

OP-15

Transcriptional and post-transcriptional epigenetic changes in male infertility

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Objective: Changes in spermatozoa, which carry genetic and epigenetic information, cause infertility and transmission of transgenerational diseases. Our study investigated the relationship between the expression of *MEST1*, *MEST*, *GNASAS*, *CEP41*, *H19*, and *IGF2AS* genes and DNA methylation in spermatozoa and infertility.

Methods: After semen analysis, DNA and RNA extraction from spermatozoa were performed in fertile (n=30), oligospermia (n=30), and normospermia (n=30) groups. Gene expressions were evaluated by the Livak method after RT-qPCR. DNA methylation was measured by the pyrosequencing. Hypermethylation rates were determined according to the cut-offs. We perform Kruskal Wallis, ANOVA, Bonferroni, and Tamhane for post hoc.

Results: In the fertile group, hypermethylation rates of the first (33.3%), third (33.3%), and last (40%) of the 5 CpG dinucleotides of *GNASAS* were significantly lower than those in the oligospermia group (66.7%, 73.3% and 73.3%) (p=0.028, p=0.005 and p=0.026). The hypermethylation rate of the third CpG dinucleotide of *CEP41* in the fertile group (16.7%) was significantly lower than in the normospermia (46.7%) (p=0.036). No statistically significant difference in age, body mass index, gene expressions, and methylation rates of other genes among the groups. Sperm concentration in the oligospermia was significantly lower. The rate of normal morphology in the fertile group was significantly higher.

Conclusion: *GNASAS* is a maternal imprint gene hypomethylated in sperm cells. Hypermethylated *GNASAS* is associated with impaired sperm production. *CEP41* is a non-imprint gene adjacent to the maternal imprint *MEST* gene. *CEP41* hypermethylation was higher in the normospermia than in the fertile. *CEP41* hypermethylation has been shown as a new candidate in the etiology of infertility with normospermia. Revealing epigenetics of infertility may reduce the risk of transgenerational epigenetic diseases.

Keywords: DNA methylation, gene expression, genomic imprinting, spermatozoa.

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