Commentary

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Selective Single Embryo Delivery Using HEED and SEED Optimizing Results from IVF While Reducing Risks and Side Effects

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Abstract

Although embryo transfer technique has been known to be a major limiting factor in accomplishing a successful live birth from IVF, there has been little progress made in embryo transfer technique in the past 40 years. Here we describe novel techniques of HEED and SEED that will optimize results and reduce risks and side effects from IVF procedures.

Keywords: *In vitro* fertilization; Embryo transfer; Hysteroscopic endometrial embryo delivery; Sub endometrial embryo delivery; Elective single embryo transfer; Maternal health; Reproductive safety

Abbreviations: IVF: *In Vitro* Fertilization; ET: Embryo Transfer; HEED: Hysteroscopic Endometrial Embryo Delivery; SEED: SubEndometrial Embryo Delivery; eSET: Elective Single Embryo Transfer

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Introduction

There has been a lot of progress made in increasing pregnancy results from IVF procedures since the world's first human IVF pregnancy in 1976 [1]. These include advanced and novel methods of ovarian stimulation [2-9], less invasive oocyte collection techniques for oocyte collection [10-16], improved oocyte culture media, sperm injection, improved media for extended embryo culture [17] and evolving techniques for preimplantation genetic screening and diagnosis. However, even after 80,00,000 IVF's done worldwide, there has been little change in embryo transfer technique that has been a bottle neck in ensuring a successful singleton live and healthy birth from IVF procedures [18].

A persistent dilemma is how to increase live, healthy pregnancy rate while decreasing major risks and side effects namely multiple pregnancies, ectopic pregnancies, lost embryos and placenta previas as a result of doing IVF.

When we look at the 2014 national ART data summary [19] more closely, eSET accounts for a mere 28.5% at best for age less than 35 and as low as 0.4% for more advanced age. Triplets and more are 80-300 times more than natural occurrence. A high rate of ectopic, previas and lost embryos are universally acknowledged.

A very recent ACOG bulletin [20] states that multiple pregnancies are major contributors to maternal morbidity and mortality in the United States.

The endoscopic embryo delivery will help minimize these risks and side effects from IVF. This is accomplished by direct visualization of the uterine cavity during the replacement of the embryo onto (HEED) [21] or into (SEED) [22] specific zone(s) of transfer. In addition, it will allow for direct embryo implantation of the embryo into the endometrium [23]. Although multiple factors including integrin's, interleukins, CSF's, LIF's and others have been implicated in the process of embryo implantation, none have proven clinically useful to neither increase implantation rate nor live pregnancies. Direct implantation will further help with the process of embryo implantation just as ICSI has helped with oocyte fertilization by sperm.

The endoscopic Sub endometrial embryo delivery (SEED) is particularly useful for implanting a single embryo in the zone of embryo delivery under direct visualization. Once implanted within the endometrium, it will be fixed in place and there will be no further migration of the embryo into the fallopian tube nor will it grow over the internal OS (placenta previa) that exposes the mother and the baby to increased morbidity and mortality [24-26] and no further lost embryo(s) [27].

Another concern is possible injury to the endometrium [28,29].

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However, this is minimized as the uterine cavity is expanded prior to entry of the flexible mini hysteron scope into the uterus as opposed to no expansion with the current "blind" method of catheter entry. Furthermore, if an injury is identified by direct visualization, embryo delivery can be made in another area while under direct visualization which is not possible with the current "blind" procedure.

Discussion

With increasing demand for IVF procedures worldwide, there are significantly increased risks and side effects from the current practice of "blind" embryo transfer techniques that are associated with increasing maternal morbidity and mortality worldwide. Human IVF procedure has evolved over the past 40 years with over 80,00,000 procedures done so far. We should curb our enthusiasm for higher Pregnancy rates at any cost and embrace safer techniques with acceptable pregnancy rate and singleton live births while reducing the incidence of ectopic, placenta previas, wasted cycles due to undetected uterine injuries and contractions and lost embryos after embryo transfer. Short term benefits of multiple pregnancies i.e. reduced direct cost to patients desiring more than one baby at a time should be abandoned against the long lasting effects on maternal health, the babies and reproductive health and public safety and the enormous cost to the society. Using a targeted single embryo delivery whether by HEED or SEED will standardize embryo transfers by allowing a visually confirmed placement of the embryo. In addition, they allow for gentle placement of the embryo at optimum zone(s) of transfer under direct visual placement. Embryo delivery by HEED is used for embryo transfers at cleavage and more advanced stages of embryo development whereas SEED is strictly for blastocyst implantation. SEED will help alleviate problems with embryo implantation and minimize ectopic pregnancies and lost embryos. It will also minimize occurrence of placenta previas from IVF. Embryo delivery whether by HEED or SEED will be deferred if uterine contractions are observed during the hysteroscopy part of the procedures. Embryo is then frozen and Embryo delivery will be performed in a subsequent un-stimulated cycle when the uterus is quiescent as confirmed by hysteroscopy. These techniques will also open the door toward further progress to understanding of the fate of the implanted embryo(s) and its interactions with the endometrial environment and take us a step further beyond the enigma of embryo implantation.

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