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Clinical outcomes of compaction stage embryo transfer versus blastocyst transfer in IVF –ET

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ABSTRACT

This study sought to evaluate the clinical outcomes of within the extended embryos sub group, compaction stage embryo transfer to that of blastocyst-embryo transfer in human in vitro fertilization- embryo transfer (IVF-ET). A total of 136 patients, fresh IVF-ET cycles were analyzed between 2012 and 2014; 79 cycles of compaction stage transfer and 57 of blastocyst transfer. There is no significant difference was observed between the compaction stage embryo transfer and blastocyst stage embryo transfer with respect to the female age (30.6+3.2 and 30.7+4.5) and the number of oocyte retrieved. This study has shown that compaction stage embryo transfer can be offered along with the other programs as it is found to yield good clinical pregnancy rates which are equivalent to the blastocyst transfer results.

Key words: Blastocyst, embryo, *in vitro* fertilization (IVF), pregnancy.

INTRODUCTION

The pregnancy rate appears to be influenced by the culture environment used for the gametes. Many clinical researchers are concerned with suboptimal culture conditions for embryo development before embryo transfer (ET). Thus, some authors have recommended day 2 or day 3 ET to avoid expected suboptimal culture conditions due to the prolonged culture time [1, 2]. Recent developments in the dynamics of embryo culture systems permit us to culture embryos beyond cleavage stage. Extended in vitro embryo culture has emerged as essential components of the advanced reproductive technology armamentarium. Sequential media that takes into account the changing metabolic requirement of the embryo, as it develops from the zygote to the cleavage, Morula and to the blastocyst stage, allows extended culture [3,4]. There by providing a customized growth environment suited to the specific needs of particular embryos, rather than expecting all embryos to adapt to a predetermined environment [5]. Having known that embryonic genome activates the 4-8 cells stage [6], extended embryo culture permit selection of more advanced embryos considered best suited for transfer and also allows chromosomally competent embryos to develop to the blastocyst stage and permits selection of embryos that have the potential for continued development under embryonic genomic control [7] In addition, selection of Day 5 embryos has the advantage of physiological synchronization with the uterine endometrium, thereby resulting in better pregnancy rates [8]. Blastocyst transfer shown to yield higher quality embryos resulting in increased implantation rates [9]. Although blastocyst transfer has

been shown to be beneficial and similar benefits were seen in compaction /Morula transfer [10]. Compaction or Morula stage embryo transfer is beneficial in several ways; the embryo is returned to the uterus, to an environment where it would normally reside. Post-genome activation will allow the embryo with the highest developmental potential to be selected from a cohort. An added advantage is being exposed to the uterine environment for the maximum time period and an in vitro environment for a minimal time period, before implantation. In addition, uterine contractility is reduced at this time, all of which maximize the potential for implantation [11, 12]. Multiple parameters contribute in the successful clinical outcome of a human IVF and nature of the association between clinical outcome and the parameters like, number and day of embryo transfer etc, bound fluctuate the outcome certainly. Present study was carried out to compare the clinical outcome within the extended embryos sub group, compaction stage embryo transfer to that of blastocyst-embryo transfer in human IVF-ET.

MATERIALS AND METHODS

A total of 136 patients, fresh IVF-ET cycles were analyzed between 2012 and 2014; 79 cycles of compaction stage transfer and 57 of blastocyst transfer. They were all under 35 years old, had more than 8 mm of endometrial thickness on the day of human chorionic gonadotrophin (HCG) administration. The data included the age of the patient, number of retrieved oocytes, fertilization rate and pregnancy outcomes were compared between compaction stage and blastocyst transfer.

Controlled ovarian hyper stimulation was performed using gonadotrophin-releasing hormone agonist/antagonist, and human recombinant follicle stimulating hormone. Human chorionic gonadotrophin (hCG) was administered when optimal follicle development was achieved, as evaluated by serial transvaginal ultrasound and serum estrogen estimations. Oocyte retrieval was performed via a transvaginal aspiration (Gynetics Single lumen follicle aspiration needle, Belgium) with ultrasound guidance 35 hours post hCG injection. The IVF or ICSI was performed with the respective male partner's spermatozoa. Fertilization was assessed 16 to 18 hours after insemination by ICSI/IVF. The fertilized oocytes were cultured with Vitrolife sequential media (Vitrolife's G-MOPS Plus, G-IVF Plus, G1 Plus, G2 Plus, Ovoil) until embryo transfer. Embryo quality assessment is done according to the Istanbul consensus workshop on embryo assessment in 2011 [13]. (The Istanbul consensus workshop on embryo assessment proceedings of an expert meeting Alpha Scientists in Reproductive Medicine and ESHRE Special Interest Group of Embryology Human Reproduction, Vol.26, No.6 pp. 1270–1283, 2011). Embryo transfer is done using Gynetics embryo replacement catheter (Gynetics Belgium & Sure Pro Wallace Embryo replacement catheter). Serum β-hCG concentration was measured 14 days after embryo transfer to confirm the pregnancy. Clinical pregnancy was confirmed by observation of the gestational sac (G-sac) on vaginal ultrasonography after 5 weeks of gestation. Statistical analysis was performed with (SPSS) program, and the average value was expressed as the mean ± standard deviation. Results were considered statistically significant if $p<0.05$

RESULTS

There is no significant difference was observed between the compaction stage embryo transfer and blastocyst stage embryo transfer with respect to the female age (30.6+3.2 and 30.7+4.5) and the number of oocyte retrieved. Similarly the fertilization rate (75.9 % and 77.4 %) and mean number of embryos transferred (2.8+0.5 and 2.5+ 0.6) also found to be no significant difference (Table.1). There was no significant difference in the clinical outcome in terms of pregnancy rate between the two groups (49.36% and 52.63%).

Table 1: Comparison of clinical pregnancy outcomes

Variables	Compaction stage Embryo Transfer N=79	Blastocyst Transfer N=57	p Value
Age of the patient	30.6+3.2	30.7+4.5	NS
Number of retrieved oocytes	549	399	NS
Number of fertilized	75.9 % (417)	77.4 % (309)	NS
Mean number of embryos transferred	2.8+0.5	2.5+ 0.6	NS
Clinical pregnancies (%)	49.36% (39)	52.63% (30)	NS
Multiple pregnancies			
Twin pregnancies	12 %(10)	10% (6)	NS

DISCUSSION

In a extended embryo sub group blastocyst transfer may lead to a higher pregnancy rate with an overall better take-home baby rate lead to reduction in multiple pregnancies [14, 15]. Day 5 ET is well-known to be the best choice for an IVF-ET program. However, day 4 ET can be a useful option in a busy IVF laboratory because day 4 embryos still have a potential for implantation even if they have not reached the morula or compaction stages [16]. The compaction stage embryo transfer had not paid enough attention in assisted reproductive technology program had been reported way back in 2002 by Jun et.al.,[10] It was practicing in limited cases where embryo biopsies were done preimplantation genetic diagnosis on day 3 embryos [17, 18]. Compaction embryo transfer can be a useful option in a busy IVF laboratory because day 4 embryos still have a potential for implantation even if they have not reached the morula or compaction stages. Consequently, day 4 ET can be chosen to avoid ET cancellation in day 5 ET resulting from suboptimal circumstances in the IVF laboratory such as an excess number of IVF cycles beyond lab capacity or other suboptimal conditions for blastocyst culture[19]. Several reports available on extended embryo culture and acceptable pregnancy rates can be achieved with day 4 embryo transfers; overall live-birth rate was reported 54.4%. Pregnancy and live-birth rates were similar across all age groups up to age 40 years [20]. Day 4 single embryo transfers were found to be a viable option or alternative to Day 5 single embryo transfers with no difference in pregnancy rates [21].

There is no significant difference was observed between the compaction stage embryo transfer and blastocyst stage embryo transfer in our observation. Similar studies have been reported by Lee *et. al*.,[19] stating that one can minimize excessive loading of culture systems and prolonged suboptimal culture conditions, day 4 ET can be chosen in a busy IVF unit. This strategy provides flexibility as to the day of ET, day 4 or 5, without affecting clinical pregnancy rates.

This study has shown that compaction stage embryo transfer can be offered along with the other programs as it is found to yield good clinical pregnancy rates which are equivalent to the blastocyst transfer results. In practical terms this indicates that instead of restricting the embryo transfers to day three or blastocyst transfer, compaction stage embryo transfer can be officered without affecting the clinical outcome benefits appears to be sane contemplation IVF program.

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