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Has the Time come for Universal PGD with IVF?

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In Vitro Fertilization (IVF) has been around for 40 years. Pregnancy outcomes, laboratory techniques, and common laboratory components of IVF have changed over time. ICSI (Intracytoplasmic Sperm Injection), available for 20 years, has morphed from a technique reserved for severe male infertility/sperm extraction utilization into a generalized technique for IVF in patients even without any male infertility. Pre-implantation Genetic Diagnosis (PGD) has now been available in primitive forms since 1990. Its use, ethics, and effectiveness have been murky at best until very recently. Prior to automated Complete Chromosomal Screening (CCS) techniques, the benefit of PGD never approached its promise. Should IVF/PGD for aneuploidy screening be the next standard part of IVF?

Clearly PGD for single gene disorders has medical and financial purposes, savings millions of health dollars on treatment of children with significant illness [1]. Uncertainty regarding the utility of PGD for aneuploidy screening stems in large part from general uncertainty about the true prevalence of aneuploidy in embryos. I believe it is fair to say that most clinicians did not believe so many morphologically good quality embryos in young women could be aneuploid. Recent CCS data confirm that aneuploidy significantly increases with age at levels exceeding 80-90%, but that even young women have baseline aneuploidy rates above 50% [2,3]. Even older FISH data from donor egg cycles showed rates of aneuploidy in excess of 50% [4]. So CCS has clarified answers that FISH data could not due to its inability to examine all chromosomes. Clearly the prevalence of aneuploidy is not unique to patients with recurrent pregnancy loss and advancing age, and therefore its benefits can now be applied to all IVF patients.

So even if we have general agreement about PGD aneuploidy results, how can universal IVF/PGD benefit patients? IVF with Single Embryo Transfer (SET) after PGD can maximize pregnancy rate and minimize risk of multiples. Assuming a high quality euploid embryo is available, pregnancy rates are exceeding high and stable across age groups [3]. Some studies have found implantation rates of greater than 60% per embryo from IVF/PGD/SET, double that from similar morphology non-PGD embryos [5,6]. So pregnancy is easier to achieve. The benefit in maternal and fetal morbidity, cost savings, and long term savings from the reduction in multiples is self evident. IVF/PGD/SET also minimizes the need for invasive testing (CVS/amniocentesis) in pregnancy which reduces third party expenses and unnecessary pregnancy risks. There is no reliable data by which to make sound recommendations for the need and benefit of invasive or even non-invasive genetic screening in pregnancy after PGD. But by reducing the use on aneuploidy embryos, PGD should greatly reduce the need for invasive antenatal genetic testing and thus reduce the number of termination procedures and related complications.

With an expansion of the use of PGD, patients must be counseled properly. The psychological role of fertility treatment failure cannot be underestimated. Reducing or eliminating the transfer of aneuploid embryos would likely reduce patient emotional discomfort. Once a transfer takes place patients tend to be more emotionally invested in the treatment process. So preventing the transfer of aneuploid embryos would decrease the number of transfers in general, reducing unnecessary medication administration, and decrease the costs of treatment. Ethically it is imperative that patients with fewer embryos available are advised that IVF/PGD may reduce negative pregnancy outcomes, miscarriages, and aneuploidy rather than increase live birth rates [7]. Patient expectations can be managed better through IVF/PGD but clinicians are forced to provide better counseling to patients now that more genetic and prognostic information is available [8].

Universal IVF/PGD will provide answers to patients and clinicians. This essentially eliminates aneuploidy as a reason for IVF failure and allows clinicians to focus on the uterus and systemic factors in patients who fail to achieve pregnancy. As PGD is applied to more patients, costs will decrease. Just as the costs of IVF, ICSI, hatching, and embryo cryopreservation have decreased with marketplace expansion over decades, PGD is at that point now. The cost-benefit role of universal PGD in total health care dollars will likely prove to be exceedingly low.

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