DOSAGGIO SIERICO DI STEM CELL FACTOR IN PAZIENTI “POOR RESPONDER” SOTTOPOSTE A CICLI DI FECONDAZIONE IN-VITRO: UN NUOVO BIOMARKER PER STABILIRE SE E QUANDO INDURRE L’OVULAZIONE ED EFFETTUARE IL PRELIEVO OVOCITARIO

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Review
The root of reduced fertility in aged women and possible therapeutic options: Current status and future perspectives

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INTRODUCTION

NO BIOMARKERS TO PREDICT THE SUCCESS OF ART TREATMENTS
IN TERM OF QUALITATIVE / QUANTITATIVE OOCYTES AND EMBRYOS COLLECTION ARE AVAILABLE

Circulating concentration of stem cell factor in serum of stimulated IVF patients

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SCF (STEM CELL FACTOR)

Pleiotropic cytokine with a molecular weight of 25–36 Kd that accomplish an effect on the target cells via the c-kit receptor, a tyrosine kinase receptor.

Data from human experimental studies investigating the expression patterns of SCF and c-kit in the ovary, as well as the actions of SCF on oocytes and theca cells, suggested that SCF may be important for many stages of follicular development and oocytes maturation.

SCF may be a candidate biomarker for the prediction of the success of a controlled ovarian hyperstimulation (COH) before ovulation induction and oocyte pick up?

Raffi F et al J Clin Endocrinol Metab, September 2012

Hu R et al Fertil Steril. 2014
Antimüllerician hormone regulates stem cell factor expression in human granulosa cells

AIM OF THE STUDY

TO EVALUATE IF THE SERUM CONCENTRATION OF STEM CELL FACTOR BEFORE OVULATION INDUCTION MAY BE CONSIDERED A NEW TOOL TO ESTABLISH WHETHER TO PERFORM FOLLICLE ASPIRATION OR NOT IN ELDERLY POOR RESPONDERS PATIENTS UNDERGOING IVF CYCLE

TO ACHIEVE THIS EVIDENCE, WE EVALUATED IF DIFFERENT PROTOCOLS OF OVARIAN STIMULATIONS MAY SIGNIFICANTLY INFLUENCE FOLLICULAR LEVELS OF SCF AND FURTHER IF THESE LEVELS MAY REFLECT THOSE OF SERUM
Pilot-observational-cohort study on 37 elderly infertile patients scheduled for IVF treatment at Padua University

Inclusion criteria

43 to 50 years
Estimated poor responders according to biochemical and sonographic features collected during ovarian reserve testing, as suggested by Bologna Criteria

Exclusion criteria

- history of smoking within the previous 12 months,
- deep endometriosis/endometrioma,
- abnormal karyotype,
- mutations of the cystic fibrosis gene,
- acquired or inherited thrombophilia and immunological disorders,
- previous chemo and/or radio therapy for neoplasia,
- untreated uterine disease,
- patients who received low-dose aspirin during treatment and cases in which oocyte retrieval was cancelled due to insufficient ovarian response

S-COH group: Patients were firstly treated by standard-protocol - long-agonist-protocol and recombinant-FSH (starting dose of 300 IU) -

LH-COH group: (in case of treatment failure) patients were secondly treated by LH- protocol within 6 months after previous cycle - different from S-COH only for the rLH supplementation (150 UI starting from the fourth day of rFSH administration).
Gonadotropin doses were adjusted according to biochemical and sonographic features of ovarian response beginning from stimulation day 5.

When at least 3 follicles exceeded 16 mm in diameter (or at least 1 follicle larger than 18 mm) were observed on transvaginal sonography, we administrated rhCG 250 for ovulation induction.

All retrieved oocytes were fertilized by ICSI technique.

All patients received high dose progesterone supplementation (600mg vaginally and 100 mg intramuscular for day) in association with valerate E2 (2mg vaginal tablet twice daily) for luteal phase support.

Both s-SCF and f-SCF were measured by ELISA Kit for SCF (R&D Systems Inc., USA, Human SCF Quantikine ELISA Kit - Catalog No: DCK00). The intra- and inter-assay coefficients of variation were <4 and <8 %, respectively, sensitivity was 9 pg/mL and the assay range was 31.2 to 2.000 pg/mL.
RESULTS

Table 1. Data regarding patients' general features and ovarian reserve test before IVF treatments.

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<th>Number of Patients</th>
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<th>Maximum</th>
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<td>Basal AMH</td>
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<td>0.1</td>
<td>0.5</td>
<td>0.219</td>
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</table>

135 MII OOCYTES RETRIEVED
FERTILIZATION RATE OF 74.8%
TOTAL 101 EMBRYOS
OF WHICH
38 (37.6%) GRADE 1
45 (44.6%) AS GRADE 2
18 (17.8%) AS GRADE 3

Figure 1. Comparison between S-COH and LH-COH treatments in term of both f-SCF and s-SCF levels.
RESULTS

Figure 2. Comparison between f-SCF and s-SCF levels using a linear correlation (cases were paired using a chromatic grey scale for number of events).

Figure 3. Stratification of MII oocytes retrieved and embryos obtained for s-SCF value.
Figure 4. Kaplan-Meier estimator curves for the estimation of events of at least 1, (fig 4a) 2 (fig 4b) or 3 (fig 4c) MII oocytes retrieved and pregnancy establishment (fig 4d) (s-SCF levels were used as a time function factors).
RESULTS

...TO SUM UP

- S-COH and LH-COH did not show statistical differences in term of f-SCF and s-SCF concentrations.

- On the contrary f-SCF and s-SCF levels showed a strong linear correlation. [p<0.001]

- Estimating the chance of collecting MII-oocytes we found that:
  - At least 3 MII-oocytes was collected with s-SCF>800 pg/mL
  - At least 2 MII-oocytes was collected with s-SCF>600 pg/mL
  - At least 1 MII-oocytes was collected with s-SCF>400 pg/mL
  - With s-SCF<400 pg/mL was not recovered MII-oocytes.

- Finally we found that all the 5 obtained pregnancies (6.9% of all treatments and 8.9% of treatments with transfer of at least 1 embryo) occurred in patients with s-SCF values >1000 pg/mL at pick-up.
THE COHORT OF ELDERLY POOR RESPONDER PATIENTS ASKING FOR AUTOLOGOUS IVF WILL INCREASE IN THE NEXT FUTURE DUE TO

- THE EXPECTED INCREASING POPULAR TREND OF DELAYING FIRST PREGNANCIES
- THE PERSISTENCE OF LEGAL, POLITICAL, CULTURAL AND RELIGIOUS BARRIERS TO OOCYTE DONATION, (IN SOME COUNTRIES IS STILL UNAVAILABLE)

THE INTRODUCTION OF S-SCF ASSAY IN THE ROUTINE MANAGEMENT OF ELDERLY POOR RESPONDER PATIENTS MAY CONTRIBUTE TO SOLVE THE DILEMMA OF WHETHER TO CANCEL OR CARRY ON THE STIMULATION CYCLE

THIS IS CRUCIAL TO SAVE THE COUPLE AN UNNECESSARY FINANCIAL AND EMOTIONAL BURDEN
... THANKS FOR THE ATTENTION...