Modifiable Nutritional and Lifestyle Factors in Sperm DNA Fragmentation

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Why test DNA fragmentation?

15% of men with a normal semen analysis have fertility issues

Men with abnormal semen analyses can have natural conceptions

1 in 4 men have a normal semen analysis but have elevated DNA fragmentation

Oleszczuk et al, 2013, Anndroloy 1, 357-60
Why test DNA fragmentation?

Sperm DNA damage caused by oxidative stress: modifiable clinical, lifestyle and nutritional factors in male infertility

C Wright a,*, S Milne b, H Leeson b

Dietary supplementation with docosahexaenoic acid (DHA) improves seminal antioxidant status and decreases sperm DNA fragmentation

Juan Carlos Martínez Soto a, b, Juan Carlos Domingo, Begoña Córdobilla, María Nicolás, Laura Fernández, Pilar Albero, Joaquín Gadea & José Landeras c

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Reduction of the Incidence of Sperm DNA Fragmentation by Oral Antioxidant Treatment

ERMANNO GRECO,* MARCELLO IACOBELLI,* LAURA RIENZI,* FILIPPO UBALDI,* SUSANNA FERRERO,* AND JAN TESARIK†‡
Causes of DNA fragmentation

Reactive oxygen species

Immature sperm
Infection
Varicocele
Inflammation
Smoking
Overweight
Heat
Xenobiotics

Antioxidants
Dietary Sources
Supplements
1. Avoid/ give up smoking

<table>
<thead>
<tr>
<th></th>
<th>Fertile Non-smokers (n=80)</th>
<th>Fertile Smokers (n=80)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Seminal ROS</strong></td>
<td>436.5 RLU</td>
<td>1180.7 RLU</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td><strong>DNA Frag (Flow cytometry - PI)</strong></td>
<td>5.86%</td>
<td>10.85%</td>
<td>&lt;0.05</td>
</tr>
</tbody>
</table>

- Taha et al. Urology. 2012
2. Avoid testicular heat

- Spermatogenic arrest

19 Healthy Volunteers – testicular warming belt
40-43°C 40min per day, two successive days per week

<table>
<thead>
<tr>
<th>DNA Frag (SCD)</th>
<th>Pre-Scrotal Warming</th>
<th>1 month post-scrotal warming</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>17.7%</td>
<td>70.7%</td>
</tr>
</tbody>
</table>

2. Avoid testicular heat

- Spermatogenic arrest

- keeping a mobile phone in trouser pocket
- cycling for long periods/ tight clothing
- laptop on the lap for extended periods, particularly with closed legs
- heated car seats
- saunas or jacuzzi

- repeat analysis 3 months after febrile illness
3. Xenobiotics

<table>
<thead>
<tr>
<th>Persistent Organochlorine Pollutants (POP, PCB)</th>
<th>Avoid farmed fatty fish</th>
</tr>
</thead>
<tbody>
<tr>
<td>Organophosphorus, pyrethroids</td>
<td>Occupational OR household exposure to insecticides/pesticides</td>
</tr>
<tr>
<td>Bisphenol A (BPA)</td>
<td>Plastic food containers, canned food, heating food in plastic containers, till receipts</td>
</tr>
<tr>
<td>SSRIs, opiates</td>
<td>History check for medication</td>
</tr>
</tbody>
</table>
4. Weight management

Correlation between central obesity and DNA fragmentation

• BMI measurement vs central adiposity/waist circumference

• Confounding factors, poor diet, low in antioxidants

Healthy weight loss, low GI diet, plenty of antioxidants...
Causes of DNA fragmentation

Reactive oxygen species

Antioxidants
Dietary Sources
Supplements
Antioxidants for male subfertility

Increased live births
OR 4.21  p<0.0001

Increased clinical pregnancy rate
OR 3.43  p<0.0001

- Showell et al. Cochrane Database Syst Rev. 2015
Antioxidants for DNA fragmentation

Vitamin C  Depletion/  Repletion Study

Depletion:  91% increase in sperm with DNA damage

Repletion:  Restored after repletion within 2-3 months

- Fraga CC et al, 1991, PNAS, 88, 24, 11003-6
# Antioxidants for DNA fragmentation

<table>
<thead>
<tr>
<th>1 g Vitamin C</th>
<th>placebo controlled double blind RCT (n=64)</th>
<th>DNA Frag (TUNEL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1g Vitamin E</td>
<td>22.1% → 9.1%</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>1 g Vitamin C</th>
<th>Uncontrolled study(n=38)</th>
<th>DNA Frag (TUNEL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1g Vitamin E</td>
<td>24.8% → 8.2% in responsive group</td>
<td></td>
</tr>
</tbody>
</table>

- Greco et al. J Androl. 2005
- Greco et al. Hum Reprod 2005
<table>
<thead>
<tr>
<th>Antioxidants for DNA fragmentation</th>
<th>DNA Frag (SCD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1500mg L-carnitine</td>
<td>28.5% → 20.12</td>
</tr>
<tr>
<td>20mg CoQ10</td>
<td></td>
</tr>
<tr>
<td>60mg Vitamin C</td>
<td></td>
</tr>
<tr>
<td>10mg Vitamin E</td>
<td></td>
</tr>
<tr>
<td>200μg Vitamin B9</td>
<td></td>
</tr>
<tr>
<td>1μg Vitamin B12</td>
<td></td>
</tr>
<tr>
<td>10mg zinc</td>
<td></td>
</tr>
<tr>
<td>50μg selenium</td>
<td></td>
</tr>
<tr>
<td>asthenteratozoospermic males (n=20) uncontrolled</td>
<td></td>
</tr>
</tbody>
</table>

Antioxidants for DNA fragmentation

<table>
<thead>
<tr>
<th>400mg Vitamin C</th>
<th>Males with DFI &gt;15% (n=58) double centred, uncontrolled</th>
</tr>
</thead>
<tbody>
<tr>
<td>400mg Vitamin E</td>
<td></td>
</tr>
<tr>
<td>33mg zinc</td>
<td></td>
</tr>
<tr>
<td>80μg selenium</td>
<td></td>
</tr>
<tr>
<td>18mg β-carotene</td>
<td></td>
</tr>
</tbody>
</table>

**DNA Frag (SCD)**

- 32.4% → 26.2
- Increase in HDS

- Menezeo et al. Reprod Biomed Online. 2007
Antioxidants for DNA fragmentation

Reactive oxygen species

Capacitation
Hyperactivation
Acrosome reaction

Caution with excess antioxidants
Antioxidants for DNA fragmentation

- Measuring blood levels
- Correcting deficiencies
- Supplementing accordingly

Antioxidants for DNA fragmentation

- 2 portions fruit per day
- 5 portions VEG per day
- Nuts and seeds
  - e.g. brazil nuts – selenium
  - pumpkin seeds, cashew nuts - zinc

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Case Study

- Poor motility, morphology, DNA fragmentation 27%
- IBS, anxiety, stress
- Low levels of Vit C, zinc, magnesium, vitamin D
- Diet low in essential fats, vegetables
- 4 month dietary & lifestyle programme

<table>
<thead>
<tr>
<th>Count</th>
<th>Pre</th>
<th>Post</th>
<th>Baby girl born in next IVF cycle</th>
</tr>
</thead>
<tbody>
<tr>
<td>Motility</td>
<td>(14 \times 10^6/\text{ml})</td>
<td>(22 \times 10^6/\text{ml})</td>
<td></td>
</tr>
<tr>
<td>Morphology</td>
<td>12%</td>
<td>39%</td>
<td></td>
</tr>
<tr>
<td>DNA frag %</td>
<td>27%</td>
<td>7%</td>
<td></td>
</tr>
</tbody>
</table>
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