

## **Advantage of Utilizing Highly Purified Human Menotropin (Possessing HCG Activity) Over Plain Recombinant FSH in High Responders Presenting with AMH $\geq$ 5 ng/ml Undergoing IVF/ICSI-A Short Communication**

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### **Abstract**

It is well understood that patients with Polycystic ovary syndrome (PCOS) possessing high anti-Mullerian hormone (AMH) amount have a higher risk of getting ovarian hyperstimulation when attempting controlled ovarian hyperstimulation (COS) in cases undergoing 'in vitro fertilization' (IVF). Although with utilization of gonadotropin releasing hormone (GnRH) agonists for trigger for oocyte maturation in Gn RH antagonist cycles helps in avoiding Ovarian hyperstimulation Syndrome (OHSS), the ideal stimulation protocol is further required to be evaluated so that we can optimize the best pregnancy rates, live birth rates (LBR), avoid preterm or other pregnancy losses secondary to the stimulation protocol, here Witz., *et al's* multicenter study points that utilizing only HPhMG (possessing HCG activity like menopur or humog against recombinant follicle stimulating hormone (FSH)) alone might yield the best results with least complications.

**Keywords:** PCOS; High AMH; HPhMG; OHSS

The ideal medicine regimen for controlled ovarian hyperstimulation (COS) in 'in vitro fertilization' (IVF) has not been accepted uniformly as well as differs depending on the individual patients properties. For decision on a stimulation protocol a lot of practitioners depend on their long term experience, besides their 6<sup>th</sup> sense, Instead of scientific results for arriving at the decision. Certain of them might debate that this constitutes partially to the art of medicine, that is reverse on the basis of proof dependent medicine. Moreover, it has greater, feasibility that arriving at the choice of a stimulation protocol based on just on ones whims and fancy might result in lesser clinical results. Albeit maximum *in vitro* fertilization (IVF) centers mostly carry out utilization of both follicle stimulating hormone (FSH) along with Luteinizing hormone (LH) activity with regards to their COS protocol, still altercation on the ideal dosage of each is present [1]. i) It has been pointed in various studies that utilization of a markedly purified human menopausal gonadotropins (HPhMG) possessing inherent LH activity might have better embryo quality, besides potential reduction in Ovarian hyperstimulation Syndrome (OHSS) that includes the studies of the the Menopur in GnRH antagonist Cycles with Single embryo transfer- High responders (MEGASET HR) [2-4]. We had further reported a case of severe Polycystic ovary syndrome (PCOS) unresponsive to stimulation with HP-hMG (humog- instead of menopur possessing hCG activity 5 instead of 9 in menopur [5]. Maximum practitioners clinically think that patients population which might have greater flexibility to alterations in the doses along the formulation regimen but minimal data is existing to draw any supposi-

tions. Although another problem exists of mixing rFSH with HPhMG-together with as separate as is occurring commonly in USA that ends in higher chances of complications like OHSS etc.

The Menopur in GnRH antagonist Cycles with Single embryo transfer- High responders (MEGASET HR) Trial that has been documented by Witz., *et al.* [6] has illustrated the advantage of scientifically analyzing the fruitfulness of COS) in IVF. They conducted a well-designed noninferiority study that evaluated a well-defined population of patients displaying a greater ovarian reaction. The observation of their study pointed to HPhMG utilization with regards to COS result in akin success rates along with lesser side effects in contrast to ovarian stimulation with utilization of recombinant follicle stimulating hormone (FSH) by itself alone. On utilization of anti-Mullerian hormone (AMH) amount  $\geq$  5 ng/ml in the form of their major inclusion criteria gives us a chance to precisely delineate a study group of patients possessing a greater chance of being high responders as well as possessing a greater risk of generation of OHSS. Despite this being a heterogeneous population of Polycystic ovary syndrome (PCOS) as well as other patients, they belong to a group where the ideal stimulation protocol is not clarified.

This study's outcome precisely illustrates the noninferiority of gonadotropin releasing hormone (GnRH) antagonist dependent COS protocols with utilization of HPhMG alone vis a vis rec FSH alone. There were akin LBR in both HPhMG alone vis a vis rec FSH alone groups in fresh (52.5% vs 48.7% respectively) as well as frozen thawed embryo transfer (FET) (63.4% vs 50.8% respectively) cycles. Intriguingly early pregnancy loss rates further significantly lesser with the HPhMG protocol vis a vis the rec FSH alone (14.5% vs 25.5% respectively) just like the rates of OHSS (9.7% vs 21.4% respectively). These observations are surprising as well as pointed to patients anticipated to be greater responders, it might be beneficial to utilize this regimen made up of HPhMG.

The strengths of this study are obvious i) it is a multicenter randomized controlled trial (RCT), with precisely marked study population, therapeutic plans along with measurable end points. RCT'S yield the maximum amount of proof as well as reduces to the least any earlier known /unknown intervening factors. iii) There was a well-defined population as well as study regimens getting easily reproduced. The observation that certain patients got  $\geq$  1 or even multiple embryo transfer (ET) off protocol might be the only real point of criticism. The decision on live birth rates (LBR), the result of maximum significance, being the primary end point further highlights how high quality study it is. Additionally, with the broad kind of centers included in the study the observations seem to be reliable for most of IVF centers, hence can generalize for all IVF practitioners. Moreover, initiation with 150iu dose of HPhMG was enough for maximum patients in trial as well as might give an initiating point for clinical utilization.

Despite the claim of the authors that fresh embryo transfer (ET) in this study yielded fruitful results, besides taking smaller time in pregnancy, it is just a gain that doesn't come without associated losses. The escalated incidence of OHSS is not warranted, knowing that utilization of GnRH agonist trigger in addition to high quality evidence to validate that cryopreservation of each embryo might prevent hyperstimulation [7]. Further these patients possess greater capacity to generate greater serum estrogen [E2] amounts, that have been demonstrated to escalate risk of poor obstetrical results [8]. Lastly the approach of cryopreservation of each embryo in the study aided in the utilization of preimplantation genetic test-for aneuploidy (PGT-A) as well as greater LBR in both HPhMG. as well as rec FSH alone groups. This particular population of great responders is the specific target population where GnRH agonist trigger in addition to cryopreservation of all embryos approach is the best approach.

A personalized strategy to medicine seems to be the path for the future. It is significant that we practice utilization of a data -based strategy towards clinical practice to decide the best therapeutic approach a specific patient. Though we are hopeful that knowledge acquired via machines as well as "big data" would yield answers despite us not acquiring that till now. In the meanwhile, we have to determine with selection of the optimum protocol for COS for the patient we have to deal with currently. The patient has maximum faith along with getting emotional physically as well as financially restrained anticipating a child from the practitioner she/he has put faith in for achieving a child. It becomes our moral duty to give the best that we can drive from the data -based strategy since human beings can waiver over their 6th sense or intuitions [9].

The marked heterogeneity of infertile patients makes generation of proof dependent studies-tough, to derive enough differentiation power in studies for the total infertility population as well as subsequently maximum research work in this field focuses a particular group constituting good or poor prognosis patients for ensuring the evaluation derives certain meaningful outcomes. This as a result hampers the generalization of the studies. Thus, Witz., *et al.* [6], have given good quality proof that patients possessing a precycle AMH  $\geq$  5 ng/ml might get advantage from a stimulation protocol with utilization of HPhMG, leading to a greater LBR besides lesser risk for complications.

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