Intervention to reduce sperm DNA damage prior to fertility treatment

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Study question:
Can changing various factors such as diet, exercise, smoking, or intake of antioxidants help to reduce the level of sperm DNA damage?

Summary answer:
The average index for sperm DNA damage (DFI) was reduced significantly from 34.1 to 25.7 (P<0.0001) for the 96 men included in this study.

What is known already:
Sperm DNA damage negatively affects the outcome of ART, including IVF and ICSI treatments. Factors such as tobacco smoking or metabolic syndrome are among the more common causes of sperm DNA damage. Furthermore, it has been shown that oral intake of antioxidants may reduce sperm DNA damage. However, DNA damage is multifactorial and many factors currently remain unknown. The overall aim of the study was to determine if sperm DNA damage could be reduced and identify the factors leading to such improvement.

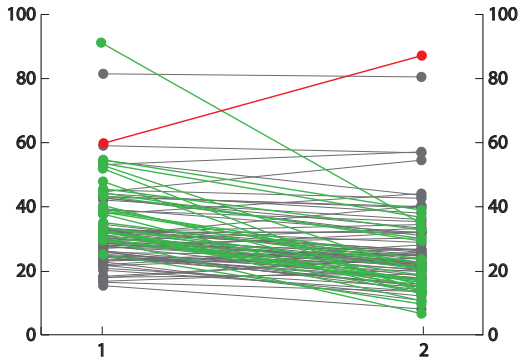
Study design, size, duration:
Sperm DNA damage was tested in 2287 male patients. The DFI was above 15 for 1178 patients (51.5%), who were then invited to participate. In total, 96 patients were enrolled in the study with interventions individually designed during consultations between physician and patient. The DFI was re-tested after a recommended period of 3 to 9 months. All changes implemented by the patient were recorded using an online self-assessment questionnaire.

Materials and methods:
Patients were enrolled at 2 fertility clinics. DFI was determined by a diagnostic laboratory using the sperm DNA integrity test (SDI-test), modified from Evenson & Jost (Current Protocols In Flow Cytometry 2000;7,13:1-27). Data from all 96 men before and after intervention was analysed using a paired t-test as well as the bootstrap method. Changes made by individuals were highlighted using the intra-individual variation of the SDI-test (estimated from control-group data of a previous RCT).

Main results and the role of chance:
The overall DFI was reduced significantly from 34.1 to 25.7 (8.4 percentage units, P<0.0001). This reduction in DFI was determined by the paired t-test and was confirmed by the bootstrap method.
Intra-individual variation (SD_w) of the SDI-test was determined using double-blinded control-group data from a previous RCT. Using the SD_w (=6.36%), 27 men were determined to have improved their DFI significantly (on average from 40.7 to 19.8). One man, however, had increased his DFI significantly from 59.4 to 87.6.

The factors implemented by the 27 men were related to dietary changes to reduce possible insulin resistance: Reductions in meat intake (13/27), white bread (13/27), soft drinks (13/27) and alcohol (24/27). In addition, an increased fruit and vegetable intake was reported (15/27), together with increased exercise levels (14/27). Out of the 27 men, 15 reported losing weight. Three men (3/27) reported stopping smoking. Twenty men (20/27) reported starting to take antioxidants. Nine men (9/27) reported taking medication, and one man, who had stopped taking a SSRI medication, achieved the highest reduction in DFI (from 92.0 to 34.1).

The man who increased his DFI significantly had taken a high dosage of various antioxidants and was confirmed to have iron intoxication.



The figure on the left shows the changes in DFI for the 96 men. The SDI-test was performed before (1) and after the interventions (2). DFI is shown on the y-axis.

One man had a statistically significant increase in DFI of 28.2 percentage units **(Red line)**. For 27 men, the reduction in DFI for the individual was statistically significant **(Green lines)**. The average reduction in DFI for the 27 men was 20.8 percentage units. The individual changes in DFI were not statistically significant for the remaining 68 men **(Black lines)**. In this group, the average reduction in DFI was 3.9 percentage units.

Before interventions, all men had DFI levels above 15. For 20 men, the DFI was between 15 and 25. The DFI was above 25 for the remaining 76 men.

After interventions, 16 men had achieved a DFI below 15. A DFI between 15 and 25 was achieved by 42 men. The DFI was still above 25 for the remaining 38 men. A reduction in DFI of more than 5 percentage units was achieved by 62 men. The average reduction in this group was 14.0 percentage units.

Limitations, reason for caution:
This prospective study is based on 96 men with an initial DFI of above 15. For most men, several factors were implemented. It should be noted that some factors, i.e. smoking, may not result in a high DFI unless other factors, i.e. lack of antioxidants, are also involved.

Wider implications of the findings:
Reduction of sperm DNA damage before ART is desirable as it may increase treatment success rates. Furthermore, such intervention may also have a positive effect on general male health as DNA damage in sperm is often linked to increased DNA damage in somatic cells.

Study funding/competing interest(s):
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