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ARTICLE

Differential effects of short co-incubation of gametes and early removal of cumulus cells in patients with different fertilizing capabilities

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Abstract The objective of this retrospective study was to evaluate the embryological and clinical outcomes of short co-incubation of gametes and early removal of cumulus cells (SCGERCC) in patients with good IVF capability and those with complete fertilization failure treated by rescue intracytoplasmic sperm injection (ICSI). The study included 257 couples with >60% fertilization rate (SCGERCC group) in the SCGERCC cycle, 72 couples with complete fertilization failure in the SCGERCC cycle given early rescue ICSI treatment (early rescue group), and 219 couples who underwent IVF cycles with overnight co-incubation of gametes with >60% fertilization rate (traditional IVF group). The results showed that the SCGERCC group had a higher multi-pronuclei rate (13.34%, $P < 0.001$) than the early rescue ICSI (5.15%) and traditional IVF (6.15%) groups. The good quality embryo rate was higher in the SCGERCC group, but implantation, clinical pregnancy and live-birth rates (37.21%, 36.92% and 38.20% for SCGERCC, early rescue and traditional IVF groups, respectively) were comparable in all three groups. The study indicated that SCGERCC followed by rescue ICSI helped couples with initial complete fertilization failure attain clinical outcomes comparable with the other two groups, but it significantly increased the multi-pronuclei rate in couples with good fertilizing capabilities.

KEYWORDS: early removal of cumulus cells, early rescue, ICSI, IVF, multi-pronuclei, short co-incubation of gametes

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Introduction

According to an evaluation by the World Health Organization (WHO) in 2004 (Mascarenhas et al., 2012), one in every four couples in 65 developing countries is affected by infertility. The overnight sperm-oocyte co-incubation method was used as the standard protocol in the traditional IVF cycle. Complete IVF fertilization failure is one of the most frustrating experiences in assisted reproductive technology (ART) treatment, which occurs in 5–10% of traditional IVF cycles (Mahutte and Arici, 2003; Zhu et al., 2012). Failed IVF fertilization may be caused by impaired spermatozoa, oocyte deficiency or a defect in the in-vitro sperm/oocyte medium. Late rescue intracytoplasmic sperm injection (ICSI) of 1-day-old oocytes generally has a limited success rate (Amarin et al., 2005; Morton et al., 1997).

The incidence of infertility in couples of child-bearing age is 10–15% in China (www.people.com.cn). There is much pressure on doctors and patients when complete IVF fertilization failure appears in the IVF treatment process. Rescue ICSI after 6 h post-insemination gave better fertilization, pregnancy and implantation rates compared with rescue ICSI after 22 h post-insemination when oocytes had become aged (Chen and Kattera, 2003).

ICSI treatment was the main solution to solve the problem of male infertility. China had strict indications of ICSI treatment due to its risk of oocyte damage and the possibility of transmission of the (epi)-genetic defect of male sterility to the next generation (Ge et al., 2010).

Short co-incubation of gametes and early removal of cumulus cells (SCGERCC) combined with early rescue ICSI can effectively avoid complete IVF fertilization failure and excessive ICSI treatment (Liu et al., 2014), and it has been adopted by many IVF centres in China.

In many SCGERCC cycles, two polar bodies are present in zygotes, indicating normal fertilizing capability of both oocyte and sperm. The SCGERCC cycle can effectively avoid complete IVF fertilization failure, but it is unknown whether this treatment would affect the outcome of patients without a fertilization barrier. This study investigated the clinical significance of SCGERCC in patients with different fertilization capabilities by analysing the IVF outcomes among patients with a greater than 60% fertilization rate in the SCGERCC cycle, patients with complete IVF fertilization failure and early rescue ICSI in the SCGERCC cycle, and patients with a greater than 60% fertilization rate in traditional IVF cycles.

Materials and methods

Patients

In this retrospective study, 548 couples (455 with their first cycles and 93 with their second cycles or more) who underwent IVF/ICSI cycles at the Department of Reproductive Medicine in Peking University Shenzhen Hospital, Shenzhen, China between July 2013 and June 2014 were included. The inclusion criteria for patients in this study: couples have a relative normal ovarian response ($1.70 <$ (oocytes recovered $\times$ 1000/total dose of FSH) < 10.07) (Huber et al., 2013) and normal sperm characteristic or mild male factor. According to the judgement of doctors and the patient's own choice, couples were randomly treated by SCGERCC or by traditional IVF. Patients with fewer than three oocytes retrieved and polycystic ovary syndrome (PCOS) patients were excluded. According to insemination programmes undergone by the couples and resulting fertilization rates, 548 couples were divided into three groups. Of these couples: 257 had a greater than 60% fertilization rate (SCGERCC group) in the SCGERCC cycle; 72 presented complete fertilization failure in the SCGERCC cycle and had early rescue ICSI treatment (early rescue group); and 219 had traditional IVF cycles with overnight co-incubation of gametes, with a greater than 60% fertilization rate (traditional IVF group). Couples were excluded from the study if they didn't have complete fertilization failure but had a fertilization rate of 60% or less following SCGERCC, because the aim of the study was to evaluate the differential effects of SCGERCC in patients with good fertilizing capabilities or patients with complete fertilization failure.

The criteria for the SCGERCC group selection were as follows: 4 h co-incubation of gametes and early removal of cumulus cells, normal sperm characteristics but infertility for more than 4 years; or mild male factor with sperm concentration ranging from 5×10^6/ml to 20×10^6/ml, percentage of grade "a + b" motility ranging from 5% to 20%, or percentage of normal head ranging from 1% to 4%. All couples in SCGERCC group had a greater than 60% fertilization rate.

The traditional IVF group included couples with overnight co-incubation of gametes, primary or secondary infertility with normal sperm characteristics, or couples with mild male factor that were similar to the patients in the SCGERCC group described above. All couples in the traditional IVF group had a greater than 60% fertilization rate.

All patients provided written informed consent to receive the SCGERCC/traditional IVF programme or early rescue ICSI treatment.

The study received ethics clearance from the ethics committee of Peking University Shenzhen Hospital, obtained approval from the institutional review board (IRB number 20130601; approval date: June 1st, 2013), and was carried out according to the regulations of university policy.

Hormonal stimulation and oocyte retrieval

Patients were given a gonadotrophin-releasing hormone analogue (GnRH-a) with recombinant follicle-stimulating hormone according to a previously described protocol (Zhou et al., 2008). Briefly, patients were treated with 1.25 mg of Diphereline (triptorelin acetate for injection; IPSEN PHARMA BIOTECH, France) on about day 21 of their previous menstrual cycle. After the serum oestradiol concentration decreased to a concentration lower than 50 pg/ml, 75–225 IU of recombinant human follitropin (GONAL-f: Merck Serono SA Aubonne Branch, Switzerland) was administered in a dosage adjusted to the individual's response. Oocyte maturation was induced by injection of 5000–10,000 IU of chorionic gonadotrophin (Livzon Pharm, China) when the two leading follicles were 17 mm in mean diameter. Oocytes were aspirated using a Wallace 17G oocyte recovery set (Smiths Medical International, Hythe, Kent, United Kingdom) 36 h after human chorionic gonadotrophin (HCG) administration under the guidance of a B-ultrasound.