FSH administration reduces significantly sperm apoptosis only in the case of high DFI value: a study in idiopathic dispermic patients

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Previous SectionNext Section

Abstract

Introduction: In the last decades sperm DNA quality has been recognized as one of the most important markers of male reproductive potential (Lewis and Aitken, 2005; Ozmen, 2007; Tarozzi, 2007), in contrast to standard semen parameters as sperm density, motility and morphology, which do not act as powerful discriminators between fertile and infertile men. DNA damage in the male germ line is a major contributor to infertility, miscarriage and birth defects in the offspring. In animal models, it has been unequivocally demonstrated that the genetic integrity of the male germ line plays a major role in determining the normality of embryonic development. In humans, many studies showed that sperm DNA damage is associated with impaired embryo cleavage (8), higher miscarriage rates (9) and also with a significantly increased risk of pregnancy loss after in vitro fertilization (IVF) and intracytoplasmic sperm injection (ICSI) (10). Specifically, above a threshold of 30% of sperms with fragmented DNA, chances for pregnancy are close to zero, either by means of natural conception or intrauterine insemination (Spano M, 2000; Bungum M, 2007). Since there is a clear relationship between sperm DNA damage and poor assisted reproduction technology (ART) outcomes, efforts should be directed in developing treatments to improve sperm DNA quality to be introduced into clinical use. The aim of this observational study was to investigate the effects of r-FSH administration on sperm DNA fragmentation of iOAT patients undergoing ICSI, comparing the DNA fragmentation index (DFI) before and after 90 days of FSH therapy.

Matherial and Methods: Fifty-three iOAT men, with a median age of 33,6 ± 7,6 years, referred to our clinics because of fertility problems after at least two years of natural attempts, were selected for the study. In all patients DNA fragmentation was evaluated sperm prior to treatment with 150 IU of recombinant human FSH (GONAL-f®, Merck Serono) three times at week for at least three months. Patients were re-evaluated after a 3-month period with semen analysis and DNA fragmentation. Sperm DNA fragmentation index (DFI) was investigated by terminal deoxynucleotidyl transferase-mediated deoxyuridine triphosphate (dUTP) in situ DNA nick end

labelling (TUNEL) assay. Data were analysed using the paired t-test and chi-square as appropriate. A p-value <0.05 was considered statistically significant.

Results: After 3 months of r-FSH treatment, no significant differences was observed between baseline and post therapy semen sample parameters including sperm count, motility, and the percentage of normal sperm forms. IThe percentage of sperm DNA fragmentation in the total of patients dropped from 20.8 ± 9.1 to 15.1 ± 8.9 ($P < 0.05$) (see Tab I). Interestingly, no statistical difference was found in sperm DFI when patients showed a baseline DFI ≤15% (10.5 ± 4.2 vs 11.4 ± 4.5). We found an evident and statistically significant DFI reduction in patients with sperm baseline DFI value ≥15% (24.37 ± 9.6 vs 15.4 ± 4.6).

Conclusion: Our data seems to demonstrate that FSH acts as a strong anti-apoptotic agent in reducing DNA fragmentation in iOAT patients. The therapy may be a specific pretreatment for infertile male partners of couples undergoing ICSI, specifically in the case that basal DFI is higher than 15%, reducing the percentage of spermatozoa with DNA integrity anomalies suggesting a positive effect on the reproductive outcome.