RBM ONLINE

ELSEVIER

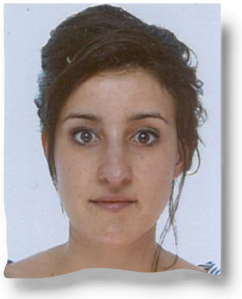
Article

Establishment and validation of a score to predict ovarian response to stimulation in IVF

Clelia Chalumeau [a], *Jessika Moreau* [a,b], *Nicolas Gatimel* [a,b], *Clementine Cohade* [a], *Florence Lesourd* [a], *Jean Parinaud* [a,b,*], *Roger Leandri* [a,b]

[a] *Médecine de la Reproduction, CHU Toulouse, 31059 Toulouse, France*

[b] *Groupe de Recherche en Fertilité Humaine EA 3694, Université Paul Sabatier, 31059 Toulouse, France*



Clélia Chalumeau is a Resident in Gynaecology at the Toulouse Medical University in France. She received her training in gynaecology and reproductive medicine. She is currently working in the Oncology Department of the Toulouse University Hospital.

KEY MESSAGE

A score, integrating clinical and biological parameters, can predict ovarian response and can be useful for customizing IVF treatments.

A B S T R A C T

This study aimed to integrate clinical and biological parameters in a score able to predict ovarian response to stimulation for IVF in gonadotrophin-releasing hormone (GnRH) antagonist protocols. A progressive discriminant analysis to establish a score including the main clinical and biological parameters predicting ovarian response was performed by retrospectively analysing data from the first ovarian stimulation cycle of 494 patients. The score was validated in a prospectively enrolled, independent set of 257 patients undergoing their first ovarian stimulation cycle. All ovarian stimulations were performed using a combination of GnRH antagonist and recombinant FSH. Ovarian response was assessed through ovarian sensitivity index (OSI). Parameters from the patients' database were classified according to correlation with OSI: the progressive discriminant analysis resulted in the following calculation: score = 0.192 – (0.004 × FSH (IU/l)) + (0.012 × LH:FSH ratio) + (0.002 × AMH (ng/ml)) – (0.002 × BMI (kg/m^2)) + (0.001 × AFC) – (0.002 × age (years)). This score was significantly correlated with OSI in the retrospective (r = 0.599; P < 0.0001) and prospective (r = 0.584; P < 0.0001) studies. In conclusion, the score including clinical and biological parameters could explain 60% of the variance in ovarian response to stimulation.

* Corresponding author.
E-mail address: parinaud.j@chu-toulouse.fr (J Parinaud).

https://doi.org/10.1016/j.rbmo.2017.09.011

Please cite this article in press as: Clelia Chalumeau, Jessika Moreau, Nicolas Gatimel, Clementine Cohade, Florence Lesourd, Jean Parinaud, Roger Leandri, Establishment and validation of a score to predict ovarian response to stimulation in IVF, Reproductive BioMedicine Online (2017), doi: 10.1016/j.rbmo.2017.09.011

Introduction

Ovarian stimulation with gonadotrophins is a key step in IVF. The response to stimulation varies widely from patient to patient and at the extremes leads either to excessive responses with the risk of hyperstimulation syndrome (OHSS) or to poor response with low results (Honnma et al., 2012; La Marca and Sunkara, 2014; La Marca et al., 2014). Therefore, there is a need for personalization of treatments to avoid cycle cancellation for inadequate response to gonadotrophins (La Marca and Sunkara, 2014).

The ovarian response is linked to the ovarian reserve (OR), defined as the number of antral follicles which can be stimulated by gonadotrophins. Its assessment is of great value to determine the prognosis of fertility treatments and the choice of protocol to be used in assisted reproductive technologies (Verhagen et al., 2008). OR can be evaluated by two direct parameters: antral follicle count (AFC) and serum anti-Müllerian hormone (AMH). These have been reported to have the best predictive value of ovarian response (Lan et al., 2013; Nelson et al., 2015). Indirect parameters, such as age and FSH, have also been shown to influence the level of response to gonadotrophins (El-Shawarby and Khalaf, 2009; Oehninger et al., 2015). Other parameters such as body mass index (BMI) (Ozekinci et al., 2015), tobacco smoking (Freour et al., 2012) or alcohol consumption (Nardo et al., 2007) can also influence ovarian response to stimulation for IVF. Therefore, ovarian response appears to be multiparametric and there is a need to integrate all parameters to benefit the choice of gonadotrophin starting dose. Such a study has already been performed by La Marca et al. (2012) for agonist protocols. The present study aimed to establish a score predicting the response in antagonist protocols, including parameters influencing ovarian response, by the use of a progressive discriminant analysis.

Materials and methods

Patients

A retrospective and prospective cohort were included in this study. The retrospective cohort (n = 494) included all patients meeting the inclusion criteria and having their first ovarian stimulation in 2014 and 2015. Patient characteristics are summarized in **Table 1**. The prospective cohort (n = 257) was a different group of patients who met the same inclusion criteria and had their first stimulation in the first semester of 2016. These patients were recruited on the first day of ovarian stimulation. All patients (n = 761) who had their first follicular puncture for IVF in 2014, 2015 and the first semester of 2016 in the Department of Reproductive Medicine of the Toulouse University Hospital entered the study, whatever the cause of infertility. Patients were included in the study if the delay between the evaluation of OR (AFC and AMH, FSH, LH and oestradiol) and IVF was less than 1 year. Out of the 761 patients, 32 had polycystic ovaries. Because the main evaluation parameter was the number of collected oocytes, attempts in which the follicle puncture appeared difficult were excluded from the study. Only the first stimulation cycle for each patient was studied.

OR was evaluated by AFC (2–10 mm using a 2D 7.5 MHz probe) and AMH (Beckman, AMH Genll kit). All hormone measurements (AMH, FSH, LH and oestradiol) were conducted in the same laboratory (ART Centre of the Toulouse University Hospital), using the same methods, between cycle day 2 and 4.

Data were extracted from the ART Centre patient database. This database was approved by the French National Commission for Information Technology and Civil Liberties (CNIL) to be used for clinical research. Patients are aware that their data can be used for anonymous clinical studies unless they specifically state otherwise. According to a recent French law (2016–1537), non-interventional studies, such as from clinical databases, do not need to be submitted to an ethical committee.

Table 1 – Demographic data in the retrospective and prospective studies.

	Retrospective study N = 494	Prospective study N = 257
Age	33.7 ± 4.2	34.1 ± 4.1
FSH (IU/l)	7.3 ± 2.2	7.4 ± 2.2
LH (IU/l)	5.9 ± 2.5	6.0 ± 2.5
LH:FSH	0.86 ± 0.43	0.86 ± 0.42
Oestradiol (pg/ml)	37 ± 17	43 ± 24
AMH (ng/ml)	3.3 ± 2.9	3.3 ± 2.8
BMI (kg/m^2)	22.9 ± 3.4	22.7 ± 3.5
AFC	22 ± 11	21 ± 11
Time between OR assessment and stimulation (months)	6.7 ± 2.7	7.1 ± 2.6
Smokers (%)	98 (20)	53 (21)
Tobacco consumption (cig/day) (range)	0–20	0–20
Stimulation length (days)	11.6 ± 2.7	11.7 ± 2.2
Total number of injected rFSH units	2149 ± 958	2299 ± 955
Mean daily number of injected rFSH units	187 ± 76	198 ± 76
Number of collected oocytes	9.4 ± 4.9	10.6 ± 5.1
Ovarian response (number of collected oocytes/100 mean daily rFSH IU)	6.2 ± 4.5	6.7 ± 4.6
Number of ICSI (%)	332 (67)	199 (77)
Origin of sperm (%)		
Husband	427 (86.4)	236 (91.8)
Ejaculated fresh	30 (6.1)	10 (3.9)
Ejaculated frozen	2 (0.4)	2 (0.8)
Urinary frozen	18 (3.6)	4 (1.6)
Epididymal frozen	3 (0.6)	3 (1.2)
Testicular frozen	14 (2.8)	2 (0.8)
Donor		
Number of obtained embryos	5.1 ± 3.5	5.7 ± 3.7
Number of transferred embryos	1.6 ± 0.8	1.7 ± 0.9
Number of pregnancies (%)	154 (31)	70 (27)
Ongoing pregnancies (%)	121 (24)	48 (19)

Values expressed as mean ± SD, n (%) or range.
AFC = antral follicle count; AMH = anti-Müllerian hormone; BMI = body mass index; ICSI = intracytoplasmic sperm injection; rFSH = recombinant FSH.

Ovarian stimulation

All patients had an ovarian stimulation for an IVF/intracytoplasmic sperm injection (ICSI) using a protocol combining recombinant FSH (rFSH) (Gonal F® Merck, Lyon, France or Puregon® MSD, Boulogne, France) and gonadotrophin-releasing hormone (GnRH) antagonist (Cetrotide® 0.2 mg, Merck, Lyon, France or Orgalutran®, MSD,

Please cite this article in press as: Clelia Chalumeau, Jessika Moreau, Nicolas Gatimel, Clementine Cohade, Florence Lesourd, Jean Parinaud, Roger Leandri, Establishment and validation of a score to predict ovarian response to stimulation in IVF, Reproductive BioMedicine Online (2017), doi: 10.1016/j.rbmo.2017.09.011