Best Practice & Research Clinical Obstetrics and Gynaecology 26 (2012) 777–788

Contents lists available at SciVerse ScienceDirect

Best Practice & Research Clinical Obstetrics and Gynaecology

journal homepage: www.elsevier.com/locate/bpobgyn

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In vitro fertilisation treatment and factors affecting success

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Keywords:
assisted reproductive technology (ART)
in vitro fertilization (IVF)
ovarian reserve
follicle stimulating hormone (FSH)
anti-Mullerian hormone (AMH)
controlled ovarian hyperstimulation (COH)
intracytoplasmic sperm injection (ICSI)
embryo transfer
ovarian hyperstimulation syndrome (OHSS)

The efficacy of assisted reproductive technologies has improved significantly over the past decades. The main indications for in vitro fertilisation include tubal obstruction, severe male-factor infertility, severe endometriosis, ovulatory dysfunction, diminished ovarian reserve, and infertility of unexplained cause. In vitro fertilisation has also become an effective treatment option for couples wishing to undergo pre-implantation genetic diagnosis or screening, and for those wishing to cryopreserve their oocytes or embryos for preservation of fertility. The management of women in late reproductive age poses a major challenge; the optimum in vitro fertilisation treatment for poor responders remains elusive. The success of in vitro fertilisation treatment can be optimised by taking an individualised, patient-centered approach to controlled ovarian hyperstimulation. Key components involve selection of an appropriate controlled ovarian protocol, close-cycle monitoring, adjustment of gonadotropin dosage to avoid hyper-response, and individualised timing of human chorionic gonadotropin injection. Future directions of assisted reproductive technologies include development of non-invasive embryo selection methods, use of transcriptomics, proteomics, metabolomics, and time-lapse imaging technologies.

Introduction

The efficacy of assisted reproductive technologies (ART) has improved significantly since the first reports of successful pregnancies and live births after in vitro fertilisation (IVF) by Steptoe and Edwards[1,2] in 1978. In the USA, the live birth rate has increased from 38% to 48% among women under

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http://dx.doi.org/10.1016/j.bpobgyn.2012.08.017

the age of 35 years treated with ART over the past decade.[3] The European IVF-monitoring consortium and the International Committee for Monitoring Assisted Reproductive Technology also observed similar trends in ART success.[4,5] Assisted reproductive technologies have also become more accessible. In 2003, the number of ART cycles carried out worldwide exceeded over 1 million.[5] To date, an estimated 3.75 million babies have been born worldwide using ART.[6]

The most common ART procedure is IVF, which involves controlled ovarian hyperstimulation (COH) with gonadotropin administration to stimulate ovarian follicle development, followed by transvaginal oocyte retrieval, fertilisation of the oocytes with sperm in vitro, culture of the resultant embryos, and transfer of the embryo(s) to the recipient. An important innovation in ART is assisted fertilisation by intracytoplasmic sperm injection (ICSI).[7] Other modalities of ART include cryopreservation of gametes, embryos, and ovarian tissue, pre-implantation genetic diagnosis (PGD) or screening (PGS), the use of donor gametes, and gestational carriers.

In this chapter, the indications for IVF and factors affecting IVF success will be reviewed, along with IVF treatment options for women of advanced maternal age. We will also provide an update on the recent advancements in, and future directions of, ART.

Indications for in vitro fertilisation

In vitro fertilisation was first reported as a treatment option for women with severe tubal disease.[1,2] With improved efficacy after the introduction of gonadotropin stimulation and ICSI, the indications for IVF have expanded to include infertility caused by severe male factor, diminished ovarian reserve, ovulatory dysfunction, severe endometriosis, and infertility of unexplained cause. In vitro fertilisation also provides a new means of preconception genetic diagnosis and preservation of fertility. In fact, IVF is the most effective treatment option for couples with multi-factorial infertility problems.

Tubal factor

Tubal-factor infertility accounts for 30% of cases of female infertility.[3] Tubal damage has classically been associated with pelvic inflammatory disease, most often with Chlamydia trachomatis and gonorrhea infections. Other causes of tubal obstruction may be either intrinsic (e.g. ascending salpingitis and salpingitis isthmica nodosa) or extrinsic (e.g. surgical sterilisation, endometriosis and peritonitis) in origin.

Before the introduction of IVF, reconstructive tubal surgery was the only treatment option for women with tubal obstruction. At present, IVF is the treatment of choice for women over the age of 35 years with significant tubal disease and those with other co-existing infertility problems.[8,9] In vitro fertilisation is also indicated in women who remain infertile for 1 year after tubal surgery.

Male factor

Abnormal semen parameters may be a contributing factor in up to 40% of infertile couples.[3,10] In cases of severe oligospermia (fewer than 5 million motile sperm/ml), severe asthenospermia (less than 5% progressive motility), and severe teratospermia (less than 4% normal morphology based on strict Kruger criteria), IVF, or a combination of IVF and ICSI, should be offered,[11] as these semen parameters are associated with poor success with artificial insemination.[12,13] For women with obstructive or non-obstructive azoospermia, IVF with ICSI are indicated to achieve fertilisation using surgically retrieved spermatozoa from either microsurgical epididymal sperm aspiration[14] or testicular sperm extraction.[14–16]

Endometriosis

The incidence of endometriosis is reported to be in the range of 9–50% among women who underwent laparoscopy for infertility evaluation.[17,18] The exact pathophysiology of endometriosis and its effects on fertility remain enigmatic. Proposed mechanisms of damage include distortion of adnexal anatomy and adverse peritoneal environment characterised by increased inflammatory cytokines and