

Wider implications of the findings: Laparoscopic uterine artery blockage effectively reduced the uterine perfusion in few hours. The procedure would make uterine surgery less bleeding from uterus itself.

Study funding/competing interest(s): no

Trial registration number: no

O-262 Specific alleles of the PRDM9 gene are a risk factor for the production of chromosomally abnormal embryos in humans

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Study question: Are PRDM9 gene polymorphisms a risk factor for the production of chromosomally abnormal embryos in infertile patients?

Summary answer: Certain genetic variants in PRDM9 influence the production of aneuploid embryos in infertile patients. Couples presenting at least one rare non-A allele (N) showed a higher proportion of embryos with chromosome abnormalities compared to those couples with the common AA genotype.

What is known already: Defective recombination is a major cause of chromosomal malsegregation during meiosis. The aneuploidies produced are one of the principal reasons for embryo implantation failure and pregnancy loss. Several studies have suggested that PRDM9 has a key function in recombination control and that certain PRDM9 alleles have reduced activity, decreasing recombination frequency. In theory, such alleles could increase the risk of non-disjunction and aneuploidy with significant repercussions for fertility and the outcome of assisted reproductive treatments.

Study design, size, duration: PRDM9 exon 11, containing the entire zinc finger (ZnF) domain, was sequenced in 70 infertile patients (43 females, 27 males) with a history of recurrent miscarriage and repetitive implantation failure. Results from the chromosomal screening of 423 preimplantation embryos produced by these patients were also available for analysis.

Participants/materials, setting, methods: Patients' DNA was extracted from blood and the polymorphic exon 11 of the PRDM9 gene was amplified. Sequences were aligned with respect to known PRDM9 ZnF types previously identified, and classified as A allele (normal) or non-A allele (reduced functionality). Chromosome screening of preimplantation embryos involved fluorescence *in situ* hybridisation.

Main results and the role of chance: Results showed significant differences in the incidence of aneuploid embryos related to PRDM9 genotype. Female patients with at least one non-A allele (i.e. AN or NN genotype), undergoing assisted reproductive treatment, produced more aneuploid embryos compared to those homozygous for the normal PRDM9 allele (AA) ($p = 0.025$). No such differences were found in males. When the genotypes of both members of a couple were studied in combination, those presenting at least one rare N allele showed rates of chromosomally abnormal embryos significantly higher than couples where both individuals presented the common AA genotype ($p = 0.026$). These results suggest that the diminished recombination rate, known to be associated with PRDM9 non-A alleles, contributes significantly to aneuploidy seen at the preimplantation stage of development.

Limitations, reason for caution: The relevance of factors such as age, referral reason or sperm quality, could not be assessed, as a larger sample size would be needed. The data indicated a greater impact of PRDM9 N-alleles in young women, but further samples are needed to confirm this statistically. Further analyses are currently underway.

Wider implications of the findings: Chromosome abnormality is common in the embryos of infertile couples, explaining many cases of implantation failure and pregnancy loss. Additionally, it has been noted that some patients produce unusually large numbers of aneuploid embryos. These observations may be explained, at least in part, by the presence of non-functional PRDM9 alleles, leading to reduced recombination and chromosomal segregation errors. Certain PRDM9 variants could be considered a risk factor for repetitive miscarriage and repetitive implantation failure.

Study funding/competing interest(s): Institutional funding. No competing interests.

Trial registration number: Not applicable

SELECTED ORAL COMMUNICATION SESSION

Session 68: The impact of genetics in andrology

Wednesday 10 July 2013

14:00 - 15:15

O-263 Clinical significance of sperm DNA damage on embryo implantation efficiency and spontaneous pregnancy loss after assisted reproductive therapy

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Study question: The study object was to correlate degree of sperm DNA damage and clinical outcomes of assisted reproductive therapy (ART).

Summary answer: Degree of sperm DNA fragmentation correlates chance of miscarriage after ART and may predict embryo implantation efficiency.

What is known already: Sperm DNA damage is more common in infertile males and may affect reproductive outcomes in selected couples (2008 ASRM committee opinion). At present, there is controversy regarding sperm DNA integrity on clinical ART outcomes.

Study design, size, duration: Retrospective cohort analysis of data from 483 fresh and cryopreserved embryo transfer cycles of 250 cases over three years at a single institution.

Participants/materials, setting, methods: The participants were less than 40 year-old. Sperm DNA fragmentation index (DFI) was evaluated by sperm chromatin dispersion test (Halosperm®, Halotech) prior to ART. DFI results were classified into three groups: L (less than 10.0%), M (10.0-30%), and H (greater than 30.0%). The study was approved by the IRB.

Main results and the role of chance: For L, M and H groups, female age (34.6 + /-3.0, 34.5 + 3.1, 36.0 + /-2.8 year-old, mean + /-standard deviation), anti-mullerian hormone (24.4 + /-16.3, 26.5 + /-21.8, 23.4 + /-16.5 pMol), average number of embryos transferred (1.5 + /-0.7, 1.4 + /-0.6, 1.7 + /-0.7), pregnancy rate (32.5, 30.9, 34.6%) were statistically similar. Embryo implantation rate showed decreasing tendency toward higher sperm DFI (for L, M and H group, 26.3, 23.2, 21.7%, respectively, $p = 0.34$). Clinical miscarriage rate after implantation was significantly higher for participants with increased sperm DNA damage: 18.4, 23.6, 33.3% for L, M and H group, respectively ($p < 0.05$).

Limitations, reason for caution: The analysis was uncategorized for fresh and cryopreserved embryos due to small sample size. Total sample size twice as large would have reached significant differences both in implantation rate and miscarriage rate.

Wider implications of the findings: The results of this study indicated value of assessing sperm DNA damage prior to ART in order to predict occurrence of negative ART outcomes, and possible future role for treatments for abnormal sperm DNA integrity. Further investigation is warranted.

Study funding/competing interest(s): None

Trial registration number: Not applicable

O-264 MicroRNA expression profile in spermatozoa from fertile donors

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Study question: Which microRNAs (miRNAs) are present in spermatozoa from fertile individuals? What is the normal miRNA expression profile?

Summary answer: 227 miRNAs were present in all sperm samples analyzed. Among them, miR-1274b, miR-720 and miR-34b were the most abundant. The full miR-30 family and most of the let-7 members were also present. Alternatively, 460 miRNAs were only detected in some fertile donors and 67 did not appear in any case.