Reproductive BioMedicine Online (2012) **24**, 532–539

www.sciencedirect.com
www.rbmonline.com

ARTICLE

Anti-Müllerian hormone for the assessment of ovarian response in GnRH-antagonist-treated oocyte donors

Nikolaos P Polyzos *, Dominic Stoop, Christophe Blockeel, Paul Adriaensen, Peter Platteau, Ellen Anckaert, Johan Smitz, Paul Devroey

Centre for Reproductive Medicine, Universitair Ziekenhuis Brussel, Vrije Universiteit Brussel, Brussels, Belgium
* Corresponding author. *E-mail addresses:* n.polyzos@gmail.com, nikolaos.polyzos@uzbrussel.be (NP Polyzos).

Dr Nikolaos P Polyzos obtained his MD (2003) and PhD (2010) degrees in the University of Ioannina in Greece. He completed his specialty training in obstetrics and gynaecology in the University Hospital of Larissa in Greece. He joined the Center for Reproductive Medicine Universitair Ziekenhuis Brussel, Vrije Universiteit Brussel, Belgium, in 2011, where he currently works as a gynaecologist visiting fellow, while he simultaneously is working on his second PhD thesis in biomedical sciences. Dr Polyzos has served as reviewer for 15 journals, as associate editor for one journal and as editorial consultant for the Physician's Information and Education Resource of the American College of Physicians.

Abstract Evidence regarding the role of anti-Müllerian hormone (AMH) among oocyte donors is limited and only involves gonadotrophin-releasing hormone (GnRH)-agonist-treated donors. This trial assessed the predictive ability of AMH for ovarian response among 108 oocyte donors treated with an antagonist protocol. In multivariate linear regression analysis, both AMH and age were independently associated with ovarian response (unstandardized coefficients 0.904 and −0.378, respectively). In receiver operating characteristic curve analysis, AMH performed better than age, but was a modest predictive marker for low (≤6 oocytes) and excessive (>20 oocytes) ovarian response (area under the curve (AUC) 0.643 and 0.695, respectively). Similarly, a multivariate logistic model including AMH and age was also modest (AUC 0.651 and 0.697 for low and excessive responders, respectively). The predictive ability of AMH did not significantly alter when different thresholds were adopted, such as <4 oocytes for low response and >25 for excessive response (AUC 0.759 and 0.724, respectively). Among oocyte donors treated with a GnRH-antagonist protocol, although AMH was correlated with the number of oocytes retrieved, it demonstrates a modest ability in discriminating women with low or excessive ovarian response.

KEYWORDS: anti-Müllerian hormone, AMH, GnRH antagonist, oocyte donation, oocyte donors, ovarian response

Introduction

Oocyte donation has become an increasingly used fertility treatment. The number of cycles using donor oocytes represents approximately 12% of all assisted reproduction cycles in the USA (Centers for Disease Control and Prevention, 2008). Nonetheless, despite the increase in cycles utilizing donated oocytes and the significant effect that this

1472-6483/$ - see front matter
doi:10.1016/j.rbmo.2012.01.024

may have for couples that are unable to conceive after assisted reproduction treatment with autologous oocytes, the financial burden related to donation remains high (Gorrill et al., 2001). First of all, managing an oocyte donor screening programme requires a great deal of time and effort and is associated with significant cost (Gorrill et al., 2001). Most women who express initial interest in the programme do not become active donors, with >70% voluntarily withdrawing from the screening process and almost 20% finally failing medical or psychological screening (Gorrill et al., 2001). Furthermore, the financial compensation of oocyte donors appears to represent a significant amount of money (Anonymous, 2007) with specific authorities even suggesting an increase in the compensation given (O'Dowd, 2010). Therefore it appears that appropriate selection of oocyte donors is of paramount importance for the proper and more cost-efficient functionality of an oocyte donation programme.

Donors' characteristics and ovarian reserve tests have been utilized to predict the level of ovarian response in oocyte donation cycles. Whereas donors' basal FSH concentrations were not associated with response to stimulation and final oocyte outcome (Barton et al., 2010), antral follicle count (AFC; Melo et al., 2009b) and age (Barton et al., 2010) appear to be correlated with the level of ovarian response.

Recently, anti-Müllerian hormone (AMH), an ovarian reserve marker proven to predict ovarian response in infertile patients (Broer et al., 2009, 2011; Gnoth et al., 2008; Nelson et al., 2007), was assessed in oocyte donors. Only two retrospective studies examined the efficacy of AMH as a predictive marker for impaired and excessive response to stimulation among oocyte donors and these were performed in patients treated with a gonadotrophin-releasing hormone (GnRH)-agonist protocol (Nakhuda et al., 2010; Riggs et al., 2011). Whereas the results were promising regarding the predictive ability of the marker for hyper-response, contradictory findings were reported regarding the accuracy of AMH in the prediction of impaired ovarian response.

Taking into account the lack of a significant amount of evidence regarding the role of AMH in oocyte donors, and the fact that the GnRH-antagonist protocol is increasingly used for the treatment of oocyte donors (mainly due to the fact that in combination with agonist triggering it totally eliminates the likelihood of ovarian hyperstimulation syndrome) (Galindo et al., 2009; Melo et al., 2009a), the current study attempted to examine the role of AMH as a predictor of the number of oocytes retrieved among donors treated with GnRH antagonists. It therefore performed a retrospective cohort trial and assessed whether AMH may be considered as a useful marker to predict lower and excessive ovarian response in oocyte donors treated with GnRH antagonists and therefore may serve as factor that could tailor the selection process for an oocyte donation programme.

Materials and methods

Eligible patients

Oocyte donors between 18 and 36 years old who underwent ovarian stimulation and oocyte retrieval between 2009 and 2011 were included in this study. This study was approved by the ethical committee of the UZ Brussel.

All donors had normal menstrual cycles between 25 and 35 days. Women with polycystic ovaries, grade III or IV endometriosis, previous ovarian surgery or with basal FSH concentrations >15 mIU/ml were excluded from the oocyte donation programme. All eligible oocyte donors were treated with an antagonist protocol (Orgalutran; MSD, Oss, The Netherlands; or Cetrotide; Merck Serono, Geneva, Switzerland) starting from day 6 of stimulation, while ovarian stimulation was performed with rFSH (Puregon; MSD; or Gonal-F; Merck Serono) or urinary FSH (Fostimon; Mithra Pharmaceuticals, Liege, Belgium) at a dose ranging from 150 to 225 IU from cycle day 2 onwards, depending on the age and body mass index (BMI) of each donor. Ovulation triggering was performed with either 0.2 mg of GnRH agonist (Decapeptyl; Ipsen NV, Merelbeke, Belgium) for the majority of the donors (85%) while the rest received 10,000 IU human chorionic gonadotrophin.

All donors' files were retrospectively reviewed and AMH values that were obtained during the preliminary examination prior to stimulation, irrespective of the day of the menstrual cycle and based on the convenience of the donor, were recorded. In addition, other baseline characteristics such as age and BMI were also recorded, given that previous trials have shown that among IVF patients treated with a GnRH antagonist, age and BMI are related to insufficient ovarian response to mild stimulation (Verberg et al., 2007).

Anti-Müllerian hormone assay

Serum AMH was determined by the Immunotech AMH enzyme immunoassay (Beckman Coulter, Marseilles, France). The intra- and inter-assay coefficients of variation were <9.5% (3.3 ng/ml). Functional sensitivity of the assay was 0.35 ng/ml.

Outcome measures

The main outcome measures were to determine whether AMH values are related to the degree of ovarian response. Additional outcomes were to determine the predictive ability of AMH in order to predict low and excessive response to stimulation. This study defined oocyte donors with ≤6 oocytes retrieved at oocyte retrieval as low responders and those with >20 oocytes retrieved as excessive responders.

The thresholds of 6 oocytes for low ovarian response and 20 oocytes for excessive response were adopted in accordance with the threshold values used in previous published trials that assessed the value of AMH as a predictor of low ovarian response in GnRH-agonist-treated donors (Nakhuda et al., 2010; Riggs et al., 2011). Furthermore, a mean number of 6 oocytes per recipient results in a good ongoing pregnancy in this study centre (43.5%; Stoop et al., 2011), and this threshold further represents the minimal demand for entering the programme for a future donation.

Statistical analysis

Baseline characteristics (AMH, FSH, BMI and age) and results related to response (total stimulation dose required and