The PICO/PECO search strategy was used.

Data extraction

The main outcome considered was the retrieval rate of viable sperm. Secondary outcomes, such as cryopreservation possibility, fertilization, and pregnancy rates were also considered

RESULTS: Literature Search

Using the inclusion/exclusion criteria previously established we had 70 studies to analyze. We used the Rayyan platform to perform the study selection, by two independent authors. At the end of this process, 11 articles were included in the systematic review.

Sperm Retrieval

Regarding the main focus of our study, 8 out of the 11 articles considered that PESA should be the first choice as a treatment. These articles advise that if the PESA approach fails, the next approach should be direct to the testes. However, when we analyze purely numerical data, in general, MESA retrieval rates are superior when compared to PESA. This can be seen on table 1.

Secondary Outcomes

Cryopreservation was the secondary outcome that most comparisons could be made, and again MESA proved to have higher rates of successful cryopreservation.

PESA's advantages, such as procedure cost, post-operative recovery, availability, and no need for hospitalization were considered in many studies.

CONCLUSIONS: The conclusion of our study points to MESA as being the best approach, considering men with obstructive azoospermia, due to its higher sperm retrieval rate and the possibility of cryopreservation.

IMPACT STATEMENT: This study has great importance because it shows the lack of articles published regarding this matter. The few published articles have a great degree of heterogeneity, so few comparisons can be made. This study is important, as it evidences that more research needs to be carried out to support and optimize treatment choices, providing the best care to our patients.

Table 1.

Author	Sperm retrieval (PESA/MESA)
Dohle	18/29 (62%); 4/4 (100%)
Tsirigotis	36/47 (76,6%); 6/6 (100%) + 2/11 (after PESA failed (18,2%)
Phillipson	6/6 (100%); 21/22 (95,4%)
Lin	66/109 (61%); 37/40 (93%) after PESA failed
Rosenlund	3/8 (37,5%) ; 3/5(60%); TESA
Patrizio	46/46 (100%); NR
Glina	65/79 (82%); NR
Tsirigotis	59/69 (85,5%); NR
Levine	6/7 (85,7%); 1/1 (100%) after PESA failed
Schroeder	NR; 88/93 (94,6%)
Borges	27/40 (67,5%); NR; TESA

NR = not realized
TESA = testicular sperm aspiration

SUPPORT: This study was financed by Fundação de Amparo à Pesquisa do Estado de São Paulo (FAPESP), process number 2020:13499-7.

P-442 6:45 AM Wednesday, October 26, 2022

STRENGTHENING THE NATURAL ANTI-OXIDANT LEVELS DURING SPERMATOGENESIS. Rachel Makloski, RN, Cristi Thompson, BS, William B. Schoolcraft, MD, Mandy Katz-Jaffe, PhD Colorado Center for Reproductive Medicine, Lone Tree, CO.

OBJECTIVE: Cellular oxidative stress is a known cause of DNA fragmentation and is brought about by natural processes of aging, lifestyle choices, and the environment (including pollutants, diet, tobacco and alcohol use). High levels of sperm DNA fragmentation have been associated with adverse reproductive outcomes. The aim of this study was to identify a highly active antioxidant species to support natural antioxidant levels in the testes prior to infertility treatment as a means to alleviate the build-up of oxidative stress and reduce the possibility of sperm DNA fragmentation.

MATERIALS AND METHODS: Male patients ($n = 50$; mean age = 38.6 ±5.2 years) with documented elevated sperm DNA fragmentation levels were recruited with IRB approval and patient consent. Semen analysis and sperm DNA fragmentation assessment (TUNEL; normal range <16%) were performed at baseline (infertility patient consult) and after 90 days of antioxidant treatment on the day of sperm collection for IVF (1800 mg/day freeze-dried acai pulp, total polyphenol content 6,618 mg GAE/100 g, oxygen radical absorbance capacity 208, 628 μmol TE/100 g). Statistical analysis of paired sperm data included two tailed Student's t-test and Wilcoxon signed rank test to compare proportions of success, with significance at $P < 0.05$.

RESULTS: Baseline TUNEL was performed approximately 90 days prior to an IVF cycle with an observed mean of 26.9 ± 9.0% (all above normal range; 16 – 52%). On the day of IVF gamete collection, post 90 day antioxidant treatment, the mean sperm DNA fragmentation had significantly decreased to 9.8 ± 8.9% (range 0 – 35%; $P < 0.0001$). Sperm concentration and morphology were comparable before and after treatment. In contrast, sperm motility significantly improved with antioxidant intervention (49.1 ±18.8% vs baseline 39.2 ±15.3%; $P = 0.0014$). In total, 38 out of 50 (76%) men were successful in recording a normal result for sperm DNA fragmentation (TUNEL; normal range <16%) on the day of fertilization for IVF. The failure of post-treatment decreases in sperm DNA fragmentation were not influenced by age, days of abstinence, sperm concentration or motility, normal morphology, BMI or baseline TUNEL. To date, there have been 22 frozen embryo transfers with 14 healthy babies delivered and 3 ongoing clinical pregnancies, reflecting treatment efficacy.

CONCLUSIONS: This study highlights the opportunity for a non-invasive, highly active antioxidant intervention in alleviating the build-up of oxidative stress in the testes prior to infertility treatment. The majority of the males in this study, post treatment, displayed normal ranges for sperm DNA fragmentation at the time of gamete collection and fertilization for IVF. This success is even more significant as the female partners were predominantly of advanced maternal age and it is conjectured that the aging oocyte has a decreased capacity to correct sperm DNA damage.

IMPACT STATEMENT: Strengthening the natural anti-oxidant levels in the testes prior to fertility treatment offers the opportunity to counter-balance oxidative stress and reduce the probability of sperm DNA fragmentation in time for fertilization.

SUPPORT: None.

P-443 6:45 AM Wednesday, October 26, 2022

PROTOCOLS DESIGNED TO IMPROVE A MAN'S OVERALL HEALTH ARE LINKED TO INCREASED CAPACITATION ABILITY: A MULTICENTRIC, PROSPECTIVE, BLINDED ANALYSIS. Fady I. Sharara, M.D.,[1] Eric Seaman, M.D.,[2] Anna Lysenko-Brockman, MS,[1] Haneen Taha, MS,[1] Cristina Cardona, PhD,[3] Garry Charles Ostermeier, PH.D.,[3] Alexander J. Travis, VMD, PhD[3] [1]Virginia Center for Reproductive Medicine, Reston, VA; [2]New Jersey Urology, MILLBURN, NJ; [3]Androvia LifeSciences, Mountainside, NJ.

OBJECTIVE: Traditional semen analysis (SA) parameters are declining; hypotheses as to the cause focus on worsening men's health due to environmental exposures and/or lifestyle. SA evaluates ejaculate volume, sperm motility, concentration, and morphology, but doesn't assess sperm fertilizing ability, which causes half the cases of male infertility. It is therefore unknown whether reported declines in SA values have any impacts on actual male fertility. Prior to fertilizing, sperm must capacitate. Cap-Score™ measures the capacitation ability of a man's sperm and prospectively predicts his probability of generating a pregnancy (PGP). Here, we evaluate the effects of protocols designed to improve a man's overall health on his SA and capacitation ability.

MATERIALS AND METHODS: 55 men questioning their fertility were evaluated for Cap-Score and SA at two independent clinics. Recommendations were made to improve overall health: Clinic 1) quit use of tobacco, marijuana, or alcohol; avoid laptops on laps or Jacuzzis/saunas; lose weight if obese; increase Vitamin D intake (≥ 2k IU/day); and start supplements (Androferti; n=30; vitamins C, E, B12, Folate, Zinc, selenium, L-carnitine, & coenzyme Q10), or Conception XR (n=8; vitamins C, E, D, Folate, Zinc, selenium, & Lycopene)): Clinic 2) limit alcohol, tobacco, marijuana; exercise ~20min/d; increase sleep, avoid foods with pesticide residues; & start supplements N acetyl cysteine & Proxeed Plus (n=17; Vitamins C, B_{12}, Folic Acid, Zinc, Selenium, L-Carnitine, Acetyl-L-Carnitine, & coenzyme Q10). A second blinded analysis was done ~13 weeks later; paired t-tests were done to compare before and after lifestyle changes.

RESULTS: All supplements impacted measures similarly ($p>0.05$; ANOVA). An increase in Cap-Score from 23.5±0.9 to 27.6±1.0 ($p=0.001$; n=55), corresponding to a 25% increase in a man's PGP, was observed. Recommended lifestyle changes had no impact on semen volume ($p=0.479$; n=54), sperm concentration ($p=0.562$; n=54), or sperm motility ($p=0.112$; n=54). Strict normal morphology was available from Clinic 1 and improved (1.7±0.2 to 3.3±0.5; $p=0.001$; n=38). No relationship was detected between Cap-Score and strict normal morphology before ($p=0.566$) or after ($p=0.156$) lifestyle changes.

CONCLUSIONS: Similar lifestyle changes recommended by two independent clinics improved capacitation ability.

IMPACT STATEMENT: Promoting a man's overall health through lifestyle change and nutritional supplementation increased capacitation ability and PGP.

SUPPORT: Androvia LifeSciences performed the Cap-Score as part of patient standard of care. Physicians received no compensation from Androvia.

P-444 6:45 AM Wednesday, October 26, 2022

SPERM GENOMIC AND EXTRAGENOMIC CARGO IN RECURRENT MISCARRIAGE AND IMPLANTATION FAILURE. Vidhu Dhawan, MD,[1] Neena Malhotra, MD DNB FRCOG,[2] Neeta Singh, MD,[3] Vatsla Dadhwal, MD,[2] Rima Dada, MD, Ph.D[4] [1]Room no. 1010, Dept. of Anatomy, First Floor, Teaching Block, All India Institute of Medical Sciences, New Delhi, India; [2]All India Institute of Medical Sciences, Obstetrics & Gynaecology, New Delhi, India; [3]Professor, New Delhi, India; [4]All India Institute of Medical Sciences, Anatomy, New Delhi, India.

OBJECTIVE: The defects in the integrity of both nuclear and mitochondrial genome, oxidative stress, shortened telomeres and dysregulation in the expression of the genes critical for early embryonic development have been implicated as a cause of pregnancy loss. Assessing the expression of the genes critical for post fertilization events and reproductive outcomes may help us better understand the unknown molecular mechanism involved in the etiology of miscarriage and implantation failure. The objective of the present case control study was to analyze the contribution of sperm genomic and extragenomic cargo in pregnancy loss.

MATERIALS AND METHODS: The prospective case control study was conducted on the male partners of couples experiencing recurrent pregnancy loss (RPL) (n=132), recurrent implantation failure (n=79), and those with previous history of conception with congenital malformations (CMF) (n=25), fertile controls (n=102). Semen samples were obtained and analyzed by WHO 2010 criteria. The sperm gene expression was analyzed by $2^{-\Delta\Delta Ct}$ method for the relative quantification of *FOXG1, SOX3, STAT4, RPS6, RBM9, RPL10A, RPS17, RPL29, WNT5A, HSP90, TOMM7, EIF5A, OGG1 and PARP1*. after normalization with internal controls *GAPDH* and β-actin. The levels of seminal ROS (RLU/sec/million sperm), DNA damage (%) and relative sperm telomere length (STL) were assessed by chemiluminescence and sperm chromatin structure assay (SCSA) and qPCR respectively. The data was analyzed by statistical software Stata 14.0. Kruskal Wallis H test followed by Bonferroni correction were used to compare outcome and markers among four group.

RESULTS: The expression of *FOXG1, SOX3, RPS6, RBM9, RPS17, HSP90, TOMM7, EIF5A,* and *OGG1* showed significant difference between RPL patients and controls ($p<0.001$***), while *SOX3, RBM9, WNT5A, HSP90, TOMM7* and *EIF5A* showed significant difference in RIF group ($p<0.001$***) and the expression of only *HSP90, TOMM7, EIF5A* varied significantly in CMF group ($p<0.001$**). The relative STL was significantly lower in all patient groups ($p=0.001$**), and ROS and DFI were significantly higher with respect to controls ($p=0.001$**, $p=0.0001$*** respectively). The STL correlated negatively with ROS and DFI.

CONCLUSIONS: The current study supports the hypothesis that there may be differential expression pattern of genes pertinent for early embryogenesis between healthy fertile males and male partners of couples with pregnancy loss.

IMPACT STATEMENT: To the best of our knowledge the present study is one of the first studies to analyse the contribution of sperm molecular factors across three patient categories.

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E-CIGARETTE AEROSOL EXPOSURE DECREASES SPERM CONCENTRATION IN MICE. Daniel Pelzman, MD,[1] Patrick Walsh, BS,[2] Miguel Brieno-Enriquez, MD, PhD,[2] Kathleen Hwang, MD[1] [1]UPMC, Pittsburgh, PA; [2]University of Pittsburgh.

OBJECTIVE: E-cigarette usage, also known as vaping, has dramatically increased in popularity over the last decade, especially in young adults. The effects of e-cigarette usage on the male reproductive system has not yet been established. We sought to evaluate the effects of e-cigarette aerosol exposure on spermatogenesis in mice.

MATERIALS AND METHODS: We exposed mice to either commercially available, nicotine-containing e-cigarette fluid (exposure) or aerosolized glycerin (control). Sixteen mice were placed in a 5-week protocol (8 control, 8 exposed), and sixteen mice were placed in a 10-week protocol. Durations were derived from normal time of spermatogenesis in mice (35 days). Exposure was performed using a commercially available, whole-body aerosolization unit (La Jolla Alcohol Research, Inc). Glycerin was chosen as the control due to its safety. After exposure was completed, the mice were sacrificed and testes/epididymides were removed. Epididymal fluid sperm concentration was measured for each mouse using a hemocytometer.

RESULTS: There was no attrition during the experiment and all mice were included in the final analysis. In the 5-week cohort, exposed mice had a lower sperm concentration than control mice, although this result was not statistically significant ($4.7\pm2.6 \times 10^6$ vs $7.4\pm4.1 \times 10^6$, $p=0.1$). Interestingly, in the 10-week exposure group, sperm counts in both cohorts were higher, and there was no difference between groups ($11.3\pm4.3 \times 10^6$ vs $10.0\pm4.3 \times 10^6$). Exposed animals demonstrated high levels of DNA fragmentation via COMET assay.

CONCLUSIONS: Five-week exposure to e-cigarette vapor reduced sperm concentrations in mice. A 10-week exposure did not appear to impact concentration. It is unclear why longer-term exposure was associated with higher sperm concentrations but may be related to compensatory mechanisms during spermatogenesis. Further research will be needed to understand other effects of e-cigarette usage on the male reproductive tract.

IMPACT STATEMENT: E-cigarettes may transiently decrease sperm concentration in mice, indicating a potentially harmful effect on spermatogenesis.

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THE EFFECTS OF COLLECTION LUBRICANT REVISITED: NEWER FORMULATIONS APPEAR TO HAVE LESS EFFECT ON POST-COLLECTION SEMEN QUALITY. Lindsay L. Penrose, PhD, Bayley Richardson, B.S., Alisa White, B.S., Samuel D. Prien, PH.D. Texas Tech University Health Sciences Center, Lubbock, TX.

OBJECTIVE: It is common for patients seeking infertility treatments to use lubricant provided by the clinic to aid in sperm collection. Although lubricant effects on sperm motility have been studied, there is no universal consensus on a "safe" lubricant. Previous research has documented that lubricant contamination at semen collection could alter the sperm analysis of men seeking infertility evaluation, and it may adversely affect fertility treatment. The objective of the current study was to compare "newer" lubricants to those currently in use, including what has been described as an "organic, plant-based lubricant."

MATERIALS AND METHODS: Semen samples were obtained from 12 individuals undergoing routine sperm analysis. Samples were obtained by masturbation at the clinic. The samples had to have a minimum of $30x10^6$ motile cells to be included in the study. Samples underwent a routine semen prep for IUI but were diluted to a final volume of 9 mL to cross all treatments. A 24-well cell culture plate was prepared with an estimated 0, 10, 50, and 100 μL of four types of lubricants: Henry Schien Lubricating Gel (standard – A), Pre-Seed™ Fertility-Friendly Lubricant (fertility – B), Überlube (silicon – C), or Fav Lubricant (water – D). The final treatment was the control utilizing semen cultured alone without a contaminant (control – E) After the plate was prepared, 0.5mL of the semen sample was added to each well. Then the culture plate was incubated at room temperature in the dark. At times 0, 1, 3, 12, and 24 hours, the plate was agitated, and a 4 μm sample of each well was analyzed using a Hamilton Thorne IVOS sperm analyzer.

RESULTS: As expected, there were differences in semen parameters based upon lubricant type, lubricate concentration, and time ($P < 0.05$). Focusing on motility as the primary outcome, a standard lubricating gel (A), caused the largest decrease in semen quality at all concentrations ($P < 0.001$). The "fertility-friendly" gel decreased motility compared to the control at moderate and high levels as early as 1 hr after exposure. Only the highest levels of contamination of the water-based lubricant had decreased motility over the 24 hrs compared to the control ($P < 0.02$), and the silicon lubricant (D) performed equally well to the control over the entire 24 hrs regardless of concentration ($P = 0.643$).