Reply of the authors: Seminal plasma exposure in IVF cycles: dripping water hollows out stone, not through force but through persistence

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Response to: Seminal plasma exposure in IVF cycles: "Dripping water hollows out stone, not through force but through persistence"

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We appreciate the interest in our article shown by dr Zhengao and colleges. Intravaginal exposure to seminal plasma has been suggested to improve the implantation rate after IVF but evidence has not been sufficient to show an increased live birth rate (1). Our study was aimed to find such an increase, depositing the male partner´s seminal plasma intravaginally at time of ovum pick-up with live birth as the primary outcome (2). The speculated effect on pregnancy outcomes has been attributed to immunologically active molecules with the ability to change endometrial receptivity. Even if no difference was found between the saline group and the seminal plasma group, it does not rule out the possibility that seminal plasma with a favorable concentration of cytokines could affect implantation rates as well as miscarriages.

We agree with Zhengao et al., that a pregnancy-enhancing effect of seminal plasma could be present in different subgroups. An assessment of pre-eclampsia after IVF with or without seminal plasma exposure at time of ovum pick-up would have been very interesting but neither peripartum complications nor subgroup analyses were aims in the study (2). A study with these primary outcomes would require a large number of couples in order to demonstrate a difference with statistical significance and is perhaps better performed in a multicenter setting. Our study of 800 couples was not powered for this type of analyses.

Many couples with recurrent pregnancy loss (RPL) and antiphospholipid syndrome have no difficulties in achieving a pregnancy and could be underrepresented in an IVF-setting. The seminal plasma in men with otherwise unexplained RPL have been shown to elicit a different immunological response than seminal plasma from control males, suggesting a causal effect on pregnancy losses (3). Intravaginal deposition at time of ovum-pick up of this type of seminal plasma would probably not elicit a different response compared with an exposure through intercourse. Instead of focusing on any possible effect of multiple exposure to seminal plasma and performing studies on infertile couples' sexual practices we would instead suggest further studies on seminal plasma itself. If the optimal cytokine concentration in seminal plasma could be determined, maybe the knowledge could be used to increase the endometrial receptivity and thereby the live birth rate after IVF, as well as decrease the risk of pregnancy losses. Our results show that random seminal plasma is not enough.

1. Ata B, Abou-Setta AM, Seyhan A, Buckett W. Application of seminal plasma to female genital tract prior to embryo transfer in assisted reproductive technology cycles (IVF, ICSI and frozen embryo transfer). Cochrane Database Syst Rev 2018;2:CD011809
2. Liffner S, Bladh M, Rodriguez-Martinez H, Sydsjö G, Zalavary S, Nedstrand E. Intravaginal exposure to seminal plasma after ovum pick-up does not increase live birth rates after in vitro fertilization or intracytoplasmic sperm injection treatment: a double-blind, placebo-controlled randomized trial. Fertil Steril 2024;122(1):131-139
3. Du Fossé NA, Lashley E, Anholts JDH, van Beelen E, le Cessie S, van Lith JMM, Eikmans M, van der Hoorn MLP. Impaired immunomodulatory effects of seminal plasma may play a role in unexplained recurrent pregnancy loss: Results of an in vitro study. J Reprod Immunol 2022;151:103500