of double-strand breaks (DSB) in sperm. Moreover, a recent study showed that DSB are not reduced during the sperm selection of an ICSI cycle.

The Fertile®ChiP-ZyMōt is a new method for sperm selection based on microfluidic properties that showed to reduce the presence of DSB in the sperm sample. In this sense, the specific reduction of DSB using Fertile®ChiP-ZyMōt could improve clinical outcomes after ICSI treatments.

Study design, size, duration: This retrospective study included 78 ICSI cycles from January 2018 to March 2019. Three groups were classified attending on the origin of the oocytes and the sperm selection method: Control group = oocytes from patients and density gradients for sperm selection (n=16); Group 1 = oocytes from patients and Fertile®ChiP-ZyMōt for sperm selection (n=22); and Group 2 = oocytes from donors and Fertile®ChiP-ZyMōt for sperm selection (n=11). All male patients presented high values of DSB.

Participants/materials, setting, methods: Patients included in the study presented high values of DSB analyzed though the Neutral CometFertility assay (CIMAB, Spain). Sperm selection was performed using conventional Density Gradients (Sperm Grad, Vitrolife, Sweden) (Control group) or the Fertile®ChiP-ZyMōt (DxNow, USA) (Groups 1 and 2). ICSI cycles were performed using oocytes from patients or donors and clinical outcomes were studied. Results were compared between groups, being the statistical significance α = 0,05.

Main results and the role of chance: Women's age was significantly lower in Group 2 (26.7 ± 4.28) compared to the Control group (35.67 ± 3.43) and Group 1 (36.17 ± 3.84), $p<0.01$.

Fecundation rates were slightly higher, even not significantly, in Group 1 (0.53 ± 0.27) and Group 2 (0.63 ± 0.21) compared to the Control group (0.51 ± 0.29), $p=0.80$. Biochemical pregnancy was significantly higher in Group 1 (12/22 (54.5%)) and Group 2 (7/11 (63.6%)), compared to the Control group (3/16 (18.8%), $p=0.03$. Clinical pregnancy was significantly higher in Group 1 (10/22 (45.5%)) and Group 2 (7/11 (63.6%)), compared to the Control group (2/16 (12.5%), $p=0.01$. Miscarriage rates were significantly higher in the Control group (2/2 (100%)) than in Group 1 (2/10 (20%)) and Group 2 (0/7 (0%)), $p=0.02$.

Even Group 2 showed the best results, there were no significant differences compared to Group 1 for biochemical and clinical pregnancies and miscarriage rates ($p=0.618$; $p=0.325$ and $p=0.418$, respectively).

Compared to density gradients, the use of the Fertile®ChiP-ZyMōt in ICSI cycles improved biochemical pregnancy rates x1,65 using oocytes from patients ($p=0,033$) and x2,32 using oocytes from donors ($p=0,054$). Fertile®ChiP-ZyMōt also improved clinical pregnancy rates x1,71 using oocytes from patients and x2,68 oocytes from donors ($p=0,036$).

Limitations, reasons for caution: Despite biochemical and clinical pregnancies presented significant better results using the Fertile®ChiP-ZyMōt, the increase in the fecundation rate was not significant. More studies analysing a larger number of ICSI cycles are needed to confirm these findings.

Wider implications of the findings: The use of the Fertile®ChiP-ZyMōt in ICSI cycles to treat high values of DSB in sperm increase biochemical and clinical pregnancy rates. These increases are even more important when oocytes are from a donor.

Trial registration number: Does not apply.

P-092 Varicocelectomy corrects sperm capacitation functions and enhances sperm genomic integrity

M. Haddad[1], P. Xie[1], A. Parrella[1], Z. Rosenwaks[1], J. Kashanian[2], G. Palermo[1]

[1]Weill Cornell Medicine, The Ronald O. Perelman and Claudia Cohen Center for Reproductive Medicine, New York, U.S.A. ;
[2]Weill Cornell Medicine, Department of Urology, New York, U.S.A.

Study question: To determine whether varicocelectomy improves spermatogenesis by enhancing semen parameters, sperm capacitation, sperm genomic integrity, and overall embryo developmental competence of the male gamete.

Summary answer: Correction of grade 2 or higher varicocele enhanced male gamete production, ameliorated sperm chromatin fragmentation (SCF), and amplified male gamete capacitation.

What is known already: Varicocele is known to induce oxidative damage to the male reproductive system, affecting semen parameters, sperm chromatin integrity, and function. Varicocelectomy has been proposed to enhance typical parameters measured in semen analysis, such as concentration and motility, and ameliorate SCF. Because the predictability of overall gamete competence through semen analysis has been debatable, new bioassays have been proposed. By surveying localization patterns of ganglioside M_1, a key regulator of capacitation and acrosomal reaction, we have been able to quantify subtle sperm function and predict probability of generating a pregnancy (PGP).

Study design, size, duration: In the past 12 months, fresh ejaculates were obtained from 6 consenting men who were initially diagnosed with varicocele of grade 2 or higher and then treated by varicocelectomy. Ejaculates were obtained again at least 3 months post-surgery to allow a full cycle of spermatogenesis. Semen parameters, SCF, CaP-Score™, and PGP were determined in a blind fashion and compared among pre- and post-operative specimens.

Participants/materials, setting, methods: Semen analysis was performed on pre-/post-operative ejaculates. Varicocele was evaluated by physical exam in standing position. Capacitation was measured by CaP-Score™ (Androvia LifeSciences) with normal thresholds of >27.6%. A corresponding PGP was previously established by analyzing pregnancy outcomes from fertile and infertile men who completed 3 IUI cycles with a normal threshold of >32.7%. Total capacitated spermatozoa were quantified by volume x concentration x CaP-ScoreÔ. SCF was assessed using TUNEL with normal threshold of <15%.

Main results and the role of chance: Men (n=6) with grade 2 varicocele or higher aiming to procreate underwent microsurgical varicocelectomy without any post-operative complication. Semen parameters such as volume and normal morphology that were assessed before surgery did not improve. For all men, sperm concentration was initially 35.0 ± 28.0 x10^6/ml and became 57.3 ± 29.5 x10^6/ml ($P < 0.05$). Sperm capacitation function, total capacitated spermatozoa, and PGP at baseline were 25.4 ± 3.4%, 18.4 ± 13.3 x10^6, and 29.3 ± 5.1%, respectively. After 3 months of post-operative recovery, sperm capacitation, number of total capacitated spermatozoa, and PGP significantly increased to 32.0 ± 4.1%, 33.2 ± 16.0 x10^6, and 41.0 ± 7.2% ($P < 0.05$), respectively. Genomic integrity as measured by SCF was originally above threshold at 17.9 ± 6.6% and significantly decreased to an average of 11.0 ± 4.8% ($P < 0.01$) after varicocele correction.

Limitations, reasons for caution: These findings support a beneficial effect of varicocele correction. However, the improvement of sperm concentration together with functional assay, as well as the amelioration of genomic integrity, needs to be confirmed by testing the embryonic developmental competence of the male gamete.

Wider implications of the findings: This analysis confirms the beneficial effect of varicocelectomy on at least one semen parameter. The utilization of a functional assay and the determination of genomic integrity by SCF provide information on an individual's ability to spontaneously reproduce or can help guide one toward the preferential method of assisted reproduction.

Trial registration number: not applicable

P-093 Andropenia precedes AML diagnosis and is associated with fatty marrow

K. Shlush[1], N. Zioni[2], N. Kaushansky[3], G. Oron[4], L. Shlush[3]

[1]fertility clinic Rabin Medical center, Obstetric and Gynecology, Herzliy, Israel ;
[2]Wiezmann institute of science, Immunology, Rehovot, Israel ;
[3]Weizmann institute of science, Immunology, Rehovot, Israel ; [4]Rabin medical center, Obgyn, Petah Tikva, Israel

Study question: What are the effects of andropenia on leukemia and bone marrow?

Summary answer: Many years before AML diagnosis testosterone levels are decreasing. Low testosterone levels after castration cause fatty bone marrow in mice.

What is known already: As human age they accumulate somatic mutations. These early mutations preleukemic mutations (pLMs) accumulate and eventually lead to different myeloid malignancies. Specific pLMs are more common among elderly males. Furthermore myeloid malignancies are more common among males. While large proportion of the population carry pLMs only a small proportion will develop myeloid malignancies. Understanding the mechanisms contributing to the progression to leukemia is of great importance. One factor possibly contributing to leukemia evolution might be the accumulation of fat in the bone marrow (BM) with age. A correlation was found between increased BM fat and low testosterone levels.