Reversibility Of Tumor Necrosis Factor (TNF-α) Induced Toxic Effects By Infliximab In Human Spermatozoa

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Objectives: Patients with endometriosis present with elevated levels of TNF-α. The presence of these pathological levels of TNF-α in the female reproductive tract may have toxic effects on spermatozoa. Infliximab a monoclonal antibody binds both soluble and membrane forms of TNF-α and neutralizes its toxic effects. The objective of our study was to evaluate the ability of Infliximab to counteract the toxic effects induced by TNF-α in human spermatozoa.

Design: Prospective-controlled study.

Materials and Methods: Semen samples were collected from 6 normozoospermic males. Following liquefaction, spermatozoa were separated on a double density gradient and resuspended in BWW media. Four aliquots of sperm suspension were incubated at 37°C for 6 hours with: 1) human recombinant TNF-α (rTNF-α, 2.5 µg/mL, R & D systems, Minneapolis, MN); 2) Infliximab (400 µg/mL, Centocor, Malvern, PA); 3) TNF-α (2.5 µg/mL) + Infliximab (400 µg/mL); and 4) BWW alone (control). Concentration of TNF-α, Infliximab and incubation were selected based on results from our pilot experiment. Sperm motility, functional integrity of plasma membrane (hypoosmotic swelling test, HOS) and DNA damage (TUNEL assay) were evaluated before and after the incubation period.

Results: Spermatozoa quality declined significantly (P<0.05) following 6 hours of incubation with TNF-α alone (percentage motility, plasma membrane integrity and DNA damage) compared to controls. The percentage of spermatozoa with DNA fragmentation was lower (P<0.05) in samples incubated with TNF-α + Infliximab compared to samples treated with TNF-α only. Infliximab was able to reverse the toxic effects of TNF-α after incubation for 6 h (Table). Similarly, sperm motility and membrane integrity was significantly improved (P<0.05) and was comparable both with controls and Infliximab alone (Table).

Conclusions: TNF-α in pathological levels exerts toxic effects on human spermatozoa. Infliximab plays a significant role in reversing and conferring protection against TNF-α induced toxic effects. Infliximab may be a potential candidate in the management of
infertility patient with endometriosis who present with elevated levels of TNF-α.

**Support:** None

Effect of TNF-α, Infliximab and TNF-α + Infliximab on sperm motility, membrane integrity and DNA damage, following 6 hours of incubation.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Control</th>
<th>TNF-α (2.5 µg/mL)</th>
<th>Infliximab (400 µg/mL)</th>
<th>TNF-α (2.5 µg/mL) + Infliximab (400 µg/mL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sperm motility (%)</td>
<td>74.9 ± 10.3</td>
<td>53.5 ± 21.52</td>
<td>70.1 ± 16.77</td>
<td>63.13 ± 18.78</td>
</tr>
<tr>
<td>HOS test (%)</td>
<td>63.83 ± 10.49</td>
<td>41.33 ± 19.11</td>
<td>59 ± 13.23</td>
<td>50.12 ± 11.98</td>
</tr>
<tr>
<td>DNA damage (% fragmentation)</td>
<td>6.26 ± 3.74</td>
<td>22.08 ± 9.14</td>
<td>8.24 ± 3.72</td>
<td>10.91 ± 5.32</td>
</tr>
</tbody>
</table>

Results are expressed as mean ± SD; \(^a\) P <0.05 considered significant compared to 0 h using Wilcoxon matched pair test; \(^b\) P <0.05 considered significant compared to corresponding control; \(^c\) P <0.05 considered significant compared to TNF-α + Infliximab.

**Author Disclosure Block:** T.M. Said, None; A. Agarwal, None; R.K. Sharma, None; M.A. Bedaiwy, None; T. Falcone, None.

**Category (Complete):** Endometriosis (GPC)

**Keyword (Complete):** tumor necrosis factor-alpha (TNF-α); endometriosis; spermatozoa; infertility

**Additional (Complete):**
- **Presenting Author Fellow:** Yes
- **In-Training Award:** True
- **ACCME Disclosure:** I will not be discussing non-FDA approved products
  - **I Agree:** True

**Status:** Complete