Five Things Physicians and Patients Should Question
by
Canadian Fertility and Andrology Society
Last updated: November 2019

1. Don't routinely perform preimplantation genetic testing for aneuploidy screening on patients undergoing IVF.

Preimplantation genetic testing for aneuploidy (PGT-A) was developed to help select the best embryos for transfer in an IVF cycle by screening out aneuploidy. However, there is no clear improvement in cumulative live birth rate compared with IVF alone. PGT-A is expensive, carries a risk of misdiagnosis, and there is no long-term data reported on childhood outcomes. PGT-A should not be performed routinely without an indication and patients should be counselled on the risks and limitations of testing.

Sources:

Forman EJ, et al. In vitro fertilization with single euploid blastocyst transfer: a randomized controlled trial. Fertil Steril 2013;100(1):100-107.

Scott RJ, et al. Blastocyst biopsy with comprehensive chromosome screening and fresh embryo transfer significantly increases in vitro fertilization implantation and delivery rates: a randomized controlled trial. Fertil Steril 2013;100(3):697–703.

Werner MD, et al. Clinically recognizable error rate after the transfer of comprehensive chromosomal screened euploid embryos is low. Fertil Steril 2014;102(6):1613–8.

Yang Z, et al. Selection of single blastocysts for fresh transfer via standard morphology assessment alone and with array CGH for good prognosis IVF patients: results from a randomized pilot study. Molecular Cytogenetics 2012;5:24.

2. Don't prescribe gonadotropins in doses of >450 units daily for controlled ovarian stimulation in IVF.

Several studies demonstrate that the use of high doses of gonadotropins (approximately 450 units daily or greater) does not result in an increased number of dominant follicles recruited, mature oocytes retrieved, nor good quality embryos produced compared with lower dosing regimens. Furthermore, higher doses of gonadotropins have been associated with an increased risk of ovarian hyperstimulation syndrome (OHSS). Given that there is a greater cost to the patient and potential for harm, with no evidence of an improved outcome, avoidance of high doses of gonadotropins is recommended.

Sources:

Friedler S, et al. An upper limit of gonadotropin dose in patients undergoing ART should be advocated. Gynecol Endocrinol 2016 Dec;32(12):965-969.

Haas J, et al. Do poor-responder patients benefit from increasing the daily gonadotropin dose during controlled ovarian hyperstimulation for IVF? Gynecol Endocrinol 2015 Jan;31(1):79-82.

van Tilborg TC, et al. Individualized FSH dosing based on ovarian reserve testing in women starting IVF/ICSI: a multicentre trial and cost-effectiveness analysis. Hum Reprod 2017 Dec 1;32(12):2485-2495.

3. Don't routinely perform laser assisted hatching on fresh embryos prior to transfer.

Laser assisted hatching (LAH) is a technique where the zona pellucida is disrupted to improve implantation and therefore live birth rates from embryos created through *in vitro* fertilization. Although there may be a benefit to performing LAH on fresh embryos in certain patient populations, the routine use of LAH for all patients undergoing a fresh embryo transfer has not been shown to improve live birth rates.

Sources:

Carney SK, et al. Assisted hatching on assisted conception in vitro fertilization (IVF) and intracytoplasmic sperm injection (ICSI). Cochrane Database Syst Rev. 2012.
Pfeifer S, et al. Role of assisted hatching in in vitro fertilization: a guideline. Fertil Steril 2014;102:348-51.
Sagoskin AW, et al. Laser assisted hatching in good prognosis IVF-ET patients: a randomized controlled trial. Fertil Steril 2007;87:283-7.

4. Don't prescribe corticosteroids, IVIG, leukemia inhibitory factor or lymphocyte immunization therapy for patients undergoing IVF, those with a history of recurrent implantation failure or patients with recurrent pregnancy loss.

Multiple studies have demonstrated no improvement in live birth rate or clinical pregnancy rate with steroids, granulocyte colony-stimulating factor (GCSF), leukemia inhibitory factor (LIF) or immunoglobulin (IVIG) in those undergoing IVF or those with a history of recurrent implantation failure (RIF). In women with a history of recurrent pregnancy loss (RPL), there is evidence demonstrating no improvement in live birth rate with IVIG or lymphocyte immune therapy.

Sources:

Achilli C, et al. The role of immunotherapy in in vitro fertilization and recurrent pregnancy loss: a systematic review and meta-analysis. Fertil Steril 2018; 110(6):1089-1100.

Boomsma CM, et al. Peri-implantation glucocorticoid administration for assisted reproductive technology cycles. Cochrane Database Syst Rev. 2012;13;(6):CD005996.

5. Don't routinely perform sperm DNA fragmentation testing.

High-grade evidence to support the routine use of sperm DNA fragmentation testing as part of initial screening investigations for infertility is lacking. Sperm DNA fragmentation tests are poor at predicting outcomes in patients undergoing assisted reproductive technologies, particularly for patients undergoing IVF or ICSI, and should not be used to guide treatment decision-making.

Sources:

Agarwal A, et al. Clinical utility of sperm DNA fragmentation testing: practice recommendations based on clinical scenarios. Transl Androl Urol 2016;5:935-50.
Cissen M, et al. Measuring sperm DNA fragmentation and clinical outcomes of medically assisted reproduction: a systematic review and meta-analysis. PLoS One. 2016;11(11):e0165125.
Pfeifer S, et al. The clinical utility of sperm DNA integrity testing: a guideline. Fertil Steril. 2013;99(3):673–7.
Zhang Z, et al. Sperm DNA fragmentation index and pregnancy outcome after IVF or ICSI: a meta-analysis. J Assist Reprod Genet. 2015;32:17–26.

How the list was created

The Canadian Fertility and Andrology Society (CFAS) Choosing Wisely National Working Group used a modified Delphi consensus approach, consisting of 5 rounds, to generate item ideas, review supporting evidence, assess clinical relevance, estimate

recommendation impact and narrow the items. The Working Group was comprised of 11 diverse clinicians with experience in the field. Round 4 of the Delphi process consisted of a National CFAS Membership Survey to rank the remaining 13 items. The top 5 items were selected based on 4 qualities: prevalence, cost, potential for harm and impact on clinical practice (round 5). The CFAS Board of Directors provided feedback which was incorporated into the composition of the final list approved by the Board.

About the Canadian Fertility and Andrology Society

The CFAS is a multidisciplinary national non-profit society that serves as the voice of reproductive specialists, scientists, and allied health professionals working in the field of Assisted Reproduction in Canada. The mission of the CFAS is to responsibly advance reproductive science and medicine in Canada through leadership, research and guidance.