [4]). So it is quite possible that the increased sperm DNA fragmentation from men with longer abstinence intervals explains much of the adverse effect on assisted reproduction outcomes observed in this study.

It is also possible that the men with longer abstinence intervals were somehow different from men with shorter abstinence intervals. As an observational study, the data in this article did not control for such alterations. For example, in Table 1 of the study (1) it is shown that men with longer abstinence intervals were older than the men with shorter abstinence intervals ($P=.05$). Increased male age certainly has an adverse effect on sperm DNA fragmentation as well (5).

In summary, this study makes important observations on the effect of male factors that adversely affected live birth rates after ICSI and IVF. It is possible, but not yet tested, that these same men could have dramatically increased the effectiveness with a simple intervention, such as providing a second semen sample (or just a semen sample with shorter abstinence) in the programmed cycle. Our acceptance of sperm as they are currently evaluated, with morphology, motility, and concentration alone, is antiquated and likely impairs our ability to optimize the effectiveness of assisted reproduction interventions. It is time to consider male factors affecting IVF success more scientifically.

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https://doi.org/10.1016/j.fertnstert.2017.09.003

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