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OBJECTIVE: Testosterone (T) is a steroid hormone responsible for the development and maintenance of male secondary sex characteristics. T exerts this physiologic function throughout by binding to the androgen receptor (AR). It is unclear how AR function varies as a function of serum T. We hypothesized that there is a saturation value for the AR above which excess serum T does not lead to increased binding or downstream signaling. This study evaluated whether varied serum T levels were associated with AR signaling in the penile tissue of men with erectile dysfunction (ED).

MATERIALS AND METHODS: Men with ED undergoing inflatable penile prosthesis (IPP) surgery were enrolled in the study. Corpus cavernosum biopsy was obtained during surgery. Serum testosterone level was also obtained the day of surgery. Penile tissue was processed and used for western blotting with downstream markers of AR function including AR, heme oxygenase (HO), inducible nitric oxide synthase (iNOS), and phosphodiesterase type IV (PDE-5).

RESULTS: The mean age of participants was 61 (IQR 8.5) years. The mean serum T level was 300.2 (IQR 231.3). The results of the western blot showed that HO and PDE-5 signaling was decreased in men with serum T less than 200 ng/dL compared to those with serum T above 200, while AR and iNOS expression was decreased in men with serum T less than 300 ng/dL compared to those with serum T above 300. These findings provide a possible explanation for why PDE5 inhibitors are most effective in men with serum testosterone levels greater than 200 ng/dL, as our western blot results indicate that PDE-5 signaling is diminished in men with lower serum testosterone levels. This suggests that maintaining eugonadal levels of serum androgens is essential for optimal functioning of PDE-5 inhibitors.

CONCLUSIONS: Within a wide range of serum T values, AR signaling was similar in penile tissue above 200-300 ng/dL. Our findings suggest that there is a limit to the effect of serum testosterone levels on AR signaling, as the downstream activity appears to plateau beyond a certain point of receptor activation.

IMPACT STATEMENT: Based on our analysis, we have observed that there is a saturation point for various AR signaling molecules. This saturation point represents a threshold level of downstream activity induced by the receptor, beyond which changes in serum testosterone level do not seem to have a significant impact on the downstream activity.

SUPPORT: This work was supported by: NIH Grant R01 DK130991 to Ranjith Ramasamy.

P-354 2:25 PM Tuesday, October 17, 2023

THE EFFECT OF SURGICALLY-DERIVED SPERM ON EMBRYO COMPACTION PATTERNS.

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OBJECTIVE: The objective of this study was to compare the embryo compaction patterns amongst embryos created with ejaculated or surgically-derived sperm from severe male factor infertility patients.

MATERIALS AND METHODS: This study was a retrospective review of prospectively collected data from a single academic center. Couples included were those with sperm counts less than two million per ejaculate, who created embryos January 2016 to December 2019 via intracytoplasmic injection of ejaculated sperm or surgically extracted from the testes or epididymis. Embryos were cultured in the Embryoscope. Embryo compaction patterns were prospectively observed by viewing time-lapse imaging videos by a researcher blinded to method of sperm retrieval. The association between compaction patterns, morphokinetic parameters, blastocyst formation, embryo disposition, and pregnancy outcomes were analyzed.

RESULTS: 1,057 embryos from 112 male infertility couples were studied. 61 males (54.4%) used ejaculated sperm to create 589 embryos (55.7%), 23 males (20.5%) had percutaneous epididymal sperm aspiration (PESA) to create 239 embryos (22.6%), and 28 males (25%) had testicular sperm extraction (TESE) to create 229 embryos (21.7%). The TESE group had significantly fewer embryos that initiated compaction ($p<0.001$) and blastulation ($p=0.017$) compared to the ejaculation and PESA groups. Embryos in the PESA group had a significantly lower cell count compared to the ejaculated group ($p=0.035$) at the start of compaction. There was no difference amongst embryos created from ejaculated, PESA, and TESE sperm regarding the uniformity of cell size. During compaction, there was no difference between the groups regarding exclusion or extrusion of cells from the compacted cell mass and the rates of synchronous or asynchronous (lobular) compaction. Percentage of full vs. partial compaction patterns was equivalent between the groups. There was no difference between the groups regarding the compacted embryo shape (spherical or irregular) and the presence of multiple fragments in the perivitelline space. Origin of sperm did not impact live birth rates for single embryo transfers.

CONCLUSIONS: Embryos fertilized with TESE-derived sperm are less likely to initiate compaction and blastulation. Embryos fertilized with PESA-derived sperm are more likely to have a low cell count at start of compaction compared to ejaculated sperm. Method of sperm retrieval does not impact embryo compaction patterns amongst severe male factor patients.

IMPACT STATEMENT: Amongst severe male factor patients, method of sperm retrieval was not predictive of embryo compaction patterns or live birth rates.

SUPPORT: N/A

REFERENCES: N/A

POSTER ABSTRACT SESSION: REPRODUCTIVE UROLOGY (2 OF 2)

P-355 1:30 PM Tuesday, October 17, 2023

EFFICACY OF DAILY EJACULATION IN MEN WITH RAISED SPERM DNA FRAGMENTATION.

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OBJECTIVE: Efficacy of Daily Ejaculation, as an active intervention to reduce raised Sperm DNA Fragmentation (SDF) and optimize reproductive outcomes in Infertile Men?

MATERIALS AND METHODS: Prospective Observational study conducted at a tertiary private teaching IVF clinic.

Men with raised SDF >25% undergoing IVF at our centre (n=40) between jan-june 2022 were recruited in the study.

Male partners aged 25-45 yrs with SDF >= 25% and had history of one previous failed IVF were included in the study. Male partners aged > 45yrs, Female >37yrs, men with BMI > 30 kg/m2 and history of chronic smoking or alcohol or were known cases of varicocele were excluded from this study.

Couples who underwent the first IVF cycle at our center and had failed to conceive and had come back for second cycle again were considered. If the SDF was >25% they were recruited for the study. Hence, their failed first IVF cycle was considered to be the index cycle.

In the study group, male partners had ejaculated daily for one week prior to oocyte retrieval procedure(OPU) and on the day of OPU, fresh sample was produced with less than 24hours abstinence. Semen sample was divided into two equal aliquots. One aliquot was processed through density gradient and used for ICSI. Another Aliquot was sent for SDF assessment. SDF assessment was done using Sperm Chromatin Structural Assay (SCSA)(flow cytometric based method). SDF of the semen sample after 7 days of daily ejaculation was assessed and compared with the initial SDF value before daily ejaculation.

One the day of OPU after ICSI, embryos were subjected to Extended Blastocyst Culture and a freeze all policy was adopted followed by frozen Embryo Transfer in the subsequent cycle with 1-2 good grade blastocysts. The primary outcome was magnitude of reduction in SDF post Daily Ejaculation. The secondary Outcomes Were Fertilization rate (FR), Blastocyst Formation Rate (BFR), Clinical Pregnancy rate (CPR), Implantation rate (IR), Miscarriage Rates (MR), Live birth rate (LBR).

RESULTS: Mean of SDF on the sample before daily ejaculation was 39.37 (SDF values ranged from 26-66) and post Daily ejaculation the value of SDF came down to 19.66 (SDF values ranged from 1-30).

SDF pot Daily Ejaculation for one week reduced by half.

Following were the embryonic and reproductive outcomes:

FR – 94.5%

BFR – 48%

CPR – 63%

IR- 56%

MR- 8%

LBR – 55%

Daily ejaculation seems to be an efficient way to reduce SDF and also optimize reproductive outcomes.

CONCLUSIONS: Daily Ejaculation seems to be an efficient active intervention to reduce raised SDF and also optimize reproductive outcomes in infertile men. Daily Ejaculation seems to be a patient friendly intervention which is economical and avoids the need for invasive interventions like testicular sperm aspiration for raised SDF.

IMPACT STATEMENT: Daily Ejaculation is an easier and economical option which can help optimize outcomes without the need of invasive methods like testicular sperm aspiration.

SUPPORT: No Conflicts of Interest to Disclose

There was no funding received for this study.

REFERENCES: NA

P-356 1:35 PM Tuesday, October 17, 2023

ASSESSING THE PROBABILITY OF SUCCESSFUL SPERM RETRIEVAL WITH MICROSCOPIC TESTICULAR SPERM EXTRACTION (M-TESE) BASED ON JOHNSEN SCORE AND THE INCIDENCE OF HYPOGONADISM POST MICRO-TESE.

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OBJECTIVE: To assess the probability of successful sperm retrieval with m-TESE based on Johnsen score and incidence of hypogonadism post m-TESE.

MATERIALS AND METHODS: Retrospective study comprising 100 patients with NOA undergoing micro-TESE at a single Tertiary level fertility clinic from January 2019 to March 2022.

Inclusion criteria: All men aged 21-55 years with NOA, Men who did not have sperm retrieval at TESA.

Exclusion criteria: Men with Obstructive Azoospermia, Cryptozoospermia

Trial TESA done as per clinic SOP and tissue sent for histopathological examination. Report interpreted as per Johnsen score on a scale(1-10).Men who were negative for TESA were taken for micro-TESE after 3 months. micro-TESE done as per clinic SOP. Upon successful sperm retrieval Intracytoplasmic sperm injection (ICSI) done. Extended blastocyst culture, freeze all policy adopted and two blastocysts transferred in a frozen embryo transfer cycle.

RESULTS: Primary outcomes : Surgical Sperm Retrieval Rate (SRR), Fertilization Rate and Blastocyst Rate, incidence of hypogonadism post procedure (3 months post micro-TESE serum testosterone analysis at 8AM) Secondary outcomes: Implantation Rate, Miscarriage Rate and Live Birth Rate.

Successful Surgical sperm retrieval seen in 51% of the study population.

SRR based on Johnsen score analyzed:

Hypo spermatogenesis men with Johnsen score of more than or equal to 9 had SRR of 70% Maturation arrest with Johnsen score of 7/8 had SRR of 31%

Sertoli cell only syndrome with Johnsen score of 5/6 had SRR of 20% .

Those with Johnsen score less than 5 had no sperm retrieval.

Reproductive outcomes: Of 51 men with positive micro-TESE

Good quality blastocyst rate 49%.

Implantation Rate:41%

LBR:31%

Mean Serum Testosterone before micro-TESE was 3.68 ng/ml and 3 months post procedure mean Serum Testosterone was 3.50 ng/ml (p-0.2) confirming no evidence of hypogonadism.

CONCLUSIONS: Johnsen score seems to help in prediction of sperm retrieval in men undergoing micro-TESE. Micro-TESE seems to be a useful and safe intervention for NOA men to father their own genetic child without the need for third party reproduction.

IMPACT STATEMENT: m-TESE SSR from this study is in accordance with published literature. Johnsen score greater than 6 seem to offer positive retrieval. Considering that Johnson score is helping in prediction of surgical sperm retrieval, this score can be used as a tool to counsel couples undergoing micro-TESE and ART.

SUPPORT: None

REFERENCES: None

P-357 1:40 PM Tuesday, October 17, 2023

SEASONAL VARIATION IN SERUM TESTOSTERONE LEVELS: EVIDENCE FROM TWO LARGE INSTITUTIONAL DATABASES.

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OBJECTIVE: Seasonal variations in testosterone levels have been reported in some studies, but the results are inconsistent. In this study, we aimed to determine if clinically relevant seasonal variability in testosterone levels exists using a large cohort of men from two different institutions, one located in an area with seasons (Pittsburgh, Pennsylvania) and one without seasons (Miami, Florida).

MATERIALS AND METHODS: Using two institutional databases, testosterone levels were obtained for men ages 18-99 from 2010-2021 who had at least 2 morning testosterone levels drawn within a 2-year period. All samples were analyzed with liquid chromatography with tandem mass spectrometry (LC-MS/MS). To avoid potential confounding by testosterone altering medications patients who were currently or previously on exogenous testosterone, endogenous testosterone stimulating medications, testosterone suppressing medications, and aromatase inhibitors were excluded from the study.

RESULTS: There were 9495 and 16171 total testosterone levels measured from Miami and Pittsburgh respectively, with all men having 2 or more levels. There was no statistically significant variation in T levels for the overall cohort in Pittsburgh or Miami, respectively (Table 1). Additionally, when stratified by age group, no individual groups were found to have significant seasonal variability.

Table 1: Changes in Testosterone Levels by Season for the Entire Cohort

	Pittsburgh		Miami	
	ΔT (ng/dL)	*p*	*ΔT (ng/dL)*	*p*
Winter	Ref	–	Ref	–
Spring	1.63	0.78	-4.28	0.47
Summer	-2.65	0.63	0.95	0.87
Fall	5.63	0.34	1.71	0.78

CONCLUSIONS: Our findings suggest that although there is differing total testosterone levels between men who reside in two different climates, there is no significant variability in testosterone levels between seasons.

IMPACT STATEMENT: Testosterone levels can be checked and interpreted without the need to account for the season during which they were drawn.

SUPPORT: none