

Mild approaches in assisted reproduction—better for the future?

Current approaches for in vitro fertilization (IVF) in the majority of assisted conception units throughout the world are aggressive, unphysiological, and expensive. Is this really necessary? There is a widespread belief among practitioners that for a woman the only consideration is a high success rate, and that the current practice of down-regulation, high-dose stimulation, and retrieval of a large number of oocytes yields a higher success rate per cycle and better outcomes. Incidentally, it also results in a higher income for the clinic, so surely, the argument goes, this is a win-win situation for both patient and practitioner. We will call this approach “conventional IVF.”

However, there are now strong reasons based on clinical results and research to challenge the philosophy underlying conventional IVF. There is little doubt that conventional IVF is associated with a high incidence of ovarian hyperstimulation syndrome (OHSS) and with increased maternal mortality due to the high estradiol levels generated. Would women prefer the conventional approach if they knew that a different method would abolish their risk of OHSS altogether? Would they be enthusiastic about the conventional approach if they realized that the majority of oocytes being collected are chromosomally abnormal? Or that the babies born as a result of conventional IVF have a higher incidence of low birth weight and stillbirth than those resulting from natural conception? Or if they knew that the situation could be improved by a different approach? There are important questions to be asked: What is the aim of IVF treatment? What is the goal of the individual couples? Is the profitability of clinics more important than the benefit of society in general? Are there good reasons to change the current trend?

There is now overwhelming evidence to support a more physiologic approach to IVF that will make it safer, more accessible, and more patient friendly toward achieving the long-term health of mother and child. We must ensure that we do no harm to the women who are undergoing IVF treatment, regardless of whether they get pregnant, regardless of whether they have a baby, and that we consider the long-term health of the offspring born as a result of IVF treatment (1). This includes preparing both the woman and the man before any IVF treatment is provided. We also have a fundamental obligation to increase the accessibility of IVF treatment by making it more affordable: reducing the cost of treatment by eliminating unnecessary interventions and decreasing the use of drugs.

We recommend a 360-degree approach to improving parental health and lifestyle before offering treatment when there is an opportunity and need. This would involve a multidisciplinary and evidence-based approach, consisting of a nutritionist, clinical psychologist (counselor), and fitness adviser working alongside a fertility specialist.

PRETREATMENT PREPARATION

Counseling patients on optimizing body weight (body mass index), improving nutrition, reducing alcohol intake, and

refraining from smoking and recreational drugs to improve general health and well-being is essential. Addressing a patient's preexisting medical and psychological conditions before embarking on IVF treatment is also of paramount importance.

MILD APPROACHES TO STIMULATION

The current conventional stimulation protocols can be complex, unphysiological, aggressive, and also unregulated. In contrast with these approaches, mild stimulation protocols can be safer and more patient friendly, with a minimized risk of OHSS and lower cost per cycle. The advances in endocrinology, ultrasound technology, and embryology have allowed us to make mild approaches to stimulation more successful and increasingly relevant in everyday practice. With increased efficacy and efficiency in the laboratory, there is less need for an increased number of eggs and embryos. Growing evidence shows that mild stimulation protocols have comparable success rates to conventional stimulation.

The primary aim of this more physiologic approach is to collect fewer but better quality oocytes. Studies have indicated that this approach is not only beneficial for oocyte/embryo quality but also for endometrial receptivity. Recent data from the analysis from the Society for Assisted Reproductive Technologies (SART) American National IVF Registry has suggested that retrieval of more than 15 oocytes significantly increases the OHSS risk without improving the live-birth rate in fresh autologous IVF cycles (2). Mild stimulation in an antagonist cycle with an agonist trigger has allowed us to eliminate OHSS. The retrospective analysis of the United Kingdom's Human Fertilisation and Embryology Authority (HFEA) data of IVF cycles performed from April 1991 to June 2008 showed a statistically significantly increased risk of adverse obstetric outcomes among hyperresponders compared with normal responders. Women who had more than 15 oocytes collected had a statistically significantly higher risk of having a low-birth-weight and preterm birth.

Segmenting IVF cycles as an egg collection cycle and an implantation cycle is recommended in high-stimulation cycles and in those with high estradiol levels to improve obstetric outcomes and neonatal health. Deferred transfer may result in better outcomes even with milder stimulation.

Natural and modified natural cycles have physiologically acceptable estradiol levels and are thus conducive for implantation and better health for the offspring. Natural cycle approaches for IVF have also proven to be effective for women with low ovarian reserve and poor responders.

Mild approaches are also beneficial for cancer patients. In vitro maturation followed by vitrification offers a realistic, safer method for fertility preservation without any delay.

MILD APPROACHES IN THE LABORATORY

Mild approaches in the laboratory would mean allowing natural selection of sperm for fertilization, without the excessive and unnecessary use of intracytoplasmic sperm injection (ICSI) wherever possible. There has been a tendency in

many clinics to use ICSI too readily and in some cases when it is unnecessary.

MINIMIZING MULTIPLE BIRTHS

Reducing multiple births is part of the strategy of mild approaches in assisted reproduction. This could be achieved by creating higher quality embryos and using a single embryo for transfer. A mild stimulation strategy is not opposed to the development of new techniques such as preimplantation genetic screening, which allows the selection of a viable single embryo for transfer.

SUMMARY

Mild approaches in assisted reproduction are aimed at achieving quality and not quantity of gametes, embryos, and endometrium with a view to protecting the long-term health and welfare of women and children at an affordable cost. The true success of IVF is in creating children who are full term and normal for gestational age without compromising the health of their mothers. Equal access to IVF treatment can only be achieved by reducing the cost and complications. The state and the society should not suffer as a consequence of IVF treatment. This is the time for change.

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