POSITIVE EFFECTS OF FSH THERAPY ON QUANTITATIVE AND FUNCTIONAL SPERM PARAMETERS IN IDIOPATHIC INFERTILE MEN



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INTRODUCTION

A number of previous studies reported that FSH administration improves quantitative and functional sperm parameters leading to a significant increase of pregnancy rate in idiopathic infertility. Hyaluronic acid (HA) binding capacity of spermatozoa is a biomarker of functional competency expressing also nuclear maturation. The percentage of HA bound spermatozoa in the ejaculate is a proxy of normal sperm maturation and fertilizing potential. No data is available on the effect of FSH therapy on HBA values and on the last phase of spermatogenesis called "spermiogenesis".

AIMS

Primary objective: evaluation of the effects of highly purified FSH (hpFSH) treatment on sperm ability to bind hyaluronic acid in relation to:

- i) 1 month therapy \rightarrow spermiogenesis;
- ii) 3 months therapy \rightarrow spermatogenesis.

Secondary objective:

- i) evaluation of the effects of hpFSH treatment on Total Motile Sperm Count (TMSC)
- ii) evaluation if $FSH\beta$ (SNP -211G>T) and/or FSHR (SNP 2039A>G) genotypes can predict response to treatment (pharmacogenetics).

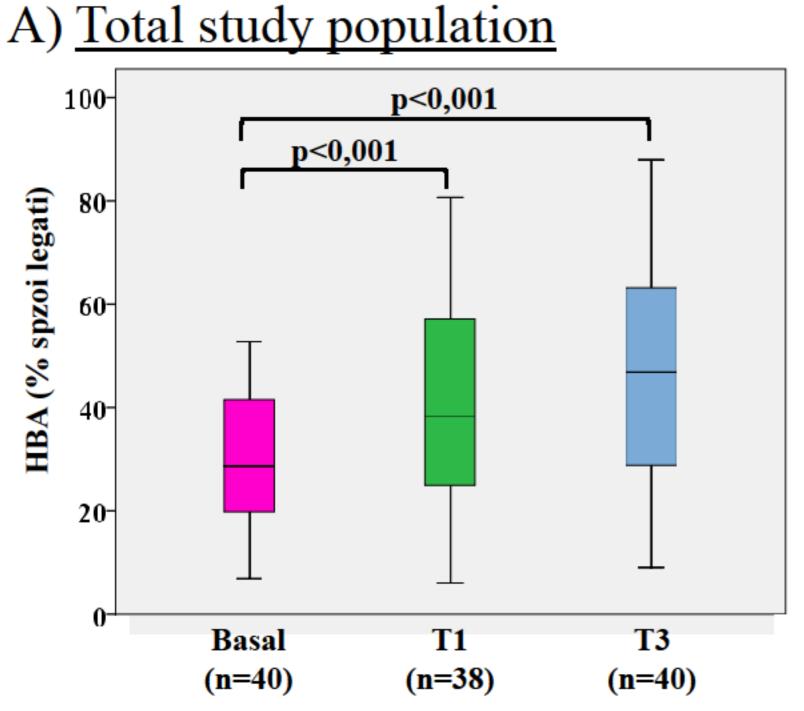
STUDY POPULATION

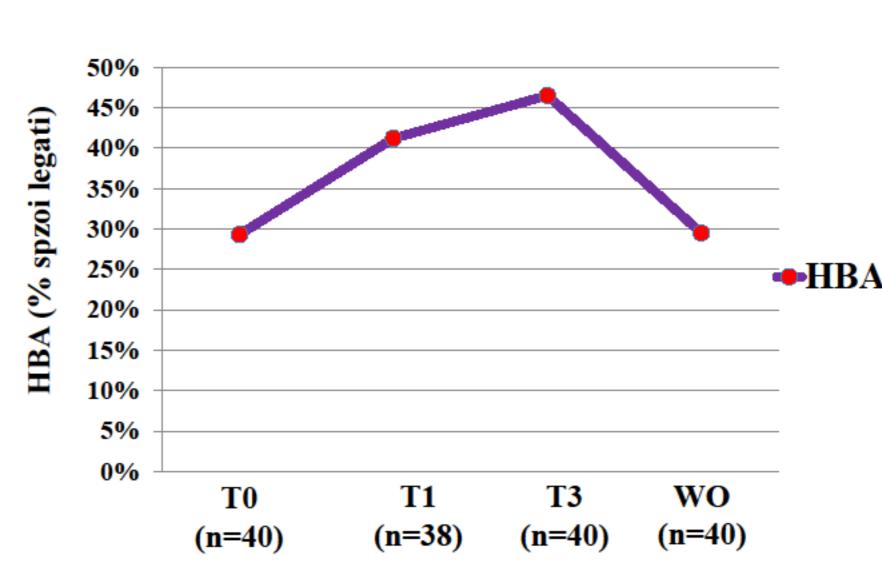
40 oligo- and/or asteno- and/or teratozoospermic male patients with idiopathic infertility, FSH <8IU/L and HBA baseline values <60% were enrolled. Patients were treated with hpFSH 75 IU/L s.c. every other day for a period of 3 months. HBA values were evaluated before (T0), after 1 (T1) and 3 months (T3) of therapy and 4-6 months after discontinuation of treatment (washout). Molecular genetic analysis was performed by PCR/RFLP ($FSH\beta$) and by PCR/HRMA (FSHR) in 39 patients.

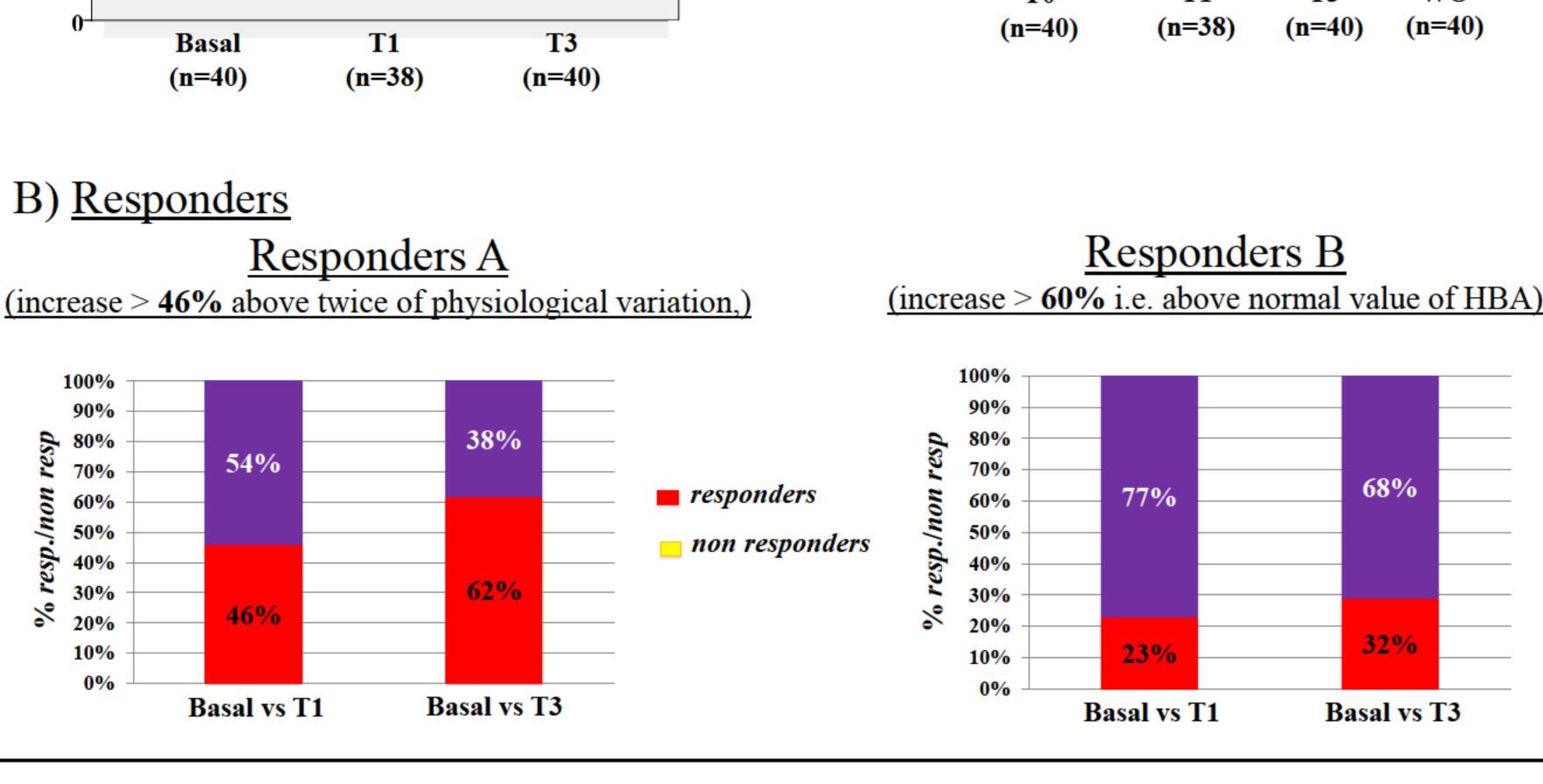
MATERIALS AND METHODS Secondary objectives: Primary objective: HA binding capacity of spermatozoa i) TMSC ii) Pharmacogenetics GG GT TT $FSH\beta$ PCR RFLP SNP -211G>T bound motile sperm TMSC = total sperm number * progressive sperm motility **% Bound** = 100 *bound motile sperm + unbound motile sperm *FSHR* PCR HRMA SNP 2039A>G PHYSIOLOGICAL VARIATION in our cohort = 84% PHYSIOLOGICAL VARIATION in our cohort = 23%

RESULTS

Primary objective: HA binding capacity of spermatozoa (HBA)

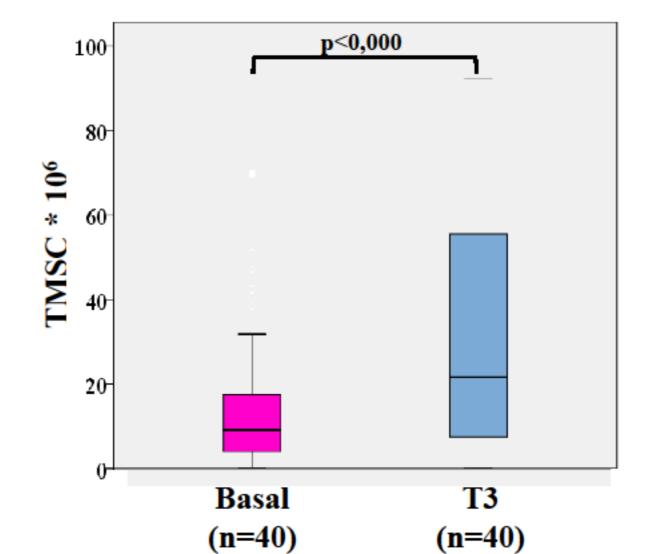


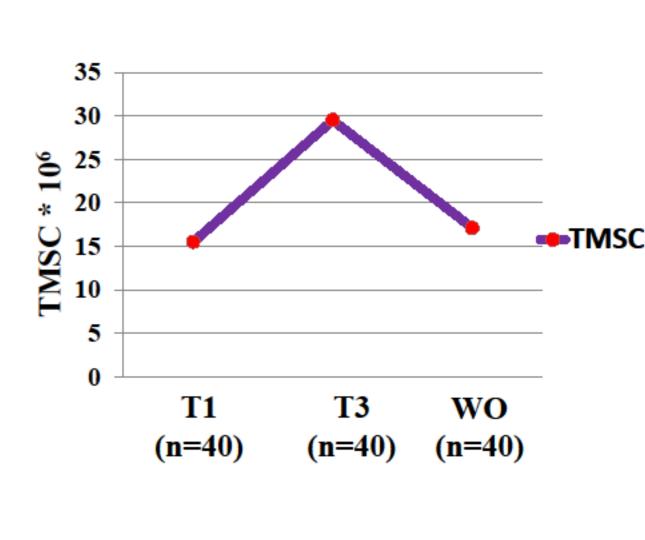




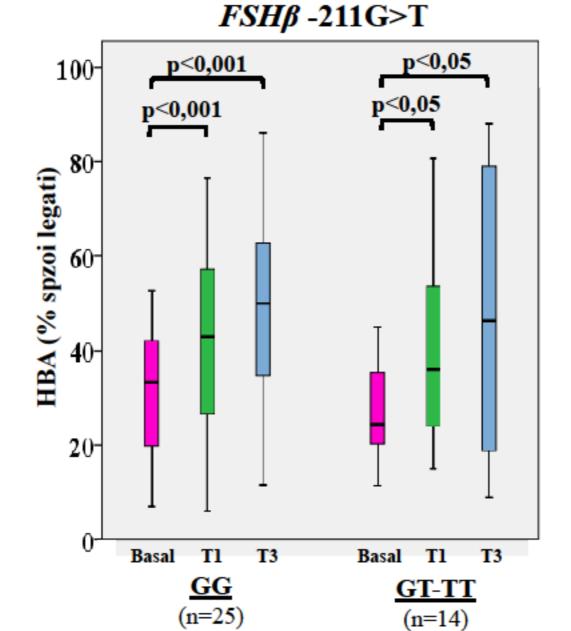
Secondary objective:

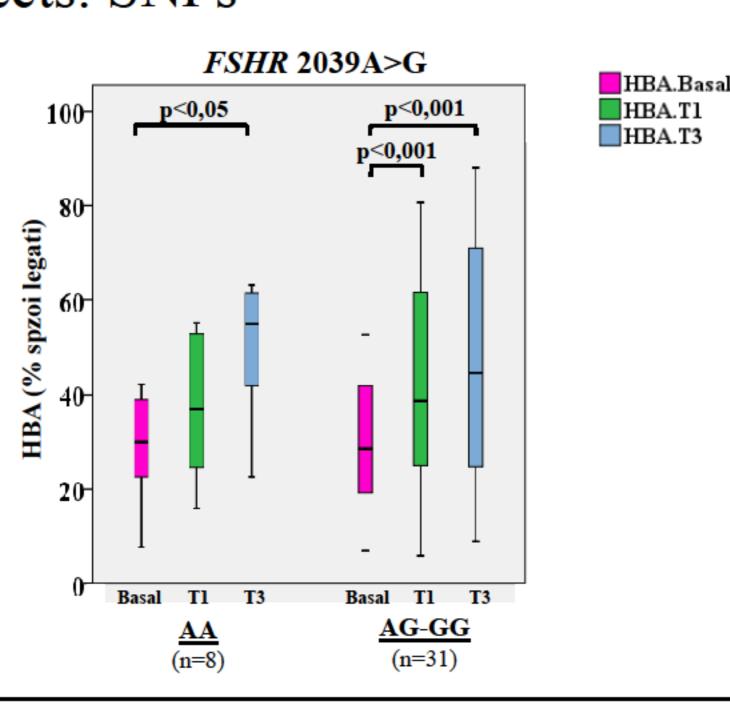
i) Effect on Total Motile Sperm Count (TMSC)





ii) Pharmacogenetic aspects: SNPs





CONCLUSION

Our study showed that hpFSH improves both the entire cycle of spermatogenesis and spermiogenesis, expressed as total motile sperm count and HBA value. The novelty of our study is that a significant positive effect on sperm maturity is already observed after 1 month, opening novel therapeutic perspectives. While the standard cycle could increase the chance of both natural or ART pregnancies we propose that the "short treatment cycle" with FSH could be useful prior ART increasing the proportion of functionally competent cells. Our preliminary data does not support a clear-cut relationship between the $FSH\beta$ and FSHR genotypes and responsiveness to the treatment.

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