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ARTICLE

Evaluation of syphilis serostatus on the safety of IVF treatment

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Abstract An increasing number of infertile syphilis-infected individuals have turned to assisted reproductive technology; however, the safety of syphilis carrier serostatus on IVF and embryo transfer outcomes has not been evaluated. Data from 482 patients who delivered singletons were analysed. In the retrospective study, the rate of IVF and intracytoplasmic sperm injection fertilization was 79.50% ± 17.57%/78.72% ± 16.66% in the *Treponema pallidum* particle agglutination assay negative (TPPA-negative) and rapid plasma reagin negative (RPR-negative) group, 76.12% ± 22.99%/74.05% ± 20.31% in the TPPA-positive and RPR-negative group, and 75.66% ± 21.72%/70.90% ± 16.11% in the TPPA-positive and RPR-positive group. The clinical pregnancy rate was 39.79% in the TPPA-negative and RPR-negative group, 46.30% in the TPPA-positive and RPR-negative group, and 36.59% in the TPPA-positive and RPR-positive group. No significant differences were found between the groups. The neonatal gestational age and mean birth weight were not significantly different between the TPPA-negative and TPPA-positive groups. Multiple linear regression analysis also showed no association between TPPA serostatus and newborn birth weight and gestational age. The present retrospective study showed that TPPA and RPR serostatus did not affect the outcomes of IVF and embryo transfer. Syphilis-infected individuals can undergo IVF and embryo transfer cycles after penicillin treatment.

KEYWORDS: IVF-ET, syphilis serostatus, pregnancy outcomes

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Introduction

Syphilis is a sexually transmitted disease that is caused by the spirochete, *Treponema pallidum*. Globally, the incidence of syphilis in adults was 10.6 million cases in 2008 (Stamm and Mudrak, 2013). If syphilis is left untreated, the disease can last for years and result in the occurrence of serious complications, such as granulomas, dementia, paralysis, blindness, and aortic aneurysm (Blencowe et al., 2011). The World Health Organization (WHO) estimates 1.4 million pregnant women had probable active syphilis infections in 2008. Pregnant women who are infected with syphilis can transfer *T. pallidum* to the neonates, and this leads to adverse outcomes of pregnancy, including stillbirths, neonatal deaths, low birth weight, and clinical evidence of syphilis (Newman et al., 2013). Gomez et al. (2013) reported that the frequency of adverse pregnancy outcomes is 52% higher among women with syphilis than among women without syphilis. Syphilis testing, coupled with appropriate and prompt penicillin treatment for infected people, is suggested by the WHO to prevent the transmission of syphilis (Kahn et al., 2014). Although these interventions have been estimated to be inexpensive and cost-effective, and have been available for over 60 years, the adverse outcomes of syphilis persist as a public health problem.

An increasing number of infertile syphilis-infected individuals have turned to assisted reproductive technology, such as IVF, intracytoplasmic sperm injection (ICSI), and embryo transfer; however, the safety of syphilis carrier serostatus on IVF and embryo transfer outcomes has not been evaluated. The objective of this retrospective study was to determine the effects of syphilis serostatus on outcomes of IVF and embryo transfer.

Materials and methods

Patients

This retrospective study was approved by the Ethics Committee of Peking University Third Hospital on 18 April 2008 (reference number 2008013). Women who underwent IVF and embryo transfer cycles between 2008 and 2012 in the Reproductive Medical Centre of Peking University Third Hospital were analysed. Women underwent ovarian stimulation with a gonadotrophin-releasing hormone agonist (GnRH) or GnRH antagonist protocol, as described previously (Gomez et al., 2013; Lin et al., 2013). Ovarian follicle development was monitored on the basis of serum oestradiol levels and transvaginal ultrasonographic measurements. When at least one follicle reached a mean diameter of 18 mm and an oestradiol concentration exceeded 500 pg/ml, 10,000 units of urinary human chorionic gonadotrophin (Serono; Aubonne, Switzerland) were administered. Thirty-six hours after the injection, oocytes were transvaginally retrieved under ultrasound guidance.

Luteal support was started on the day after oocyte retrieval (Progesterone Injection; Xianju Pharmacy, Zhejiang, China).

Laboratory protocols

In accordance with routine laboratory procedures, IVF and intracytoplasmic sperm injection (ICSI) were carried out on the day of oocyte retrieval (D 0). The presence of two pronuclei was observed 16–18 h after insemination or injection, and the zygotes were then cultured in 25 μl of pre-equilibrated cleavage medium droplets. The embryos were cultured in incubators at 37°C under 5% or 6% CO_2. The morphology of embryos was evaluated 68–72 h after insemination (e.g. cell number, fragmentation and symmetry). The number of embryos transferred was determined on the basis of patient age, number of IVF cycles and embryo quality.

Data collection

In the present study, only patients 40 years of age or younger with a body mass index (BMI) less than 30 kg/m^2 were analysed. Patients were excluded if they received pre-implantation genetic diagnosis. Furthermore, only data from singletons born alive after the 20th week gestation were included in the data analysis. The criteria were the same as used in previous reports; specifically, gestational age, low birth weight and high birth weight were defined as described previously (Nelissen et al., 2012). Clinical pregnancy was diagnosed by a gestational sac with fetal heart beat at 7 weeks of gestation. **Spontaneous abortion** was defined as any pregnancy loss before 20 weeks gestation. The spontaneous abortion rate was also analysed to evaluate the effects of syphilis serostatus on outcomes of IVF and embroy transfer.

Analysis design

Serologic screening for syphilis is routinely carried out when couples undergo assisted reproductive technologies. The patients were treated with benzathine penicillin G if the *T. pallidum* particle agglutination assay (TPPA) and rapid plasma reagin (RPR) test were positive. Patients may receive assisted reproductive technology treatment if the RPR test is negative or the RPR titre is less than 1:4 after 1 year. Among the 482 patients, 387 were TPPA and RPR seronegative couples ($TPPA^-$ RPR^- group), 54 were TPPA-positive and RPR-negative ($TPPA^+$ RPR^- group), and 41 were TPPA-positive with a RPR titre less than 1:4 ($TPPA^+$ RPR^+ group). Only one partner was seropositive in all couples. The percentage of female seropositivity was 46.30% (25/54) in the $TPPA^+$ RPR^- group and 48.78% (20/41) in the $TPPA^+$ RPR^+ group.

Statistical analysis

The Statistical Package for Social Sciences (SPSS) version 16 (SPSS Inc., USA) was used for all statistical analyses. The basic characteristics of patients were compared using analysis of variance followed by the Student–Newman–Keuls testing, and categorical variables were evaluated with chi-squared tests. Multiple linear regression analyses were used to evaluate the association between TPPA serostatus and birth weight, whereas controlling for the effects of possible confounding factors, including maternal age, paternal age, maternal height, paternal height, maternal weight, paternal weight, causes of subfertility, subfertility types, duration of subfertility,