A Multicentre trial comparing the tWE lab laboratory system with standard IVF culture techniques

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Introduction

In our pursue to achieve the millennium development goals among others, the improvement of maternal health (United Nations Millennium Development Goals, 2008) in the form of reducing maternal deaths and providing comprehensive reproductive health service, global partnership for development should be considered one of the instrumental strategy.

Approximately 15% of couples worldwide (Boivin et al., 2007) suffer from childlessness with significant and at times catastrophic consequences (Dyer et al., 2004, 2005; Fathalla et al., 2006). Severe tubal damage and male infertility are common reasons for infertility in the developing countries as a result of sexually transmitted infections, septic miscarriages and/or puerperal sepsis (Adetoro and Ebomoyi, 1991; Ericksen and Brunette, 1996; Van Balen and Gerrits, 2001). Unfortunately these patients can only be managed by assisted reproduction technology such as IVF (Ombelet et al., 2008). Of major concern is the inaccessibility to these effective treatment options due to high costs and complex laboratory services.

There are 3 cost drivers in assisted reproductive programs. Ovulation induction, laboratory cost and personnel. For the service to be widely available and affordable the ovarian stimulation protocols have to be modified to milder forms to reduce the cost of medication needed and the risk of complications such as OHSS (Verberg et al., 2009). The laboratory set up also needs to be simplified.

Therefore the aim of the study is to compare the standard incubator IVF outcomes with the tWE Lab (Ombelet, 2014; Van Blerkom et al., 2014) IVF outcomes in a multicentre prospective randomised study.

Research question:

Is simplified embryo culture system as effective as standard incubator embryo culture system in IVF?

*Hypothesis***:**

Our hypothesis is that simplified tWElab embryo culture system may be as effective as standard incubator culture system in IVF.

Aims of the study:

Evaluate the effectiveness of tWE Lab embryo culture system versus standard incubator culture system in IVF.

Objectives of the study are:

Primary outcomes:

To evaluate the fertilization rates, clinical pregnancy rates (CPR), and on-going pregnancy rates (OPR) per cycle of tWE Lab embryo culture system versus standard incubator culture system in IVF.

Secondary outcomes:

To evaluate the total number of oocytes collected,
To evaluate the miscarriage rates,

Methods and Materials

Study Design: Randomized Controlled Multicentre Trial in Southern Africa.

Target Population: All patients with bilateral tubal occlusion, mild male infertility (1 million motile sperms after washing and three previously failed artificial inseminations (IUI)).

Study Population: All patients who require ART in the form of IVF.

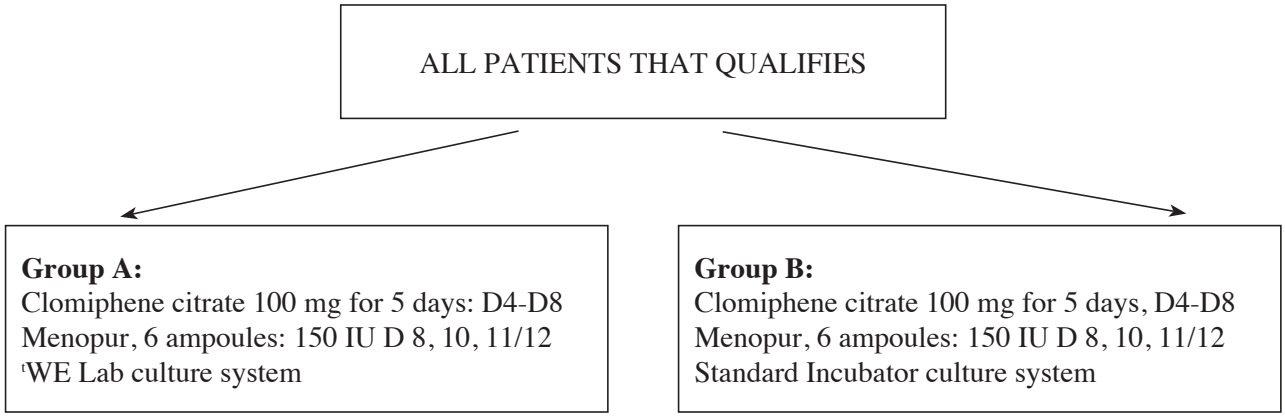
- *Setting:* The trial will be conducted at Tygerberg Hospital, Reproductive Medicine Unit, Aevitas Clinic Cape Town and 2 other centres to be recruited.
- *Inclusion criteria:* Female patients age between 18-37 years. It must be their first IVF treatment, with regular menstrual cycle (25-32 days) and a BMI (kg/m^2) of 18-29.
- *Exclusion criteria:* Female patients > 37 years. Patients with previously failed IVF treatment and the presence of large ovarian cyst of ≥ 3 cm on ultrasound were excluded. Patients with severe male infertility, moderate to severe endometriosis and vaginal and/or uterine abnormalities were also excluded.

Study sample: Consecutive patients who qualifies for ART in the form of IVF

Randomization method: Balanced block design following patient information assessment. No new patients will be enrolled once the sample size is reached.

Sample size: A statistical program (Epi-info, UMassAmherst) was used to do a sample size calculation for this study. Using given parameters-confidence (95%) and the power (80%) it was evident that using one hundred and seven per treatment group would be sufficient.

Data Source: The groups will be separated into two, Group A, minimal stimulation IVF with CC 100mg for 5 days and ≤ 6 ampoules of Menopur with tWE Lab culture system and Group B, minimal stimulation IVF with CC 100 mg for 5 days and ≤ 6 ampoules of MenopurIVF with standard incubator culture system.



Data collection and handling:

Patient information will be handled safely and confidentially. We will do double entry to ensure accurate collection.

Statistical processing:

Descriptive statistics: We will use Statistical Package for Social Sciences (SPSS) for overall analysis and specific tests for specific data. *Analytic statistics:* Outcomes will be analysed at the end of the trial.

Ethics and Permission:

Consent form will be signed by all participants before the study begins. There will be consent forms in English, Afrikaans, and Xhosa to accommodate predominant languages in the area. Interviews and questionnaires will be administered on one by one basis to ensure patient's privacy and confidentiality. The drugs used in this trial are registered and used according to the manufacturer's recommendations.

This protocol forms part of the approved PhD study by the Faculty of Health Sciences at Stellenbosch University ethics committee meeting: *N11/08/256 but permission must be obtained for this new protocol*

Results: to be obtained

Conclusion and Discussion: We anticipate favourable outcomes with the tWe Lab culture system.

References

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Addendum

All patients will have a pre treatment ovarian assessment using antral follicle count, AFC.

Ultrasound will be done between the cycle day 1 and cycle day 3 thereafter on cycle day 8 and repeated every other day or daily for follicle tracking and endometrial thickness assessment. Urine sample will be taken for assessment of LH on the days the ultrasound. Ovulation trigger will be performed with subcutaneous injection of Ovitrelle® when a lead follicle has atleast 18 mm diameters. Transvaginal ultrasound-guided follicle aspiration will be performed 34-36 hours after the hCG administration.

Generally embryo transfer will be performed on the third day after oocyte retrieval for both groups. Luteal phase will be supported with vaginal progesterone from the day of embryo transfer until the day of pregnancy test.

Implantation is defined by positive pregnancy test, serum b-hCG ≥ 25 IU on the tenth day following embryo transfer. Clinical pregnancy is defined as the ultrasound presence of foetal cardiac activity at 7 weeks gestation and on-going pregnancy is defined as the presence of a foetus of > 12 weeks on ultrasound.

The cycle will be cancelled if < 2 dominant follicles are present and the LH > 20IU/L and there are no quality embryos to transfer.