P-042 Impact of semen parameters, sperm DNA fragmentation and sperm aneuploidy in male infertility

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Study question: Should sperm aneuploidies and sperm DNA fragmentation (sDNAfrag) be included as valid tests in the routine investigation of male infertility?
Summary answer: Sperm DNA fragmentation was associated with male age, oligozoospermia (OZ), oligoteratozoospermia (OT), astenoteratozoospermia (AT) and oligoastenoteratozoospermia (OAT). Sperm aneuploidies were associated with OT and OAT.
What is known already: Semen parameters assist male infertility diagnosis and treatment, but sDNAfrag and aneuploidy analysis could add useful information, as abnormal values compromise fertility. To include these tests in the routine diagnosis it should be determined if behave as informative parameter and add information regarding the fertility status. For that, further studies comparing these tests to semen parameters are needed, since previous results are not consensual. Additionally, standardization of a sDNAfrag cut-off is needed, as different sample sizes and techniques originate distinct results. Also, until a standardization of the protocol is missing, a cut-off value should be defined for each laboratory.
Study design, size, duration: A retrospective and prospective investigation was performed, within a 12 years period (April 2007-December 2019). A total of 835 infertile males with a normal karyotype (46,XY) were included. Karyotyping and evaluation of sDNAfrag and sperm aneuploidies were made at a public Genetic unit. All normozoospermic (NZ) patients with a born child and patients whose infertility treatments were done due to female factors were selected from our database and used as controls (60 individuals).
Participants/materials, setting, methods: Semen analysis followed WHO-2010 guidelines. sDNAfrag was evaluated using the TUNEL assay. Sperm aneuploidies were detected using FISH (chromosomes 13, 18, 21, X, Y). Several tests were applied: correlations for linear associations between numerical variables, ANOVA for comparisons between means, Dunn-test for post-hoc comparisons. To determine the sDNAfrag cut-off value, the area under the ROC curve, sensitivity and specificity, were calculated, with the Youden-Index used to find a threshold that maximizes both sensitivity and specificity.
Main results and the role of chance: Regarding male age, it was observed a positive correlation with sperm concentration, a negative correlation with sperm vitality (VT) and hypoosmolality, and a positive correlation with sDNAfrag. Regarding sDNAfrag, it was observed negative correlation with sperm concentration, total progressive motility (TPM), morphology, VT and hypoosmolality. Regarding sperm aneuploidies, both total sperm aneuploidy and total sperm disomy exhibited a negative association with sperm concentration, TPM and morphology. It was also investigated whose groups of individuals could be indicated for sDNAfrag or sperm aneuploidy testing. The NZ group evidenced significant lower sDNAfrag, total sperm aneuploidy and total sperm disomy in relation to the non-NZ group. In the NZ group, sDNAfrag was significantly lower in relation to the OZ, OT, AT and OAT groups. The NZ group presented significant lower percentages of sperm aneuploidy in relation to the OT and OAT groups, and significant lower percentages of sperm disomy in relation to the OAT group. Additionally, sDNAfrag was positively correlated with total sperm aneuploidy and total sperm disomy. From the present large population, ROC curve analysis allowed estimating a cut-off value of 18.8% for the TUNEL-assay (sDNAfrag), with 0.658 of area under the curve, 53.9% sensitivity and 76.7% specificity.
Limitations, reasons for caution: Although presenting a high number of cases and strict controls, the present study was unable to include as controls healthy men with proven fertility. Additionally, the present study did not take into account life-style factors and male associated pathologies besides infertility

Wider implications of the findings: Semen parameters were shown to be negatively correlated with sDNAfrag and sperm aneuploidies. As sDNAfrag testing and sperm aneuploidy testing were associated with semen abnormalities and male age, it is suggested their inclusion in the routine evaluation of infertile men, thus adding important complementary information about the fertility status.
Trial registration number: Not Appliable