Results were compared with 82 embryos (13 IVF-PGD cycles) from a control group of patients (egg donation cycles, normal karyotypes no male factor associated) analyzed also by aCGH.

Main results and the role of chance: The group of patients with a polymorphisms in the karyotype have a maternal age mean of 30.27 y.o, and the control group of 30.07 y.o ($p = 0.9048$), allowing further comparisons.

In the study group, the percentage of euploid, aneuploid and other abnormalities (complex abnormalities with >12 aneuploid events and polyploidy) was 27.16%, 49.38% and 23.45%, respectively. The corresponding values observed for the control group were 58.53%, 37.80% and 3.66%.

A statistically significant increase in the percentage of abnormal embryos was observed in the studied group compared with the control one (72.84% vs. 41.46%, $p < 0.0001$). In 3 out of 11 cycles (27%) no euploid embryos were found.

The study group involved embryos from couples with heteromorphisms in the karyotype, showing increased heterochromatin at the chromosome centromere, telomere or at the short arm. It's been suggested that heterochromatin variation in these regions may cause partial asynapsis, defects in centromere function and kinetochore assembly, difficulty in homologous chromosome pairing, and impact on cell division. All of the above events could affect cell division and gamete formation and might cause the increased aneuploidy observed. Embryo aneuploidy consequences as implantation failure, miscarriage could explain the high percentage of patients with these altered karyotypes referring reproductive failures.

Limitations, reasons for caution: As per the difficulty in recruiting patients with this type of karyotype undergoing IVF-PGD cycle the sample size of this study is limited. More studies should be added.

Wider implications of the findings: This study shows high increase of aneuploidy in embryos from carriers of heterochromatin variant. This finding could explain the high percentage of polymorphisms carriers in infertile population. More attention must be directed to infertile couples with a karyotype revealing those chromosomal variants, and an IVF-PGS cycle should be considered.

Trial registration number: not applicable.

O-185 Reevaluation of the Frequency and Characteristics of Aneuploidy of Surgically Retrieved Spermatozoa in Light of Enhanced Molecular Genetic Techniques

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Study question: We challenged the notion that sampling epididymal and testicular tissues yields spermatozoa with a higher incidence of aneuploidy than those retrieved in the ejaculate.

Summary answer: With the implementation of advanced molecular genetic techniques, we confirmed that surgically retrieved spermatozoa have at least comparable incidence of aneuploidy than those ejaculated.

What is known already: Previous studies, including our own, evidenced, on about 100 testicular spermatozoa in 8 to 13 men and by only 4 chromosome probes, that these spermatozoa have a remarkably higher (13%) occurrence of aneuploidy. This notion, however, did not translate into a higher incidence of miscarriages nor a lower rate of pregnancy. Moreover, ICSI offspring generated from surgically retrieved gametes did not suffer from increased aneuploidy than those generated from ejaculated specimen. In light of the availability of more accurate molecular genetic techniques, we have decided to challenge this dogma.

Study design, size, duration: From December 2014 to November 2016, FISH aneuploidy was carried out on the specimens 2 donor controls, on the ejaculates of 67 men, and on surgical specimens of 6 azoospermic men. To confirm our findings, DNA sequencing technology was carried out on the ejaculates and surgical samples of 20 men. A simultaneous assessment was performed on non-azoospermic men with high DNA fragmentation in their ejaculate. ICSI pregnancy outcome was also analyzed and compared.

Participants/materials, setting, methods: Consenting men treated for infertility provided their specimens. FISH was performed on at least 1000 spermatozoa with a threshold of >1.6% with 2-3% FISH error. DNA was extracted and amplified from a comparable number of spermatozoa by PCR-based random hexamer amplification (average DNA concentration 610 ± 102 ng/ul and quality of 1.7 ± 0.1 nm). By Next Generation Sequencing (NGS), duplications and deletions by Copy Number Variants (CNVs) were then calculated for all chromosomes by CASAVA and VarScan2 software programs.

Main results and the role of chance: A total of 67 couples were included in our study (maternal age 99.9 ± 9yrs and paternal age 39.4 ± 3yrs). Sperm concentration of 9 ± 0.2x10^6/ml, 25 ± 21% motility, and 1.6 ± 2% normal morphology. Aneuploidy by FISH yielded 0.9% for the donor control but rose in the study group to 3.6% in the ejaculated, 1.2% for the epididymal, and 1.1% for testicular spermatozoa. There were no differences in autosomal or gonosomal disomies, nor nullisomies. In this group, the ejaculated spermatozoa yielded 22% clinical pregnancy rate and 50% with the surgically retrieved specimen.

NGS yielded 1.2% for the control while in the study was 11.1% for the ejaculated specimen and decreased to 1.8% in the epididymal and 1.5% for the testicular ($P < 0.0001$). The pregnancy rate for the ejaculated specimen was 47.2% and 50% for the surgically retrieved.

Simultaneous aneuploidy assessment on the ejaculated and testicular samples in the same individual evidenced a sperm chromatin fragmentation (SCF) of 20% in the ejaculate while on the testicular spermatozoa was only 8%. The pregnancy rate was 0% with ejaculated while 100% with the testicular spermatozoa. Aneuploidy assessment by FISH evidenced 2.8% in the ejaculated and 1.2% in testicular biopsy while with NGS became 8.4% and 1.3% in testicular biopsy ($P = 0.02$), respectively.

Limitations, reasons for caution: This is still a limited number of observations carried out on men screened for infertility. If confirmed, this study may suggest that testicular sampling may be beneficial even in non-azoospermic men where retrieving spermatozoa with lower SCF may also control for sperm aneuploidy.

Wider implications of the findings: This study challenges the dogma that testicular spermatozoa conceal a higher proportion of aneuploidy. This implies that testicular gametes do not contribute to chromosomally related pregnancy losses. Moreover, this may explain why offspring from testicular biopsy do not evidence higher autosomal or gonosomal aneuploidy than those resulting from ejaculated spermatozoa.

Trial registration number: Not applicable

SELECTED ORAL COMMUNICATIONS
SESSION 51: TRAVELS THROUGH IMPLANTATION

Tuesday 4 July 2017 Room C 15:15–16:30

O-186 Sperm transcript dysregulation: role in recurrent pregnancy loss

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Study question: Do sperm transcripts have any relevance in recurrent pregnancy loss?

Summary answer: Paternal transcripts delivered to the oocyte at fertilization are responsible for regulating the critical processes involved in early embryonic development

What is known already: Substantial literature has previously been cited regarding the molecular and cellular events underlying fertilization and early embryonic development. Apart from the previous studies on extensive embryo-maternal interface, the role of paternal factors in embryonic development is being brought to surface. Sperm with disrupted DNA integrity do fertilize an oocyte but on account of being transcriptionally inert and limited repair mechanisms the damage exists post fertilization. It not only affects the outcome of pregnancy but also exert profound impact on the health of the future progeny.