Title: OXIDATIVE STRESS AND MITOCHONDRIAL MUTATION IN IDIOPATHIC ASTHENOZOOSPERMIC MEN
**Objective:** Since mtDNA is the key factor that produces energy in the form of ATP that helps in the sperm motility, any change in mtDNA nucleotides could affect the ATP production. As mtDNA is both the source and target of ROS, it is believed that ROS damages mitochondrial membrane and further mtDNA. Hence, the aim of our study is to find the role of OS and mtDNA mutation in infertile men.

**Design:** Prospective study

**Materials and Methods:** The present study included 40 infertile men with idiopathic asthenozoospermia and 35 fertile controls. ROS activity was estimated by measuring the level of lipid peroxidation in semen samples by malondialdehyde (MDA) assay. DNA from semen was isolated from both patients and controls. Mitochondrial genome was sequenced by standard PCR-DNA sequencing protocol.

**Results:** 72.5% (29/40) of the infertile patients showed significant nucleotide changes in their sperm mtDNA compared to the controls. Sperm MDA levels of infertile group was significantly higher when compared to the controls (p<0.0001), where normal sperm parameters of infertile patients were significantly decreased compared to the controls.

**Table 1.** Comparison of sperm parameters, MDA level and nucleotide changes in Asthenozoospermic and control men

<table>
<thead>
<tr>
<th>Subjects</th>
<th>Sperm Count X 10^6/mL</th>
<th>Progressive motility (%)</th>
<th>MDA (nmol/dL)</th>
<th>Number of subjects harbored nucleotide changes in the ATPase6 &amp; ATPase8 gene</th>
</tr>
</thead>
<tbody>
<tr>
<td>Asthenozoospermic (n = 40)</td>
<td>52.3 ± 4.5</td>
<td>12.6 ± 7.0</td>
<td>0.271 ± 0.032</td>
<td>29</td>
</tr>
<tr>
<td>Controls (n = 35)</td>
<td>60.8 ± 17.8</td>
<td>65.3 ± 12.7</td>
<td>0.131 ± 0.026</td>
<td>5</td>
</tr>
<tr>
<td>P value</td>
<td>P&lt;0.0005</td>
<td>P&lt;0.0001</td>
<td>P&lt;0.0001</td>
<td>-</td>
</tr>
</tbody>
</table>

P <0.005 was significant by Student’s t-test

**Conclusions:** Oxidative stress appears to impair sperm motility both by depleting ATP and by lipid peroxidation of sperm plasma membrane. Increased ROS activity in the semen (based on elevated MDA levels) may be responsible for the nucleotide change in the mtDNA and for impairment of sperm motility. Our preliminary study highlights the need to analyze mitochondrial genome in sperm samples for mutations and to assess the free radical levels in order to have better insight into pathophysiology of infertility.
Support: None.

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