Intravaginal culture using INVOCELL: Is it a viable treatment option for infertility?

Since the first successful birth in 1978 from in vitro fertilization (IVF) treatment, it has rapidly become the mainstay of therapy for infertility. Today, couples undergo IVF treatment either directly following consultation and workup or following several unsuccessful ovulation induction cycles with or without intrauterine insemination, depending on the indication for treatment. There are significant cost differences among different fertility treatment options, with IVF being the most expensive. Affordability of this treatment was shown to be correlated with access to infertility care. Even a slight reduction in the cost was associated with improved access (1).

IVF treatment has evolved in the last 40 years and now, in most cases, includes ovarian stimulation, transvaginal oocyte retrieval, conventional insemination or intracytoplasmic sperm injection in the IVF laboratory, followed by embryo culture and embryo transfer either at cleavage or blastocyst stage. The complexity of the overall treatment and the demand for resources contribute to the high cost, and this treatment is especially financially demanding in the United States. Furthermore, the use of preimplantation genetic testing for aneuploidies and IVF add-ons can further increase the cost of the treatment (2). Strategies that would decrease the cost of IVF can include decreasing the gonadotropin dose and number of monitoring visits and avoiding IVF add-ons with limited evidence. Another option would be decreasing the demand for IVF laboratory services, such as embryo culture. Intravaginal culture (IVC) emerged as an option to circumvent the need for embryo culture in the laboratory and has evolved since its first implementation in 1988 (3). In 2015, the US Food and Drug Administration cleared INVOCELL (Ferring Pharmaceuticals, Parsippany, NJ) for IVC. INVOCELL is a small 1.5 in. × 1 in. device that is placed in the vagina, allowing the patient to effectively become an incubator for gametes during fertilization and for embryos during preimplantation development.

In this issue of *F&S Reports*, Jellerette-Nolan et al. present the experience of 463 patients from 5 fertility clinics who underwent 526 IVF cycles using INVOCELL for IVC (4). The authors describe that INVOCELL was most commonly offered to women <38 years old with body mass index <35 kg/m^2 and adequate ovarian reserve, excluding women with antimüllerian hormone <0.8 ng/mL in most cases. Stimulation protocols varied among centers and 9–16 oocytes were retrieved on average per cycle. INVOCELL was loaded with 1–30 oocytes, 95% of the embryos were cultured to the blastocyst stage, and most transfers were fresh (>60% in all but 1 center). The blastocyst development rate per inseminated oocyte ranged from 19%–34%, implantation rates were 39%–51%, and 78% of cycles proceeded to transfer.

Bypassing the need for IVF laboratory services seems to be an attractive strategy to decrease the cost of the treatment as long as clinical outcomes are not significantly compromised. The numbers of the current study speak for themselves and to date, only 1 other study from the United States assessed the efficacy of extended intravaginal embryo culture (5). In 40 good prognosis patients who underwent mild predetermined ovarian stimulation with single ultrasound and randomization on stimulation day 10, IVC resulted in 31% good quality blastocyst (≥2BB) development rate compared with 51% for IVF (primary endpoint). Live birth rates were not significantly different between groups. Future research with a greater granularity of data, controlling for the heterogeneity associated with different centers and analysis of patient subgroups can help identify the patients who are most likely to benefit from this technology.

Although IVC decreases the cost of IVF treatment by obviating the need for embryo culture in an IVF laboratory, possible decreased blastocyst formation rates and subsequent lower number of embryos available for transfer and cryopreservation need to be considered. Formal cost-effectiveness analysis with this technology is yet to be published, and this analysis will need to take the family building goals of the patients into account and will also potentially point to patient subgroups who are most likely to experience the decreased cost associated with this treatment.

The available limited data showed that blastocyst development rates with IVC appeared inferior to those of conventional IVF, highlighting the importance of appropriate patient selection. Future well-designed prospective controlled studies are needed to better examine the efficacy of IVC in its current form. Although IVC promises to be a viable treatment alternative for infertility, questions regarding its cost-effectiveness and outcomes in various patient populations need to be answered. As our understanding of fertilization and preimplantation development grows, progress will certainly be made in conditions required to support these processes. Improved fertilization and embryo development rates can make IVC an important part of infertility treatment in the years to come.

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