

TITLE: Altered FISH in sperm, would you be indicated Preimplantation Genetic Diagnosis (PGD)?

AUTHORS: Fabregat A., Baeza N., Ortiz JA., Lledó B., Morales R., Ten J., Tió MC., Llácer J., Bernabeu R.

STUDY QUESTION: Is there a correlation between sperm aneuploidy and transmission of chromosomal abnormalities to their offspring?.

SUMMARY ANSWER: The analysis of our results indicates that probability of finding a chromosomally altered embryo is significantly higher in those men with altered sperm FISH to at least one of the chromosomes analyzed respect for those men with normal FISH specially in couples with young women.

WHAT IS KNOWN ALREADY: The development of more sophisticated techniques such as ICSI, revolutionized the management of male infertility, allowing the use of sperm from men with severely compromised semen parameters. Nevertheless, approximately 20% of pregnancies end in miscarriage. Aneuploidy has a negative effect on reproductive outcomes and represents one of the main causes of implantation failure and miscarriage. PGD has been applied for the selection of euploid embryos aiming to improve clinical outcomes.

STUDY DESIGN, SIZE, DURATION: We performed a retrospective observational study. Overall, 834 embryos (140 cycles) were biopsied and diagnosed. Of these, 634 embryos were analysed by FISH after biopsy on day 3 and 200 embryos were analyzed using a-CGH after biopsy on day 5. Study was performed from January 2007 to April.

PARTICIPANTS/MATERIALS, SETTING, METHODS: PGD (SGP or a-CGH) was performed to couples who attended the Instituto Bernabeu with recurrent miscarriage, implantation failure, severe male factor or altered karyotypes. We analyzed 7 chromosomes in spermatozoa and 9 in the blastomeres by FISH (SGP). For a-CGH, trophoectoderm genome was amplified and performed Agilent SurePrintG3 8x60K.

MAIN RESULTS AND THE ROLE OF CHANCE: Globally, 412 out of 834 biopsied embryos were aneuploid (49.4%). Significant differences were reported in terms of embryonic aneuploidy among those embryos from men with altered sperm FISH (64.5%) and normal (49.4%) ($p < 0.05$).

For embryos diagnosed by a-CGH, we also found significant differences in the rate of embryonic aneuploidy depending on whether the man had altered sperm FISH (68.6%) or normal (39.6%) ($p < 0.05$).

However, not significant differences were found ($p = 0.196$) when analyzing the embryos by SGP.

We also considered other parameters such as semen quality, DNA fragmentation and implantation rate in relation to embryonic aneuploidy. We only obtained significant differences for semen quality ($p < 0.05$, $p = 0.736$ and $p = 0.26$ respectively).

LIMITATIONS, REASONS FOR CAUTION: One limitation of the study is the use of FISH to determine aneuploidy in sperm and embryos biopsied on day 3, since in this way we only study a certain number of chromosomes.

This could be the reason why no significant differences in SGP were found.

WIDER IMPLICATIONS OF THE FINDINGS: This study shows that altered sperm FISH could be an indication in itself for the performance of a PGD by a-CGH to reduce implantation failure and recurrent miscarriage .

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