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P-064 Clinical outcomes of 127 patients with recurrent implantation failure treated with testicular sperm aspiration (TESA)

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**Study question:** Are the embryological, clinical and newborn outcomes using aspirated testicular sperm improved in cases with recurrent implantation failure previously treated with ejaculated sperm?

**Summary answer:** Aspirated testicular sperm enabled to obtain significant higher embryological, clinical and newborn outcomes in cases with recurrent implantation failure previously treated with ejaculated sperm.

What is known already: High levels of sperm DNA fragmentation (SDF) were associated to poor clinical outcomes (1-Simon et al., 2017). Testicular sperm display lower SDF than ejaculated sperm (2-Sakas and Alvarez, 2010), improving clinical outcomes in cases with abnormal semen parameters (3-Awaga et al., 2018; 4-Kang et al., 2018), recurrent implantation failure (RIF) and pregnancy loss (RPL) (5-Esteves et al., 2017), and elevated SDF (6-Ambar et al., 2021). As only a few studies are specifically dedicated to RIF, we expanded the number of cases and first provided full demographic, stimulation, embryological, clinical and newborn outcomes.

References: I-(https://doi.org/10.4103/1008-682X.182822);

2-(https://doi.org/10.1016/j.fertnstert.2009.10.046);

3-(https://doi.org/10.1016/j.rbmo.2018.08.017);

4-(https://doi.org/10.1038/s41598-018-26280-0);

5-(https://doi.org/10.1016/j.fertnstert.2017.06.018); 6-(https://doi.org/10.5534/wjmh.200084

**Study design, size, duration:** We retrospectively evaluated during consecutive years (2010-2020) 63 patients with recurrent implantation failure, which accepted to perform testicular sperm aspiration (TESA) as an alternative treatment. These patients presented a long history of failed treatments (153 cycles) using ejaculated sperm. From these cycles, no pregnancy ensued. The present study compares 127 treatment cycles, 80 with testicular sperm (17 cases repeated TESA) and 47 with ejaculated sperm from the same patients performed at the present IVF clinic.

**Participants/materials, setting, methods:** Patients were screened for karyotype abnormalities, for Y-chromosome microdeletions (7-Gonçalves et al., 2016), and for SDF with the TUNEL assay (8-Sá et al., 2015). Conventional semen analysis was performed according to World Health Organization guidelines (9-WHO, 2010). Male evaluation and TESA was performed by the same experienced urologist (LF) according to established protocols (10-Madureira et al 2014). The procedure was performed entirely on an outpatient basis, with no complications reported.

References: 7-(https://doi.org/10.4103/1008-682X.172827);

8-(https://doi.org/10.1016/j.rbmo.2015.06.019); 9-(https://apps.who.int/iris/handle/10665/44261); 10-(https://doi.org/10.1111/j.2047-2927.2014.00231.x).

Main results and the role of chance: The mean ages were 35.5±3.4 (26-42)-female and 38.1±5.7 (29-59)-male. There were 4 abnormal karyotypes (3-female, I-male), all without known relevance. Most cases had asthenozoospermia and teratozoospermia (65.1%), or oligoasthenoteratozoospermia (41.8%). Of the 19 cases with <5M/ml, none presented Y-chromosome microdeletions. Although we do not routinely perform SDF testing, 15 patients had previous SDF values (12, >20%; 8, >36%). Female basal characteristics and testicular evaluation were under normal values. The TESA procedure took about 15-20 min, and the time of laboratorial search around 30-60 min. Cases using testicular sperm showed significant higher rates of fertilization (64% vs 73%-p=0.005), blastocyst development (47% vs 62%-p=0.010), implantation (6% vs 27%-p=0.000), clinical pregnancy (10% vs 39%-p=0.001), live birth delivery (5% vs 28%-p=0.005) and newborn (5% vs 32%-p=0.000) than ejaculated sperm. No significant differences were observed regarding the rates of embryo cleavage (95% vs 94.8%) and high quality embryos (89.4% vs 94%), in the mean number of transferred embryos ( $1.8\pm0.4$  vs  $1.9\pm0.4$ ), or in the abortion rate (2 cases-50% vs 7 cases-25.9%). Cases using testicular sperm had 22 frozen-thawed embryo transfer cycles, enabling per initiated cycle a cumulative pregnancy rate of 45%, live birth delivery rate of 31.3% and newborn rate of 37.5% (32 newborn).

**Limitations, reasons for caution:** Although presenting the higher number of cycles using TESA in the treatment of RIF, this number needs to be increased for drawing more definitive conclusions, as these women present a diversity of conditions, rendering subgrouping difficult. In the future, it would also be important to evaluate SDF in all cases.

Wider implications of the findings: In conclusion, the present results gave further evidence for the superiority of using testicular sperm instead of ejaculated sperm in cases with recurrent implantation failure. Data also evidences the security of using testicular sperm aspiration, as there were no pregnancy or delivery complications, or congenital anomalies among the 32 newborn.

Trial registration number: Not Applicable