Current Strategies in Management of Infertile Couple

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ABSTRACT

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Infertility can be defined as the failure to achieve a pregnancy within 1 year of regular unprotected intercourse; Advances in our understanding of the causes of infertility and ART have facilitated the development of increasingly complex diagnostic tools, prognostic models and treatment options.

Personalized management strategies, based on individual patient characteristics, have been proposed and the further development of these strategies may represent real progress towards individually tailored fertility treatment.

The uses of hysteroscopy and Ultrasonography in the assessment of infertile women id discussed. The role of ovarian stimulation is controversial but often needed.

Keywords: Infertility, Semen analysis, Ultrasonography, ART, Ovarian stimulation.

Infertility can be defined as the failure to achieve a pregnancy within 1 year of regular unprotected intercourse (Evers, 2002; Zegers-Hochschild et al.,2006). Despite the inherent difficulties of estimating the prevalence of infertility (Greenhall and Vessey, 1990), it is generally accepted that one in four women are affected at sometime (Gunnell and Ewings,1994). Moreover, 20% of couples consult their general physician because of difficulty conceiving, and half of those couples (10%) require specialist care (Hull et al., 1985; Beurskens et al., 1995).

Assisted reproductive technology (ART) treatment for infertile couples now results in reasonably high pregnancy rates but may be associated with risks of ovarian hyperstimulation syndrome (OHSS) and multiple pregnancy (Van Voorhis, 2006). The variability in patient characteristics and response to ART dictate the need for proven, personalized diagnostic and therapeutic approaches to optimize efficacy and safety outcomes (Fauser et al., 2008).

Advances in our understanding of the causes of infertility and ART have facilitated the development of increasingly complex diagnostic tools, prognostic models and treatment options. It is hoped that the identification of reliable baseline demographic, disease or genetic characteristics that are predictive of treatment outcome will enable selection of the most appropriate management strategy for each couple. Furthermore, new laboratory techniques may facilitate the transfer of

single embryos while maintaining existing pregnancy rates (Van Voorhis, 2006).

Personalized management strategies, based on individual patient characteristics, have been proposed and the further development of these strategies may represent real progress towards individually tailored fertility treatment.

Individualized pretreatment assessment- The accurate detection of underlying reproductive abnormalities helps to guide individual management decisions and maximize ART treatment outcomes. Clinical evaluation of the infertile couple may be grouped into following categories: semen analysis, the post-coital test (PCT), assessment of ovulation, uterine and tubal evaluation, and laparoscopy (Balasch, 2000). Of these, semen analysis, mid-luteal phase serum progesterone level and tubal patency evaluation comprise the initial basic patient work- up (Crosignani and Rubin, 2000). However, the use of several fundamental elements of infertility testing is still contentious, and evidence suggests that the current World Health Organization (WHO) recommendations for the standard investigation of the infertile couple are poorly followed in Europe (Rowe et al., 1993; Balasch, 2000).

Semen analysis- Humans have a low proportion of 'normal' sperm compared with many other species. Although relatively few studies of semen analysis have been performed in men with proven fertility, there

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is a high degree of overlap in semen characteristics between fertile and infertile men (Guzick et al., 2001). High-quality semen analysis has diagnostic value for gross male infertility conditions (such as azoospermia or globozoospermia), but the predictive value of an individual semen analysis is less robust when moderate numbers of motile sperm are present (Comhaire, 2000). Semen analysis comprises sperm concentration, motility and morphology. No isolated semen analysis measures have been shown to be diagnostic of infertility in large studies (Guzick et al., 2001).

Greater quality control and standardization of clinical and laboratory evaluations are required to optimize ART practices and improve individual patient outcomes. Well-designed, good-quality studies are required to drive improvements to the diagnosis and management of ART processes.

There is no compelling evidence that either routine use of hysteroscopy before IVF or correction of identified pathology leads to better treatment outcomes. Compared with hysteroscopy, HSG has high sensitivity (81-98%) but low specificity (23-35%), and high falsenegative (10-90%) and false-positive (22-44%) rates. Although hysteroscopy is considered the gold standard for identification of intrauterine pathology (Bozdag et al., 2008), recent advances have enabled ultrasonographic techniques to increasingly substitute for invasive screening procedures (Ekerhovd et al., 2004). Late follicular phase TVS has proved to be a useful tool for the detection of intrauterine abnormalities such as polyps, synechiae, fibroids and Mullerian anomalies (Van Voorhis, 2008). SIS offers enhanced visualization of the endometrium and better detection of intrauterine pathology than does standard TVS, and may be as effective as hysteroscopy in detecting intracavitary abnormalities (Ragni et al., 2005; Valenzano et al., 2006). MRI may be used for patients with suspected complex Mullerian anomalies (Deutch and Abuhamad, 2008).

Uterine fibroids occur in 20–50% of women aged over 30 years and are the most common benign tumour of the female genital tract (Eldar-Geva et al., 1998; Okolo, 20 08). These tumours are heterogeneous in composition, size, location and number (Pritts, 2001), thus complicating the identification of women who would benefit from myomectomy prior to ART treatment. Retrospective data suggest that the presence of fibroids, 4 cm in diameter does not affect the outcome of ART treatment cycles (Vimercati et al., 2007). Additional retrospective analyses suggest that only fibroids that encroach on the uterine cavity negatively affect implantation rates and pregnancy

outcomes in ART (Farhi et al., 1995; Eldar-Geva et al., 1998). A meta- analysis suggested that compared with infertile women without fibroids, women with submucosal fibroids have significantly lower rates of clinical pregnancy [relative risk (RR 0.36, 95% CI 0.18–0.74), implantation (RR 0.28, 95% CI 0.12–0.65) and live birth (RR 0.32, 95% CI 0.12-0.85) (Pritts, 2001). Removal of submucosal fibroids improves clinical pregnancy rates (RR 2.03, 95% CI 1.08-3.83), but the limited available data suggest no improvement in treatment outcomes after removal of intramural fibroids (Pritts, 2001). Endometrial polyps have been identified by hysteroscopy in 16-27% of women with otherwise unexplained infertility (Kim et al., 2003; de Sa Rosa e de Silva et al., 2005). The benefit of hysteroscopic polypectomy on pregnancy rate has been demonstrated in a prospective, randomized study of women with ultrasonically diagnosed endometrial polyps who were undergoing IUI (Perez-Medina et al., 2005), in which patients who underwent polypectomy had a significantly higher cumulative pregnancy rate than those who underwent hysteroscopy plus polyp biopsy (63.4% versus 28.2%, P < 0.001) (Perez- Medina et al., 2005). An association between polypectomy and improved spontaneous pregnancy rates was also shown in nonrandomized studies (Varasteh et al., 1999; Spiewankiewicz et al., 2003; Shokeir et al., 2004; Stamatellos et al., 2008; Yanaihara et al., 2008). Retrospective data suggest that hysteroscopic polypectomy improves pregnancy rates in previously infertile women, regardless of the number or size of polyps present (Stamatellos et al.,2008), and that resection of polyps located at the utero-tubal junction may improve pregnancy rates in infertile patients (Yanaihara et al., 2008). Although the effect of endometrial polyps on IVF is unclear (Lass et al., 1999; Isikoglu et al., 2006), data suggest that women with otherwise unexplained infertility may still benefit from polypectomy (Stamatellos et al., 2008). In summary, prophylactic salpingectomy improves ART outcomes for patients with a fluid filled hydrosalpinx. However, there are currently insufficient highquality data on the optimum screening modality and management of other uterine and tubal abnormalities prior to ART on which to base personalized patient care. Good-quality, prospective studies are warranted to evaluate the relative merits of uterine and tubal screening tests and management approaches prior to ART treatment.

The use of ovarian stimulation in combination with IUI is a controversial and heavily debated topic (Fauser et al., 2005; Goverde et al., 2005; van Rumste et al., 2006). Biologically, the use of ovarian stimulation would

be expected to increase the likelihood of a multiple pregnancy because the development of multiple dominant follicles and ovulation of multiple oocytes is the aim of this intervention. However, published literature contains conflicting reports, which may be related to failure to induce multifollicular development or cycle cancellation after the detection of three or more pre- ovulatory follicles in half of the patients in some studies (Goverde et al., 2005; Verhulst et al., 2006; van Rumste et al., 2006). Nonetheless, a recent systematic literature review of studies of controlled ovarian stimulation and IUI clearly demonstrated that multiple pregnancy rates correlated positively with the number of pre-ovulatory follicles (van Rumste et al., 2008).

No differences in live birth rates were demonstrated with IVF or IUI either with (OR 1.15,95% CI 0.55–2.4) or without (OR 1.96, 95% CI0.88–4.4) ovarian stimulation in a Cochrane meta- analysis of clinical trials of unexplained infertility (Pandian et al., 2005). ICSI is associated with a significantly lower rate of complete fertilization failure in cases of unexplained infertility than conventional IVF (0.8% versus 19.2%; P < 0.001) (Jaroudi et al., 2003). However, data from three randomized controlled trials indicate that clinical pregnancy rates are similar following IVF or ICSI: 11% and 28%, respectively, per oocyte retrieval (P < 0.09)

(Jaroudi et al., 2003); 32% and 38% (RR 0.83, 95% CI 0.48–1.45) (Bhattacharya et al., 2001); and 50% for both [not significant (P-value not provided)] (Foong et al., 2006).

END NOTE

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