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ARTICLE

Cost-effectiveness of assisted conception for male subfertility

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Abstract Intrauterine insemination (IUI), with or without ovarian stimulation, IVF and intracytoplasmatic sperm injection (ICSI) are frequently used treatments for couples with male subfertility. No consensus has been reached on specific cut-off values for semen parameters, at which IVF would be advocated over IUI and ICSI over IVF. The aim of this study was to evaluate the cost-effectiveness of interventions for male subfertility according to total motile sperm count (TMSC). A computer-simulated cohort of subfertile women aged 30 years with a partner was analysed with a pre-wash TMSC of 0 to 10 million. Three treatments were evaluated: IUI with and without controlled ovarian stimulation; IVF; and ICSI. Main outcome was expected live birth; secondary outcomes were cost per couple and the incremental cost-effectiveness ratio. The choice of IVF over IUI with ovarian stimulation and ICSI over IVF depends on the willingness to pay for an extra live birth. If only cost per live birth is considered for each treatment, above a pre-wash TMSC of 3 million, IUI is less costly than IVF and, below a pre-wash, TMSC of 3 million ICSI is less costly. Effectiveness needs to be confirmed in a large randomized controlled trial.

KEYWORDS: cost-effectiveness, intracytoplasmic sperm injection, intrauterine insemination, in vitro fertilization, male subfertility

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Introduction

Male subfertility is a common condition, diagnosed as the sole cause in 30% of all couples presenting with subfertility and as a contributory factor in another 20% (Crosignani and Walters, 1994; Hull et al., 1985). Intrauterine insemination (IUI) with or without ovarian stimulation, IVF and intracytoplasmatic sperm injection (ICSI) are frequently used treatments for couples with male subfertility (Cohlen, 2005; Goverde et al., 2000; Tournaye, 2012). Despite their widespread use, their cost-effectiveness has never been compared.

In a large prospective study among subfertile couples on the prognostic capacity of semen quality for fathering a child after natural conception, a strong correlation was observed between semen parameters and the probability of natural conception (van der Steeg et al., 2011). A population-based study in first-time pregnancy planners found a strong predictive capacity of semen volume, sperm motility and sperm concentration for natural conception (Bonde et al., 1998). Furthermore, the total motile sperm count (TMSC) seems to have a consistent, direct relationship with the pregnancy rate per cycle after IUI, but no definite predictive threshold exists for success (Tijani and Bhattacharya, 2010).

Knowledge of the effectiveness of the available treatments, i.e. IUI, IVF and ICSI for male subfertility with different grades of severity, is limited. The role of IUI with or without ovarian stimulation in couples with mild male subfertility has been subject to much debate. No evidence of difference between the probabilities of pregnancy rates per woman was found when IUI was compared with timed intercourse in both natural cycles (odds ratio [OR] 5.3; 95% confidence interval [CI] 0.42 to 67). No statistically significant difference between pregnancy rates per couple for IUI with ovarian stimulation compared with IUI in natural cycle could be found (OR 1.5; 95% CI 0.92 to 2.4) (Bensdorp et al., 2007). In couples with moderate or severe male subfertility, i.e. a TMSC between 1 and 3 million, carrying out IUI before IVF is not based on comparative studies. It also remains unclear at which TMSC ICSI becomes more effective than IVF (Repping et al., 2002; Rhemrev et al., 2001). As a consequence, ICSI is recommended when extreme male subfertility is present (TMSC below 1 million), although epidemiological data to support such cut-offs are lacking. The few studies that compared IVF with ICSI in couples with male subfertility showed a higher incidence of fertilization failure in IVF compared with ICSI (Pisarska et al., 1999; Plachot et al., 2002; van der Westerlaken et al., 2006). A meta-analysis showed that the risk ratio for an oocyte to become fertilized was 1.9 (95% CI 1.4 to 2.5) in favour of ICSI, and 3.1 ICSI cycles may be needed to avoid one complete fertilization failure after conventional IVF (95% CI 1.7 to 12.4) (Tournaye et al., 2002). The probability of total fertilization failure is, therefore, crucial in the choice between IVF or ICSI treatment in couples presenting with male subfertility. Once fertilization occurs, pregnancy rates between IVF and ICSI do not differ (Repping et al., 2002).

Cost-effectiveness studies on interventions for male subfertility are scarce. A randomized controlled trial with a subset of 77 couples with mild male subfertility (TMSC between 1 and 20 million), reported IUI to be more cost-effective compared with IUI with ovarian stimulation and IVF (Goverde et al., 2000). The costs per pregnancy resulting in at least one live birth were US$ 4511–5710 for IUI and IUI with ovarian stimulation, and US$ 14,679 for IVF. This study, however, was conducted 15 years ago, when IVF success rates were rather low, and the small subset of couples with mild male subfertility did not allow robust conclusions to be drawn on this issue. A retrospective cohort study evaluated 3479 IUI cycles and 551 IVF cycles,and evaluated their cost-effectiveness (Van Voorhis et al., 2001). This study concluded that if the pre-wash TMSC was below 10 million, IVF–ICSI was more effective and less costly than IUI. As further comparative studies on IUI, IVF and ICSI are lacking, a computer-simulated cohort study was conducted on the subject. The aim was to compare the cost and effectiveness of IUI, IVF and ICSI in subfertile women aged 30 years with a partner with a pre-wash TMSC between 0 and 10 million.

Materials and methods

Three Markov decision trees were constructed for couples presenting with male subfertility who completed their basic fertility work-up. To evaluate the most cost-effective treatment, one cycle of IUI with ovarian stimulation was compared with one cycle of IVF; one cycle of IUI in the natural cycle was compared with one cycle of IVF; and one cycle of IVF was compared with one cycle of ICSI according to pre-wash TMSC.

A Markov model is a more complicated decision model used to analyse recurring events over time. Therefore, it is a useful tool for the evaluation of cost-effectiveness analyses in reproductive medicine, because in every cycle there is a new chance to conceive. Markov models can be used to compute the costs per live birth and the incremental cost-effectiveness ratio (ICER). The ICER represents the extra costs per live birth between two scenarios. These costs are calculated by dividing the differences in costs by the differences in live births of two scenarios. Normal practice is to order strategies or scenarios from the least to the most effective. Dominated strategies are then eliminated and the ICERs are calculated for each strategy compared with its next best alternative.

Details of computer simulation model

Patient characteristics

The base-case calculation was centred on a 30-year-old woman with a regular menstrual cycle, normal Fallopian tubes and a partner with a pre-wash TMSC between 0 and 10 million. A 30-year-old woman was selected, as the studies of pregnancy probabilities according to pre-wash TMSC were based on couples in whom the woman had a mean age near 30 years (Campana et al., 1996; Cohlen et al., 1998; Dickey et al., 1999; Dorjpurev et al., 2011; Van Voorhis et al., 2001; Zhao et al., 2004).

Models

Three decision trees were built. In model one, one cycle of IUI with ovarian stimulation was compared with one cycle of IVF. In model two, one cycle of IUI in the natural cycle was compared with one cycle of IVF. In model three, one cycle of IVF was compared with one cycle of IVF–ICSI. The used probabilities are presented in **Table 1**.