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Research Article

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IVF-ET Does Not Improve Live Delivered Pregnancy Rates vs Intrauterine Insemination Despite Mild Oligoasthenozoospermia in Women with Very Severe Diminished Oocyte Reserve

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ABSTRACT

Background: Though fecundity is markedly reduced in women with severely diminished oocyte reserve (DOR), nevertheless live deliveries are still possible. The objective of this study was to determine how much, if any, does in vitro fertilization (IVF) increase the chance of a live delivery in the presence of DOR complicated by the male partner having oligoasthenozoospermia. Though a reasonable pregnancy rate is usually found in the presence of oligoasthenozoospermia with intrauterine insemination (IUI) and even intercourse, lower egg quality could make it more difficult for lower quality sperm to achieve a pregnancy naturally.

Materials and Method: The study group consisted of women with marked DOR as evidenced by a serum anti-mullerian hormone (AMH) level <0.5ng/ml whose male partner had mild oligoasthenozoospermia. They were given the option of IVF or IUI. If they chose IVF, they were randomly assigned to have intracytoplasmic sperm injection (ICSI) or conventional oocyte insemination. Only women with one dominant follicle were selected.

Results: The results showed a 3% chance of a live delivery from IUI to IVF in one treatment cycle. ICSI did not improve outcome any better than conventional oocyte insemination.

Conclusion: These results thus suggest that with infertile couples where the female partner has severe DOR and the male has mild oligoasthenzoospermia, there does not appear to be any advantage of spending much more money to have IVF with or without ICSI.

Keywords: Diminished Oocyte Reserve, Oligoasthenozoospermia, In Vitro Fertilization, Intracytoplasmic Sperm Injection, Ethinyl Estradiol

Introduction

Women with moderate to severe diminished oocyte reserve (DOR) have a poor prognosis for achieving a live pregnancy even with in vitro fertilization-embryo transfer (IVF-ET). It is not clear that IVF-ET would improve the chance of a live delivery vs. natural cycles with correction of follicular maturation defects and luteal phase support with progesterone (P) without the advantage of the production of several embryos and the transfer of multiple day 3 embryos or the selection of a top-quality single blastocyst. Thus, for couples without insurance coverage for IVF-ET it may not make sense to spend the extra money for IVF-ET if there are a bilateral tubal patency and the absence of a severe male factor issue e.g., severe oligoasthenozoospermia. It is not clear how much does mild oligoasthenozoospermia negatively affect fecundity. Thus, this study evaluated women with such severe DOR that only one embryo was likely from either IVF or intrauterine insemination (IUI) cycles. The objective was to determine if IVF would lead to a higher live delivered pregnancy rate than IUI.

Materials and Methods

Couples were selected with a minimum of one year of infertility, whose female partner age <42 had a serum anti-mullerian hormone (AMH) level of <0.5 ng/ml and whose male partner had a motile density of 5 to 8 million and or % motility <30% and or 2% or less sperm with rapid linear motion (RLM).

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Couples were not included if morphology using strict criteria was 0%. Couples performing IVF using a follicle stimulating hormone (FSH) receptor upregulation technique for ovarian stimulation were excluded if more than one egg was retrieved [1,2]. Half of those choosing IVF were randomly assigned to ICSI and 50% conventional oocyte insemination. IUI was performed in natural cycles or with a small boost of exogenous FSH if the follicle was not mature. IUI cycles were not included if the serum estradiol (E2) did not reach 200 pg/ml or more, or the egg did not release by pelvic sonography [3]. Females received 10,000 units human chorionic gonadotropin (hCG) prior to IVF or IUI. The IUI was generally performed 40 hours after the hCG injection. A pelvic ultrasound was performed to check egg release from the follicle.

Results

The primary objective was to compare the live delivered pregnancy rates (LDPRs) in those women having IUI vs. oocyte retrieval. A second objective was to determine if ICSI was superior to conventional oocyte insemination during IVF.

There were 135 IUIs performed, leading to 4 live delivered babies (3.0%) per cycle.

There were 201 egg retrievals and in 169 an egg was retrieved (84.4%). This led to 74 transfers (43.8%). In 19 cycles an egg was atretic or immature, 49 had no fertilization and in 21 there was poor cleavage and 6 froze the embryos for the future. Subtracting the 6 frozen cycles 195 oocyte retrievals led to 6 live deliveries (3%). Three pregnancies resulted from conventional insemination and 3 from ICSI. The average serum AMH was 0.375ng/ml for the IUI group and 0.176 for the IVF group and respective average ages of the female partners were 39.1 for IUI and 38.7 for IVF.

Discussion

IVF does not seem to provide any benefit over IUI in couples where the female partner has marked DOR and the male partner has a slightly subnormal semen analysis as evidenced by a mild low motile density. Perhaps there were some couples that would have had failure to conceive had ICSI not been performed, but others may have failed to conceive with ICSI because the oocyte may be better able to select the normal sperm [4,5]. Also, possibly the mechanical invasion of the eggs by ICSI could have harmed the egg in some cases [4,5]. Thus, when women have marked DOR there does not seem to be justification to suggest IVF with or without ICSI compared to IUI if there are patent fallopian tubes and only a mildly subnormal semen analysis. With similar pregnancy rates per procedure, the low cost of IUI vs. IVF with or without ICSI gives the couple many more chances to conceive.

There are slight differences in the FSH receptor up-regulation technique used for IVF vs. IUI [1-3]. In the former, recombinant FSH is added when the serum FSH approaches a normal level to purposely try to recruit more than 1 follicle, if possible. In contrast, for IUI, to save money, expensive gonadotropins e.g., recombinant FSH or Menopur is only given if the follicle does not attain maturity (average diameter 18mm and serum E2 >200pg/ml naturally).

Nevertheless, these conclusions of no improvement in success with IVF vs IUI may not apply to patients with DOR of less severity since transfer of an extra embryo may provide a better chance of it being a euploid embryo.

Most studies find that IVF-ET results in a higher pregnancy rate per cycle than natural conception or IUI. We have found a 2.5-fold increase in live deliveries per treatment cycle with IVF-ET even in women of advanced reproductive age with DOR [6]. However, the DOR was less severe than in the present study, so the average number of embryos transferred was 2.1 per cycle [6]. The question is whether the IVF is more effective because of guarantee of sperm and oocyte contact as opposed to a natural or IUI cycles where sperm oocyte contact is less certain. There may be some cycles that there are adequate numbers of sperm reaching the egg but there is inadequate binding of the sperm to the zona pellucida leading to failed fertilization [7]. Possibly this could be overcome by the larger numbers of sperm contacting the zona pellucida with conventional oocyte insemination. Another possible reason for failure to conceive naturally is that some embryos die in the fallopian tube in natural cycles, or there may sometimes be failure of the fimbria of the fallopian tube to grab the egg. Another possible reason for higher pregnancy rates per cycle with IVF than natural where there is adequate egg reserve or only mild DOR is that there may be a higher chance of pregnancy related to multiple embryos transferred or a better selection of a good quality blastocyst from a cohort of embryos.

The equal pregnancy rates of this study suggest that failed fertilization is not a common event in natural cycles if sperm exposure occurs at the proper time. Similarly, these data suggest that lack of egg pick-up in natural cycles, or death of the embryo in the fallopian tube, or defects in the tube not allowing the embryo to teach the uterus at all, or at the right time, are not frequent causes of infertility. Thus, this study suggests that the higher pregnancy rates found in IVF vs natural cycles are mostly related to the creation of multiple embryos. Mother nature may not be able to select a chromosomally normal egg from a given cohort of antral follicles.

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