FSHR genotype is associated with different response to wild type FSH versus recombinant FSH

Lledo B (b), Dapena P (b), Morales R (b), Ortiz JA (b), Turienzo A (b), Guerrero J (a), Llacer J (a), Bernabeu R (a).
a: Reproductive Medicine, Instituto Bernabeu, Alicante, Spain. b: Instituto Bernabeu Biotech, Alicante, Spain.

INTRODUCTION

Previous studies have reported conflicting results for the comparative doses of recombinant FSH (rFSH) and highly purified FSH (wtFSH or FSH-HP) required for an adequate ovarian stimulation. Clinical studies have demonstrated that N680S polymorphism determines ovarian response to FSH stimulation in patients undergoing IVF. Patients with the S680 allele need more FSH during the stimulation. Nothing is known about the clinical efficacy of rFSH or FSH-HP depending on the N680S FSHR polymorphism.

METHODS

This retrospective study includes 382 cycles performed at Instituto Bernabeu (Alicante. Spain) from 191 oocyte donors genotyped for N680S. All donors carried out two cycles: one with rFSH and the other one with FSH-HP (n=63 group1), both with FSH-HP (n= 100 group2) or both with rFSH (n=25 group3). We compare the results in pair from each. The ovarian stimulation protocol was GnRH antagonist with starting doses 150, 225, 300 IU/day according to donor age, body mass index, clinical features and antral follicle count.

RESULTS

A total of 191 women were examined for the FSHR variant N680S in this study. In total, the results indicated that 83 patients had SS genotype (43%), 70 showed NS genotype (37%) and in 38 patients NN was detected (20%). (Figure 1).
The main outcome measures were oocyte yield, MII, days of stimulation and gonadotrophin dosages. No significant differences were reported when we compared the cycles for each donor in group 1. However, according to FSHR polymorphism statistical differences were shown in oocyte yield and MII. For SS genotype more oocytes (18 vs 17) and MII (16 vs 13; p<0,05) were yielded in a HP-FSH cycle. For NS genotype more oocyte (20 vs 16) and MII (17 vs 14; p<0,05) were yielded in a rFSH cycle (Table 1). For NN genotype no differences were reported. No significant differences were reported when we compared the cycles for each donor in group 2 and 3 regardless of the FSHR polymorphism.

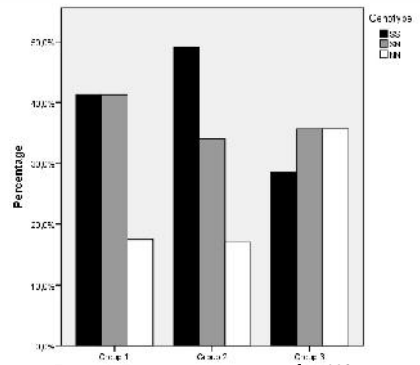

Figure 1. Frequency comparison of N680S.

Table 1. Group 1 donor ovarian stimulation data in relation to FSHR S680 genotype.

GENOTYPE		SS (52)	NS (52)	NN (22)
	Cycle	Average±SD	Average±SD	Average±SD
Donor age (y)	rFSH	25.4±4.1	26.0±3.6	25.0±4.3
	HP-FSH	25.6±3.8	26.4±3.8	25.6±4.0
Stimulation length (days)	rFSH	9.1±1.2	8.5±1.4	8.9±1.7
	HP-FSH	9.2±1.2	9.0±1.3	9.6±1.3
Gonadotropin used (IU)	rFSH	2071±524 [a]	1866±391	2030±686
	HP-FSH	1988±403	1884±458	2107±633
No. of retrieved oocytes	rFSH	16.9±6.8	20.1±8.6 [a]	19.3±7.0
	HP-FSH	18.4±8.0 [a]	16.9±6.5	20.6±8.1
No. of MII oocytes	rFSH	12.8±5.2	17.4±7.9 [a]	16.7±6.6
	HP-FSH	15.5±7.2 [a]	14.2±5.4	17.9±6.5
IU gonadotropin / MII oocyte	rFSH	162±101[a]	107±50	122±104
	HP-FSH	128±56	133±85[a]	118±97

Test performed for statistical analysis T-student for paired samples, [a]Differences between cycle with rFSH and HP-FSH. p<0.05

CONCLUSIONS

For the first time we show in a population of egg donors 680FSHR gene polymorphism affects the efficacy of wtFSH or rFSH. Genotyping FSHR N680S could help us to choose not only the doses of gonadotrophin but also the form of administration (rFSH vs HP-FSH) particularly in poor responders where the optimization of protocol is very important to achieve a high number of oocyte retrieval. A possible explanation could be different affinity to the FSH receptor. FSHR genotype is an important factor to determine the doses and the gronadotrophin administration in ovarian stimulation.