Differential Contribution Of Reactive Oxygen Species And Tumor Necrosis Factor-α To The Peritoneal Fluid-Induced Embryotoxicity In Endometriosis Patients

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Objectives: Alterations in the production of peritoneal fluid cytokines and oxidative stress parameters contribute to the evolution of endometriosis. Peritoneal fluid (PF) TNF-α and reactive oxygen species (ROS) are indirect measures of both pathogenic mechanisms. Peritoneal fluid embroyotoxicity is a presumptive mechanism of endometriosis-associated infertility. The objectives of this study were to study the embryotoxic effects of PF in women with endometriosis, and to relate any embryotoxicity to the PF levels of ROS and TNF-α.

Design: Experimental study in a research laboratory in a tertiary care facility.

Materials and methods: Reactive oxygen species levels were measured in laparoscopically obtained PF of 12 endometriosis patients by enhanced chemiluminescence assay using luminol as the probe. Concentrations of TNF-α in PF of those patients were measured using quantitative ELISA kits. Two hundred eight four thawed mouse embryos were pooled and randomly distributed between 5 groups: (A) composed of plain HTF without PF as a control group, (B) HTF supplemented with 10% PF, (C) HTF supplemented with 15% PF, (D) HTF supplemented with 25% PF, and (E) HTF supplemented with 50% PF for each patient. The numbers of embryos were from 62 to 132 embryos per concentration. Blastocyst development rates (BDR) were checked after 72 hours of incubation. Logistic regression with generalized estimating equations (GEE) to assess the effect of ROS, TNF-α and PF concentration on blastocyst development rate while adjusting for correlation between embryos grown together and embryos grown in PF from the same patient was performed.

Results: Higher PF concentration was significantly associated with lower BDR (P<0.001), both with and without adjusting for ROS and TNF-α (Figure). The median and interquartile ranges of PF ROS and TNF-α were 1.21 (0.66-2.32) x10^6 cpm and 1.69 (0.21-6.33) pg/mL respectively. There is no evidence that either ROS or TNF-α was associated with BDR after adjusting for PF concentration.

Conclusions: Peritoneal fluid embroyotoxicity may be a contributing factor to endometriosis associated infertility. Peritoneal fluid ROS or TNF-α was not the culprit. The embryotoxic effect may be due to dilutional effects. Given the fact that this is an interim analysis, the results may change when we analyze data from the planned sample size of 25 endometriosis patients.
Commercial Relationship: J. Noriega, None; M.A. Bedaiwy, None; S. Worley, None; R.K. Sharma, None; A. Agarwal, None; T. Falcone, None.

Topic (Complete): 13. Endometriosis

Keyword (Complete): endometriosis ; tumor necrosis factor-alpha (TNF-α) ; embryotoxicity

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

Status: Complete