Editorial

Trends in IVF

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Introduction

The birth of Louise Brown in 1978 was undoubtedly an event of historical significance, both for the medical community as well as for society. Since that time, *In Vitro* Fertilization (IVF) has revolutionized reproductive medicine. In just over three decades, IVF has evolved from a laboratory curiosity to a commercialized medical technology responsible for more than 5 million births worldwide. Indeed, the use of assisted reproductive technologies has dramatically increased since the first successful IVF cycle. In the United States, use of IVF grew approximately 90% between 1995 and 2010; nearly 150,000 fresh cycles were performed in 2010, accounting for over 1% of live births in the United States. In Greece, a staggering 5.8% of live births in 2007 were from Assisted Reproductive Technology (ART) with this proportion continuing to grow.

The last four decades have provided increased knowledge of the hormonal control of reproduction, thus allowing for the development of novel approaches to fertility treatment. However, these very strategies that aim to assist patients have contributed to elevated risk of multiple pregnancies and Ovarian Hyperstimulation Syndrome (OHSS), causing emotional, physical and economic harm to patients.

Reduction in multiple pregnancies

To improve the safety of IVF and in response to the increased risk of multiple pregnancies, IVF practitioners began transferring fewer embryos. In the United States, the average number of embryos transferred per cycle declined from 4.0 in 1995 to 2.3 in 2010, while pregnancy rates increased from 24% in 1995 to 30% in 2010. This decrease in the number of embryos transferred resulted in >60% reduction in the number high-order multiple pregnancies. A similar trend has been seen worldwide with the average number of transferred embryos being 1.78 in Australia/New Zealand, 2.67 in Asia, 2.16 in Europe, 2.97 in the Middle East, and 3.01 in Central/South America with an associated improvement in live birth rate. More recently, many fertility centers worldwide have instituted the concept of a single embryo transfer. To support this management, multiple observational studies comparing single Embryo Transfer (ET) with double ET have shown a lower incidence of multiple pregnancies with essentially no change in pregnancy rate. However, the patients included in these studies tended to be young with a good prognosis, thereby possibly limiting the applicability of this management to a specific patient population.

Reduction in ovarian hyperstimulation syndrome

While Ovarian Hyperstimulation Syndrome (OHSS) is a relatively uncommon iatrogenic complication of fertility treatment, its development can have serious consequences. In the past, OHSS was prevented/ ameliorated by gonadotropin 'coasting', cycle cancellation, and freezing all embryos. While these interventions are still utilized, recent novel stimulation strategies to specifically reduce this complication have developed. Use of low doses of gonadotropin ('mini-IVF'), natural IVF cycles, GnRH antagonists, and GnRH-analogue triggers have shown marked reductions in the incidence of OHSS. Further adjustments in protocols will trend toward improving the overall safety of IVF.

As we enter the fourth decade of this field, we are faced with ongoing technological advances to help patients achieve reproductive success.

In a short lifespan, the field of assisted reproductive technology has allowed patients to overcome essentially any form of infertility. The serendipitous discovery of intracytoplasmic sperm injection (ICSI) by Andre van Steirteghem in 1998 has provided a means to treat men with little or no sperm. Egg donors have allowed postmenopausal women to have families. Preimplantation genetic diagnosis/screening (PGD/S) has given us the option to screen embryos for inherited disease and has enabled couples with recurrent pregnancy loss to deliver a healthy child at term. Improvements in oocyte freeze-thaw technology have provided women a means to electively preserve their future fertility. Numerous centers are actively investigating methods of 'embryo profiling', predicting an embryo's genetic and developmental competence using proteomic and genomic technology. The current pace of innovation suggests that we will be seeing even more advances in the coming decades.

With these accomplishments and with the recognition of Professor Robert Edwards as a Nobel Laureate, IVF is now firmly established in the mainstream of medicine and society. Increasing the safety and success of IVF therapy in the setting of continuing technological innovation is the prime objective of all IVF practitioners. As providers within this medical field, we bear responsibility as we 'push the envelope' with assisted human reproduction. Indeed, we must always abide by the dictum, 'primum non nocere', or 'first do no harm.' As a field, we have adhered to, and will continue to follow, this command by striving to reduce the complications associated with IVF by decreasing the number of embryos transferred and by implementing safer stimulation regimens. Further improvements in the IVF laboratory, enhancements in stimulation protocols, and advancements in predicting an embryo's potential will continue. In the end, these innovations will provide the ability to safely stimulate patients and assure transfer of a single developmentally competent embryo, thus leading to the ultimate goal of a successful singleton pregnancy.

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Received September 28, 2012; Accepted September 28, 2012; Published September 30, 2012

Citation: Dayal MB (2012) Trends in IVF. J Fert In Vitro 2:e117. doi:10.4172/2165-7491.1000e117

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Continued innovation