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Original article

Individualization of controlled ovarian stimulation in vitro fertilization using markers of ovarian reserve: a systematic review

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ABSTRACT

Introduction: The main objective of individualization of treatment in IVF is to offer every single woman the best treatment tailored to her own unique characteristics, thus maximizing the chances of pregnancy and eliminating the iatrogenic and avoidable risks resulting from ovarian stimulation. Personalization of treatment in IVF should be based on the prediction of ovarian response.
Objective: To summarize the predictive ability of ovarian reserve markers, and the therapeutic strategies that have been proposed in IVF after this prediction.
Methods: A systematic review of the existing literature was performed by searching Medline, LILACS, SciELO and Pubmed, for publications related to ovarian reserve markers and their incorporation into controlled ovarian stimulation (COS) protocols in IVF.
Results: 251 articles were found. Ten articles published between 2010 and 2015 were selected.
Conclusion: Antral follicle count (AFC) and anti-Mullerian hormone (AMH), the most sensitive markers of ovarian reserve, are ideal in planning personalized COS protocols. These markers permit prediction of the ovarian response with reliable accuracy. Following the categorization of expected ovarian response clinicians can adopt tailored therapeutic strategies for each patient.

Individualização da estimulação ovariana controlada na fertilização *in vitro* com o uso de marcadores da reserva ovariana: uma revisão sistemática

Palavras-chave:
FIV
Individualização

RESUMO

Introdução: O principal objetivo da individualização do tratamento na fertilização *in vitro* é oferecer a cada mulher o melhor tratamento sob medida para suas próprias características

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Reserva ovariana
Contagem de folículos antrais
Hormônio anti-Mülleriano

únicas, maximizar, assim, as chances de gravidez e eliminar os riscos de iatrogenia durante a estimulação ovariana. A personalização do tratamento na fertilização *in vitro* deve basear-se na predição da resposta ovariana.

Objetivo: Avaliar o uso de marcadores da reserva ovariana para individualização da dose inicial do FSH nos ciclos de FIV.

Métodos: Revisão sistemática da literatura feita por meio de pesquisa Medline, Lilacs, SciELO e PubMed, para publicações relacionadas com marcadores reserva ovariana e sua incorporação, estimulação ovariana (COS) e protocolos controlados em fertilização *in vitro*.

Resultados: Foram achados 251 artigos. Foram selecionados dez artigos publicados entre 2010 e 2015.

Conclusão: Contagem de folículos antrais (AFC) e hormônio anti-Müulleriano (AMH), os marcadores mais sensíveis da reserva ovariana, são ideais no planejamento de protocolos individualizados. Esses marcadores permitem previsão da resposta ovariana com confiança. De acordo com a resposta ovariana esperada, os clínicos podem adotar estratégias terapêuticas sob medida para cada paciente.

Introduction

It is well established that successful IVF and embryo transfer requires both stimulation of the ovary and suppression of the pituitary. Thus, exogenous gonadotropins and gonadotrophin-releasing hormone (GnRH) analogues are considered the hormones required to maximize IVF success.[1]

The daily dose of gonadotrophin administered in assisted reproduction technology may be fixed but usually it is progressively increased or tapered according to the given patient's response.[2]

A key issue in the management of cycles is defining the optimal starting dose of FSH for each patient in order to obtain the optimization of response and outcomes whilst minimizing the risks.[3–5]

In this article we discuss the use of the most recently identified markers of ovarian reserve, to categorize women based on their anticipated ovarian response. The marker-based strategy of assessing ovarian reserve in women in order to select the ideal therapeutic approach in IVF is reviewed.

Methods

A systematic review was conducted of studies published from January 2010 to December 2015 in English, Portuguese and Spanish. The following databases were consulted: Medical Literature Analysis and Retrieval System Online (MEDLINE), Literature Latin American and Caribbean (LILACS), Scientific Electronic Library Online (SciELO), and US National Library of Medicine (PubMed).

The descriptors used were: anti-Mullerian hormone (AMH), antral follicles, antral follicle count (AFC), ovarian reserve and several synonyms of IVF and ICSI. Among the studies identified, prospective studies, systematic reviews and retrospective studies that addressed ovarian reserve markers as predictors of ovarian response and individualized optimal dose of follicle stimulating hormone (FSH) to reduce inappropriate responses in an IVF cycle were selected. Inclusion criteria were studies with a sample composed of women <40 years of age with regular menstrual cycles, without ovarian anatomical changes and with causes of infertility treated by assisted reproduction techniques (ART).

The studies were selected independently and blindly by two authors according to the inclusion and exclusion criteria. Where there was disagreement between the two authors, the opinion of a third author was employed.

Two hundred and fifty-one published articles were identified from the descriptors and filters used. One hundred and one articles were excluded by the title, by reading the abstracts, or because of repetition in the databases, and 150 articles were selected that related ovarian reserve markers as predictors of ovarian response to individualized optimal dose of FSH to reduce inappropriate responses.

From these 150 articles, six that respected the inclusion criteria defined for this study were selected. The reference lists of the selected articles were analyzed to investigate the existence of new articles addressing the topic that could be incorporated.

Four more articles fitting the proposed inclusion criteria were included, making a total of 10 articles analyzed in this study.

Fig. 1 shows the flow chart summarizing the strategy adopted to identify and include the studies. Because this study used only data published in the literature, approval by an institutional review board was not required.

Results

Using the data from the articles, Table 1 was constructed for comparative analysis. Six of the ten articles analyzed were prospective studies dealing with clinical trials and cohort studies, and two was case–control studies with retrospective design. Furthermore, two systematic reviews were included in this study.