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Research Article

Comparison Intracytoplasmic Sperm Injection and *In Vitro* Fertilization in Patients with Only Few Oocyte Retrieval and Non-Male Infertility

Papageorgiou S* and Cima G
Department of Obstetrics and Gynecology, Ospedale Versilia Centro procreazione medical mente assistita "Ettore Barale", Italy

***Corresponding author:** Savvas Papageorgiou, Department of Obstetrics and Gynecology, Ospedale Versilia Centro procreazione medical mente assistita "Ettore Barale", Lido di Camaiore (LU), Italy

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Abstract

The aim of this work was to compare the efficacy of Intracytoplasmic Sperm Injection (ICSI) and conventional *In vitro* Fertilization (IVF) in patients with only few oocytes was available for insemination.

A total of 333 cycles with only one or two retrieved oocytes performed in 303 non-male infertile couples were retrospectively reviewed. Cycles were divided in two groups by different techniques: ICSI group (147 cycles) and IVF group (186 cycles). Groups were compared in terms of cycle cancellation rates, fertilization rates, cleavage rates, good-quality embryo rate, implantation rates, clinical pregnancy rates and miscarriage rates. The results showed that the clinical pregnancy rate (12.2% versus 22.5%) and implantation rate (11.8% versus 19%) were significantly lower in the ICSI group compared with the conventional IVF group. No significant differences were found in terms of cycle cancellation rate (23.1% versus 17.2%), fertilization rate (71% versus 77.6%), cleavage rate (97.4% versus 99%) and good-quality embryo rate (65% versus 60%) respectively. Our results suggest that, in patients with only few oocytes and in the absence of a male factor, conventional IVF might be the technique of choice.

Keywords: Assisted reproduction; ICSI; IVF; Oocyte insemination; Low responders; No-male infertility

Introduction

Intracytoplasmic Sperm Injection (ICSI) was introduced in 1992 to improve fertilization in couples with severe male factor infertility or in couples with fertilization failure in a previous *In vitro* Fertilization (IVF) program [1]. Recently, however the use of ICSI for patients with non-male factor has been increasingly [2,3], but the advantage of this technique is still controversial, in fact Kim et al. [4] have reported no differences in terms of fertilization and implantation rates between IVF and ICSI in contrast, other authors [5] recognize the efficacy of ICSI in terms of the number of fertilized oocytes and good quality embryos.

Also when a low number of oocytes are available for insemination the literature is divided, in fact some authors [6] have found that using ICSI is possible improves the fertilization rate and the formation of good quality embryos while others showed no differences between conventional IVF and ICSI in these patients [7-10]. However, some recent studies [11,12] suggest that IVF could be used as a technique of choice in young low responder patients, in fact the authors found the clinical pregnancy rate and implantation rate was higher in conventional IVF group.

The aim of this study is to evaluate whether there is different results between ICSI and conventional IVF when only one or two oocytes are available in patients with favorable semen quality.

Materials and Methods

We retrospectively analyzed data from a total of 333 cycles (303 patients) at the Ospedale Versilia Centro procreazione medical mente assist it a "Ettore Barale" between January 2008 and December 2013. All patients were considered eligible according to European Society of Human Reproduction and Embryology (ESHRE) consensus [13]. The patients with only one or two oocytes retrieved during ovarian pick-up were included in this study. All partners had normal semen parameters on the retrieval day. The couples signed an informed consent form approved by the Institutional Review Board, allowing retrieval of clinical data from patients' records, in accordance with Good Clinical Practice guidelines.

The cycles were divided into two groups by different fertilization techniques: the IVF group, insemination with conventional IVF and ICSI group, insemination with ICSI. The patients were treated with Gonadotropin-Releasing Hormone (GnRH) agonist (Enantone die; Takeda, Rome, Italy), which was started during the luteal phase (21°-23° day) of the previous cycle. Ovarian stimulation were administered on day 2 of the cycle with 300-450 UI of recombinant Follicle Stimulating Hormone (FSH) (Gonal F; Serono, Rome, Italy), according to basal FSH and Anti-Mullerian Hormone (AMH) levels; the dose was then adjusted according to individual responses, estimated by oestradiol assays and ultrasound scanning every other day. Recombinant human chorionic gonadotropin (Ovitrelle; Serono, Rome, Italy) was administered when at least one or two follicles reached a mean diameter of 17-18 mm. Oocytes were retrieved by ultrasound-guided transvaginal follicular aspiration 36h later.

All semen samples were collected following masturbation after 3-5 days of sexual abstinence and were allowed to liquefy for at least

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30 min. at 37°C. After liquefaction, volume, sperm count, forward motility and morphology were analyzed according to the World Health Organization criteria [14]. Sperm not meeting the defined threshold was classified as sub fertile sperm and the couples were excluded from the study. The semen samples were processed using a two-layer density gradient separation technique.

In the IVF group, the oocytes were incubated in culture medium (G-IVF™ Plus, Vitrolife, Sweden) and inseminated, 4-5 h after oocyte retrieval, with 150.000 motile washed spermatozoa. While in the ICSI group, oocytes were incubated in hyaluronidase (Hiase™-10X, Vitrolife, Sweden) for 20 s at a concentration of 80 UI/ml. Cells of the corona radiate were removed by gently pipetting in and out. Subsequently, the maturity of the oocytes was observed. Only oocytes in metaphase II were used for the ICSI technique.

Fertilization was confirmed by the observation of two pronuclei about 16-18 after fertilization technique. All the fertilized oocytes were transferred into a fresh cleavage medium (G-1™v5 Plus, Vitrolife, Sweden) and cultured until transfer. On day 2 (44-48h post insemination) the embryos were evaluated for cell number and rate of fragmentation by a single expert embryologist.

Embryo transfer was performed after 48-72h under the guidance of abdominal ultrasound, using K-Soft 5001 embryo transfer catheter (Cook, Ireland Ltd.). All patients had luteal phase support with daily vaginal progesterone (Prometrium 200 mg, Rottapharm, Italy) and intramuscular progesterone every day (Prontogest, AMSA, S.r.l., Italy), starting on the day of embryo transfer until both serum pregnancy test result was negative and gestational sac was confirmed on ultrasound. For patients with a positive serum pregnancy test, progesterone was confirmed until the 12th week of pregnancy.

Clinical pregnancy was defined as the presence of a gestational sac as well as at least one fetal heartbeat on ultrasound screening.

Statistical Analysis

The data were analyzed using the Student's t-test and all variables were expressed as mean ± Standard Deviation (SD). To compare proportion, we used the Fisher's exact test. A p value < 0.05 was considered to be statistically significant.

Results

A total of 333 cycles performed in 303 patients were reviewed. The 333 cycles consisted of 186 in the IVF group and 147 in the ICSI group.

The number of oocytes retrieved was similar between the two groups. The fertilization rate was higher in IVF group compared with the ICSI group (77.6% *vs* 71%), but this was not significantly different (p=0.123) (Table 2).

The percentage of cycles cancelled was 17.2% (32/186) in the IVF group compared with 23.1% (34/147) in the ICSI group (p=0.217) (Table 2).

The cleavage rate and good quality embryo rate did not differ between IVF and ICSI group (99% *vs* 97.4%; p=0.223 and 60% *vs* 65% p=0.335 respectively) (Table 2).

The clinical pregnancy rate for cycles in the ICSI group was significantly lower than in the IVF group (12.2% *vs* 22.5% p=0.015 respectively), also implantation rate was significantly lower in ICSI group in comparison with IVF group (11.8% *vs* 19% p=0.046) (Table 2).

The abortion rate was similar between the two groups (45% *vs* 38% p=0.77 IVF *vs* ICSI) (Table 1).

Table 1: Comparison of cycle characteristics among group (IVF *vs* ICSI).

	IVF-ET	ICSI	p-value
Age	38.6± 4.7	39.0 ± 3.8	0.43
FSH	10.5 ± 7.8	9.71 ± 4.5	p = 0.730
LH	6.46± 3.53	6.04±3.37	p = 0.749
E2	50.70 ±36.78	49.14±38.62	p = 0.782
PRG	1.05±0.83	1.14 ±0.31	p = 0.823
PRL	27.23 ± 22.57	26.04 ± 19.13	p = 0.837
Duration of infertility	2.88 ± 2.0	2.98 ± 2.1	p = 0.345
Numberof previous treatments	0.58 ± 0.77	0.99 ± 0.84	p = 2.29

Values are expressed as mean ± SD, *n*

Discussion

ICSI was originally indicated for cases with severe male factor infertility [15], but many studies indicated that this technique can provide a higher fertilization, a higher embryo quality and higher pregnancy rates in non-male factor couples [5,16] and the use of ICSI in patients with normal semen parameters has become more common [17].

However, the fact that ICSI may replace IVF in non-male factor infertility is still controversial [18].

Also in patients with low oocytes retrieval at the pick-up the ICSI is commonly used [4,7,9,16] but no differences were found, in fact the only advantage, is in theory to increase the number of embryos and to minimize the risk of complete fertilization failure [18,19]. On the other hand Ludwig et al. [6] demonstrated that ICSI, in the absence of male factor and with low oocytes recruited, increase the fertilization rate and the formation of good-quality in comparison with conventional IVF. Similar results are reported in a study by Khamsi et al. [5] but, recently Artini et al. [11] show that the analysis, on cohorts of low responder younger patients, reveals that the use

Table 2: Comparison of outcomes among group (IVF *vs* ICSI).

	IVF-ET	ICSI	p-value
n° cycles	186	147	-
n° of oocytes retrieved	1.6 ± 0.4 (309)	1.6 ± 0.4 (238)	0.42
Cycle cancellation rate, % (n)	32/186 (17.2%)	34/147 (23.1%)	0.217
Fertilization rate % (n)	233/ 300 77,6 %	156/218 71%	0.123
Cleavage rate % (n)	231/233 99%	152/156 97,4 %	0.223
Good quality embryo rate % (n)	139/231 60%	99/152 65%	0.335
Implantantion rate % (n)	44/231 19.0%	18/152 11.8%	0.046 *
Clinicalpregnancy rate % (n)	42/186 22,5 %	18/147 12,2%	0.015 *
Miscarriage rate % (n)	19/42 45%	7/18 38%	0.77

Values are expressed as mean ± SD, *n,* or *n* (%). *p<0.05

of ICSI decrease reproductive potential in fact IVF was significantly more advantageous than ICSI for what concerns implantation and pregnancy rates while no significant differences in fertilization and cleavage rates were observed. Also our retrospective results showed that when ICSI was used to treat non-male infertile couples with low oocytes recruited, no significant differences were observed in term of fertilization and good-quality rates but it resulted in significantly lower pregnancy and implantation rates. The same results were observed by Xi et al. [12] who retrospectively analyzed 406 cycles with three or fewer oocytes retrieved from women with the same age, in fact the authors showed that the pregnancy rate and implantation rate were significantly lower in the ICSI group compared with the IVF group. The higher pregnancy rate and implantation rate after IVF may be explained with the lacking of natural sperm selection when most steps of the fertilization process are bypassed by sperm injection in fact in conventional IVF the sperm that fertilizes is further selected through the biological process of sperm-oocyte interaction beginning at zona pellucida or during sperm penetration through the cumulus matrix [20]. Indeed, the finding that majority of sperm bound to the zona pellucida have a normal nuclear chromatin DNA [21] strongly suggest that embryologist subjectively selected sperm during ICSI may have a lower quality compared to zona pellucida-bound sperm. Moreover, increased knowledge in the biology of fertilization process has revealed that sperm-oocyte interaction at membrane level involves numerous molecular actors with a possible role in sperm fusion and gamete selection. All these mechanisms may explain the higher pregnancy and implantation rates in IVF group in comparison with ICSI group observed in our study.

Conclusion

We suggest that IVF could be used as a technique of choice in the patients with one or two oocytes recruited and normal semen parameters. However, since ours is a retrospective study, only further randomized trials will be able to confirm our result.

References

1. Palermo G, Joris H, Devroey P, Van Steirteghem AC. Pregnancies after intracytoplasmic injection of single spermatozoon into an oocyte. Lancet. 1992; 340: 17-18.
2. Oehninger S, Gosden RG. Should ICSI be the treatment of choice for all cases of in-vitro conception? No, not in light of the scientific data. Hum Reprod. 2002; 17: 2237-2242.
3. van der Westerlaken L, Helmerhorst F, Dieben S, Naaktgeboren N. Intracytoplasmic sperm injection as a treatment for unexplained total fertilization failure or low fertilization after conventional *in vitro* fertilization. Fertil Steril. 2005; 83: 612-617.
4. Kim HH, Bundorf MK, Behr B, McCallum SW. Use and outcomes of intracytoplasmic sperm injection for non-male factor infertility. Fertil Steril. 2007; 88: 622-628.
5. Khamsi F, Yavas Y, Roberge S, Wong JC, Lacanna IC, Endman M. Intracytoplasmic sperm injection increased fertilization and good-quality embryo formation in patients with non-male factor indications for *in vitro* fertilization: a prospective randomized study. FertilSteril. 2001; 75: 342-347.
6. Ludwig M, al-Hasani S, Küpker W, Bauer O, Diedrich K. A new indication for an intracytoplasmic sperm injection procedure outside the cases of severe male factor infertility. Eur J Obstet Gynecol Reprod Biol. 1997; 75: 207-210.
7. Moreno C, Ruiz A, Simón C, Pellicer A, Remohí J. Intracytoplasmic sperm injection as a routine indication in low responder patients. Hum Reprod. 1998; 13: 2126-2129.
8. Borini A, Gambardella A, Bonu MA, Dal Prato L, Sciajno R, Bianchi L, et al. Comparison of IVF and ICSI when only few oocytes are available for insemination. Reprod Biomed Online. 2009; 19: 270-275.
9. Gozlan I, Dor A, Farber B, Meirow D, Feinstein S, Levron J. Comparing intracytoplasmic sperm injection and *in vitro* fertilization in patients with single oocyte retrieval. Fertil Steril. 2007; 87: 515-518.
10. Fang C, Tang J, Huang R, Li LL, Zhang MF, Liang XY. Comparison of IVF outcomes using conventional insemination and ICSI in ovarian cycles in which only one or two oocytes are obtained. J Gynecol Obstet Biol Reprod (Paris). 2012; 41: 650-656.
11. Artini PG, Obino ME, Carletti E, Pinelli S, Ruggiero M, Di Emidio G, et al. Conventional IVF as a laboratory strategy to rescue fertility potential in severe poor responder patients: the impact of reproductive aging. Gynecol Endocrinol. 2013; 29: 997-1001.
12. Xi QS, Zhu LX, Hu J, Wu L, Zhang HW. Should few retrieved oocytes be as an indication for intracytoplasmic sperm injection? J Zhejiang Univ Sci B. 2012; 13: 717-722.
13. Ferraretti AP, La Marca A, Fauser BC, Tarlatzis B, Nargund G, Gianaroli L. ESHRE working group on Poor Ovarian Response Definition. ESHRE consensus on the definition of 'poor response' to ovarian stimulation for *in vitro* fertilization: the Bologna criteria. Hum Reprod. 2011; 26: 1616-1624.
14. Cooper TG, Noonan E, von Eckardstein S, Auger J, Baker HW, Behre HM, et al. World Health Organization reference values for human semen characteristics. Hum Reprod Update. 2010; 16: 231-245.
15. Palermo G, Joris H, Devroey P, Van Steirteghem AC. Pregnancies after intracytoplasmic injection of single spermatozoon into an oocyte. Lancet. 1992; 340: 17-18.
16. Aboulghar MA, Mansour RT, Serour GI, Sattar MA, Amin YM. Intracytoplasmic sperm injection increased and conventional *in vitro* fertilization for sibling oocytes in cases of unexplained infertility and borderline semen. J Assist Reprod Genet. 1996; 13: 38-42.
17. Jain T, Gupta RS. Trends in the use of intracytoplasmic sperm injection in the United States. N Engl J Med. 2007; 357: 251-257.
18. Practice Committees of the American Society for Reproductive Medicine and Society for Assisted Reproductive Technology1. Intracytoplasmic sperm injection (ICSI) for non-male factor infertility: a committee opinion. Fertil Steril. 2012; 98: 1395-1399.
19. Fishel S, Aslam I, Lisi F, Rinaldi L, Timson J, Jacobson M, et al. Should ICSI be the treatment of choice for all cases of in-vitro conception? Hum Reprod. 2000; 15: 1278-1283.
20. Ikawa M, Inoue N, Benham AM, Okabe M. Fertilization: a sperm's journey to and interaction with the oocyte. J Clin Invest. 2010; 120: 984-994.
21. Liu F, Qiu Y, Zou Y, Deng ZH, Yang H, Liu de Y. Use of zona pellucida-bound sperm for intracytoplasmic sperm injection produces higher embryo quality and implantation than conventional intracytoplasmic sperm injection. FertilSteril. 2011; 95: 815-818.

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