Commentary

Ovarian Sensitivity Index: A Cost Effective Marker for Assessing Ovarian Response

F Yadav A, Neena Malhotra*

Department of obstetrics and Gynaecology, All India Institute of Medical Sciences, New Delhi, India

DESCRIPTION

"More the Merrier" holds good for ovarian stimulation in in-vitro fertilization (IVF) cycle, but with a caution on hyper stimulation. In quintessence, the ideology to get more oocytes lies in not just getting the surplus embryos to cryofreeze for future use, but make them available for extended culture allowing selection of the best "Buddy" for transfer, and hence improving pregnancy rates in the index cycle [1]. So, to say controlled ovarian stimulation (COS) is not only crucial but an imperative step in determining success rates of IVF cycle. Therefore, it is vital to monitor the cycle during the COS gauging the response to stimulation, avoiding possible tribulations that could result in cancellation with a poor or excess response to gonadotropins.

While initiating COS during the IVF/ICSI cycle, some principles that guide us in individualizing the accurate protocol and the starting dose and the type of gonadotropins are the ovarian reserves that decipher the responsiveness of the ovaries to a given stimulation. The markers which are conventionally being used for determining ovarian reserve are age, antral follicle count(AFC), anti-Mullerian hormone (AMH), basal levels of estradiol (E2), Follicle stimulating hormone(FSH), Luteinizing hormone(LH) and inhibin-B [2-7]. These markers are being used for stratifying patients in to risk categories prior to start of the IVF/ICSI cycle. It was found that the these markers when used in large group of cohorts for determining ovarian response the correlation was reasonably good but failed to do so in individual cases(8). Presently, AMH is quite promising marker with excellent correlation to the antral follicle numbers with better inter-cycle reproducibility in comparison to the conventional markers like AFC and FSH [9,10].

Of all the available markers, AFC and AMH are the most routinely used for grouping women into response categories with their inherent limitations. Defining a woman into a designate response category may seem plausible with available bio-markers but unexpected surprises like poor response in expected normal responder and vice a versa should always be kept in mind. Is there any other predictor of response during COS?

Another way of ovarian response measure is the retrieved oocytes number, total gonadotrophins dose required in the cycle or better still the ratio of the two called the ovarian sensitivity index(OSI). It is being inversely related to the dosage of gonadotrophins used. OSI recently has proven to be a refined predictor of response to COS, rather than the individual or combined ovarian reserve tests (ORT).The lower the FSH dose used during the stimulation cycle, the higher will be the ovarian sensitivity. Deciding the optimum and accurate dose for ovarian stimulation cycle has been a double-edged sword in which the lower dose might result in a poor response and the higher dose in to a hyper-response. So, with all these pitfalls with the individual markers the newer combined marker like OSI appears to be more reliable for determining the response to stimulation cycle, because it involves the amount of stimulation given also in to account.

OSI has been in use since its first mention in the pioneer study by Biasoni et al, who found that it has a significant correlation with response markers AFC and AMH, which were traditionally considered the best markers for assessing the same. Also, AMH and OSI were found to have a significant inverse correlation even stronger than that between AMH and the oocyte yield, or independently between total FSH dose and AMH. So, they advocated it as a stand-in marker to AMH assays in cost constrained areas for assessing ovarian response in IVF cycle [11].

Following this another study by Li et al, also found similar results in addition they have also seen that OSI has a significantly stronger correlation across the index and the subsequent cycle as compared to the oocyte yield [12]. Huber et al, found that OSI shows a logarithmic distribution, and they also determined cut off levels for poor and hyper response. And also found to have good predictive power in determining live birth than oocyte yield alone. The cut-off values given may be used for coalescing studies involving ovarian response patterns [13].

In our study [14], which was a large retrospective cohort, a significantly higher correlation of OSI with BMI and age was found, and it seems that these combined markers along with the traditional markers could be assimilated in forecast models for ovarian response prediction. It appeared to be a valuable and reliable index of ovarian responsiveness to gonadotrophins and can be useful to estimate the FSH dose [14].

Corresponding Author:

Neena Malhotra, Department of obstetrics and Gynaecology, Professor, All India Institute of Medical Sciences, New Delhi, India, Tel: 011-26593361; E-mail: malhotraneena@yahoo.com

While OSI measures the inherent characteristic which is not subjected to variation with gonadotropin dose manipulations in comparison to the oocyte yield which varies with the dose of gonadotrophins, reaching a potential only at maximal stimulation, OSI is easy to calculate and free of cost method for determining ovarian response and deciding the dose for the next IVF cycle. The biggest drawback being that it cannot be used for the index IVF cycle. It is potentially a valuable marker and can be used in the dose determining models to optimize IVF cycles. We are looking forward to larger randomized controlled trials to support the use routinely.

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