Scholars Journal of Applied Medical Sciences
Abbreviated Key Title: Sch J App Med Sci
ISSN 2347-954X (Print) | ISSN 2320-6691 (Online)
Journal homepage: https://saspublishers.com

OPEN ACCESS

Obstetrics & Gynecology

Comparison of Trans-Resveratrol (98% Pure) with Resveratrol (40%) as Rejuvenation Therapy on Ovarian Reserve Parameters and Pregnancy Outcomes in Infertile Adult Women with Poor Ovarian Reserve, Undergoing Assisted Conception Cycles – A Double Arm, Randomized, Open Label Study

Dr. P. M. Gopinath[1*], Dr. Sahityalakshmi Manoharan[2]

[1,2]Department of Obstetrics, Gynaecology & Reproductive medicine, SRM Institutes for Medical Science, Vadapalani, Chennai, India

DOI: 10.36347/sjams.2023.v11i12.010 | **Received:** 08.11.2023 | **Accepted:** 13.12.2023 | **Published:** 16.12.2023

***Corresponding author:** Dr. P. M. Gopinath
Department of Obstetrics, Gynaecology & Reproductive medicine, SRM Institutes for Medical Science, Vadapalani, Chennai, India

Abstract **Original Research Article**

This is a Phase IV Randomized, double arm Open labelled trial, conducted at SIMS hospital, Vadapalani, Chennai. It involves all women seeking fertility treatment with poor ovarian reserve, who are planned to undergo assisted conception cycles, including IUI & IVF. The study included women aged between 21 and 45 years, with Poor ovarian reserve with regular menstrual cycles (21–35 days), prestimulation parameters (AFC<5, AMH<1.2 ng/ml), History of previous poor ovarian response </= 5 oocytes with a conventional stimulation protocol, Couples undergoing the ICSI cycle with ejaculated sperm. The data collected was subjected to statistical testing. The groups were compared in terms of their demographic features and both the groups was found to be equally distributed. Trans-Resveratrol shows that this drug has no advantage over Resveratrol, therapeutically or statistically advantage.

Keywords: Resveratrol, rejuvenation, Low AMH, Poor ovarian reserve, Transresveratrol, Ovarian parameters, Assisten conception, ART.

INTRODUCTION

Resveratrol is a plant-based compound derived from red wine, grapes, berries and peanuts. It is known for its anti-oxidant activity [1], activating SIRT1 (regulator to stressors, longevity) [2], activating AMPK (regulates cellular energy homeostasis) [3].

The wide range of benefits are Selective anti-bacterial activity, Mitochondrial biogenesis, blood homeostasis, vasodilation and cerebral blood flow, bone formation. It is also known to improve Bone Strength, Oral Health, Gut Microbiota, Cardiovascular Health, Cognitive Support, Skin Preservation, Blood Glucose Regulation, Eye Health.

ANTI OXIDANT PROPERTY:

- Scavenge reactive oxygen species (e.g. O2-, HO·, HO2)
- Inhibition of lipid peroxidation and reduced malondialdehyde (MDA) production
- Inhibition of DNA, RNA or protein oxidative damage (e.g. oxygenation)
- Upregulation of endogenous oxidative defense systems (e.g. SOD, catalase, GSH)
- Measured using different methods (e.g. TEAC, FRAP, TRAP‡)

From the above mentioned anti-oxidant properties, Resveratrol has a better effect as an antioxidant when compared to astaxanthin [4], butylated hydroxyanisole (BHT) [5, 11] butylated hydroxytoluene (BHT) [5], tocopherol (VitE) [5, 11] quercetin [6], curcumin [7], hydroxytyrosol [8], catechin [9], galicic acid [9], ascorbic acid (VitC) [10].

The drug is produced from enhanced baker's yeast that undergoes several steps of fermentation and purification to give a Natural, Non- GMO, contaminant free resveratrol.

Key Benefits:

1. Natural
2. Consistent Quality with a purity of >98% trans-resveratrol
3. Free from contaminants
4. No Emodin/ polycyclic aromatic hydrocarbons (PAHs) / pesticides/ herbicides
5. No alflatoxins/ dioxins/ furans
6. No unwanted organic solvents/ toxic heavy metals (e.g. Cadmium)
7. Allergen free

METHODOLOGY

This is a Phase IV Randomized, double arm Open labelled trial, conducted at SIMS hospital, Vadapalani, Chennai. It involves all women seeking fertility treatment with poor ovarian reserve, who are planned to undergo assisted conception cycles, including IUI & IVF.

Inclusion Criteria

1. Poor ovarian reserve with regular menstrual cycles (21–35 days),
2. Patients < 45 years with prestimulation parameters (AFC<5, AMH<1.2 ng/ml).
3. Previous poor ovarian response </= 5 oocytes with a conventional stimulation protocol.
4. Aged between 21 and 45 years,
5. Couples undergoing the ICSI cycle with ejaculated sperm.

Exclusion Criteria

1. Male factor
2. Mechanical factor infertility (Mechanical infertility is defined in women following bilateral salpingectomy or women with bilateral tubal occlusion diagnosed by hysterosalpingography and/or laparoscopy)
3. Past or present malignancy, history of cytotoxic chemotherapy and/or radiotherapy, history of ovarian surgery such as oophorectomy or cystectomy, current usage of dehydroepiandrosterone (DHEA) or testosterone supplement use.
4. Uncontrolled metabolic and endocrine disorders
5. Known allergy to the utilized drug.
6. Preexisting medical conditions such as bleeding disorders, septicemia, TB.
7. Patient unlikely to be available for follow-up as specified in the protocol.

A total of 30 patients were enrolled in the study as per the inclusion and exclusion criteria after counselling and obtaining written consents. The group was divided into 2 arms by randomization.

ARM 1: The Therapy Group

Trans-Resveratrol (98% pure) given orally twice daily (250 mg) for 60 days along with standard care of treatment.

ARM 2: The Comparative group

Resveratrol (40%) given orally twice daily (250 mg) for 60 days along with Standard care of treatment

The duration of the study is 90 days, out of which 60 days of medication were given. Participant followed up for outcome assessments (AMH) assessed in 2nd /3rd day (+15days) of their 3rd menstrual cycle.

VISIT SCHEDULE

Hospital Visit-1 (Day-0) - Pre-evaluation study: Blood collection and imaging as desired by the clinician.

Hospital Visit-2 (Day –1) - Screen subjects and enrol by inclusion/exclusion criteria; Obtain informed consent and enrol the consented subjects into the study. Based on the randomization list the subject will be randomized to either of the two arms and receive the investigational product along with the standard care of therapy. Participants in both the group will receive 60 days of the medication.

Telephone visit 1(at 30 days)- to check for drug compliance and any drug related side effects.

Hospital Visit-3 (day 60) – after 60 days of treatment +/- 15 days. To report 2/3rd day of their cycle to repeat the blood tests and the ultrasound. Chemical Pregnancy assessment by beta HCG levels.

Hospital Visit-4 (32 Days after V3) - Clinical pregnancy assessment at 12 weeks by Ultrasonogram

Hospital visit-5 (2 weeks after V4) Clinical examination will be done by principal investigator and confirm viability of fetus.

Unscheduled Visit - Unscheduled visits will be documented and informed to the IEC.

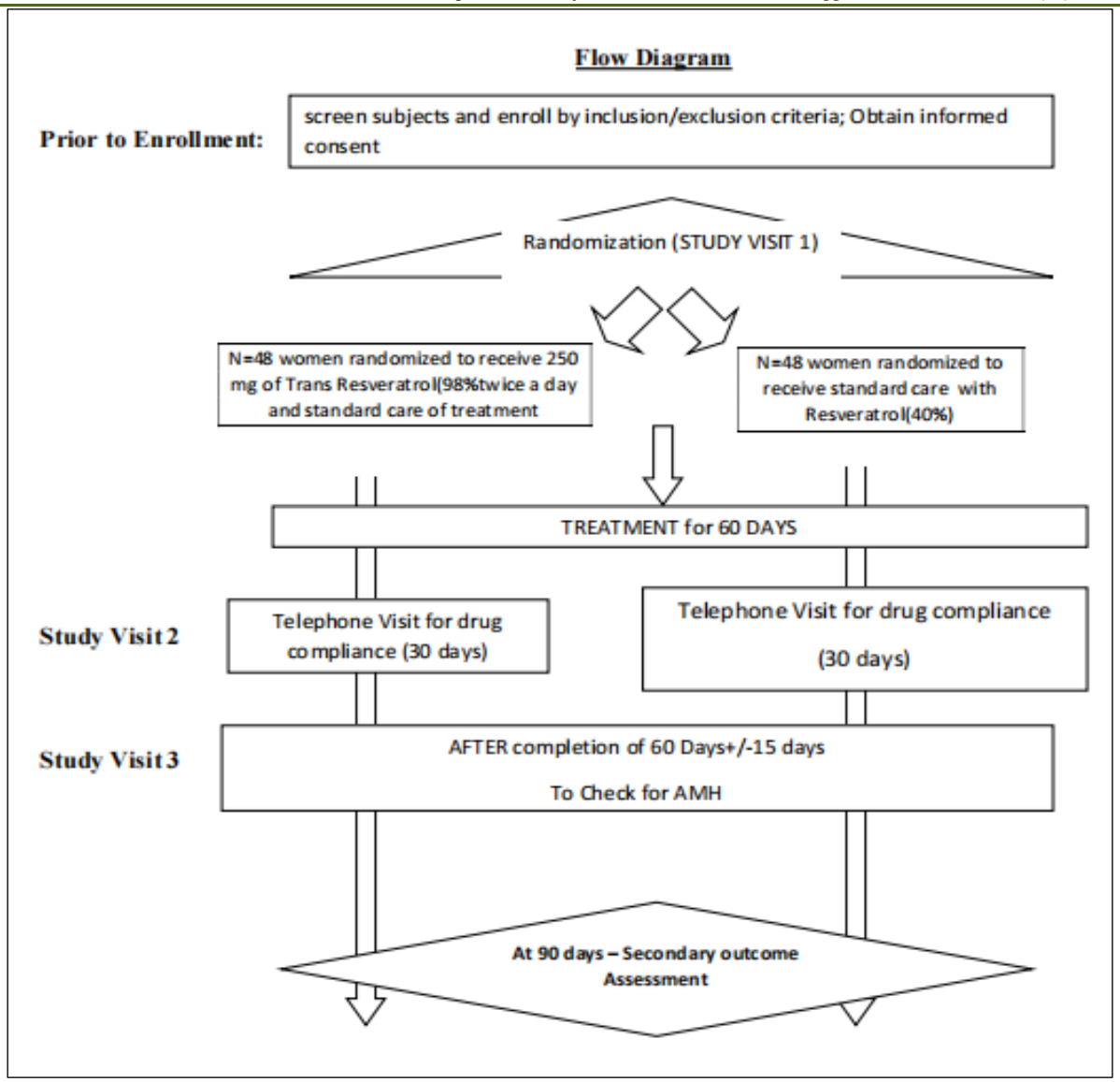

Fig 1: Methodology

Primary outcome was to study the Increase in ovarian reserve in terms of AMH between the two study groups at the end of 60 days of medication.

Secondary outcomes included Chemical pregnancy rate, Clinical Pregnancy Rate, Implantation rate, Oocyte quality, Embryo quality.

STATISTICAL ANALYSIS

A total of 30 patients participated in the study.

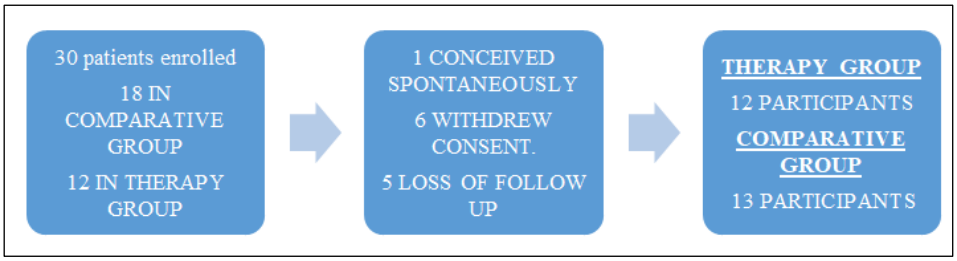

Fig 2: Sample size

The data collected was subjected to statistical testing. The groups were compared in terms of their demographic features and both the groups was found to be equally distributed.

THERAPY GROUP:

As per the study, this group was prescribed and AMH values were compared (Table 1). The mean AMH value pre-therapy was 1.43 with a SD of 1.32 and the value post therapy was 1.4078 with SD of 1.23. while comparing both the mean, the p value is .762 denoting that the values are statistically not significant.

Table 1: Comparison of serum Anti - Mullerian hormone in therapy group

AMH VALUE	MEAN	STANDARD DEVIATION	STANDARD ERROR MEAN
Pre- Transresveratrol	1.4315	1.32337	.36704
Post Transresveratrol	1.4078	1.23675	.34301

COMPARATIVE GROUP:

Similarly, the AMH values were compared before and after administering the control drug-Resveratrol (Table 2). The mean AMH pre trial was 1.5558 ± 1.303 and post trial was 1.4101 ± 1.36257. The p value while comparing both the mean was .401 denoting that it was statistically not significant.

Table 2: Comparison of serum Anti - Mullerian hormone in comparative group

AMH VALUE	MEAN	STANDARD DEVIATION	STANDARD ERROR MEAN
Pre- Resveratrol	1.5558	1.30381	.37638
Post Resveratrol	1.4101	1.36257	.39334

CONCLUSION

This double arm, randomized, open label study, comparing the trial drug Trans-Resveratrol shows that this drug has no advantage over Resveratrol, therapeutically or statistically advantage. There was one spontaneous conception during the course of the study however it was under the effect of the control drug, Resveratrol.

REFERENCES

1. Gülçin, İ. (2010). Antioxidant properties of resveratrol: A structure–activity insight. *Innovative food science & emerging technologies*, *11*(1), 210-218.
2. Borra, M. T., Smith, B. C., & Denu, J. M. (2005). Mechanism of human SIRT1 activation by resveratrol. *Journal of Biological Chemistry*, *280*(17), 17187-17195.
3. Lan, F., Weikel, K. A., Cacicedo, J. M., & Ido, Y. (2017). Resveratrol-induced AMP-activated protein kinase activation is cell-type dependent: lessons from basic research for clinical application. *Nutrients*, *9*(7), 751.
4. Sueishi, Y., Ishikawa, M., Yoshioka, D., Endoh, N., Oowada, S., Shimmei, M., ... & Kotake, Y. (2012). Oxygen radical absorbance capacity (ORAC) of cyclodextrin-solubilized flavonoids, resveratrol and astaxanthin as measured with the ORAC-EPR method. *Journal of Clinical Biochemistry and Nutrition*, *50*(2), 127-132.
5. Gülçin, İ. (2010). Antioxidant properties of resveratrol: A structure–activity insight. *Innovative food science & emerging technologies*, *11*(1), 210-218.
6. Boydens, C., Pauwels, B., Decaluwé, K., Brouckaert, P., & Van de Voorde, J. (2015). Relaxant and antioxidant capacity of the red wine polyphenols, resveratrol and quercetin, on isolated mice corpora cavernosa. *The journal of sexual medicine*, *12*(2), 303-312.
7. Eybl, V., Kotyzova, D., & Koutensky, J. (2006). Comparative study of natural antioxidants–curcumin, resveratrol and melatonin–in cadmium-induced oxidative damage in mice. *Toxicology*, *225*(2-3), 150-156.
8. Bigagli, E., Cinci, L., Paccosi, S., Parenti, A., D'Ambrosio, M., & Luceri, C. (2017). Nutritionally relevant concentrations of resveratrol and hydroxytyrosol mitigate oxidative burst of human granulocytes and monocytes and the production of pro-inflammatory mediators in LPS-stimulated RAW 264.7 macrophages. *International Immunopharmacology*, *43*, 147-155.
9. Yilmaz, Y., & Toledo, R. T. (2004). Major flavonoids in grape seeds and skins: antioxidant capacity of catechin, epicatechin, and gallic acid. *Journal of agricultural and food chemistry*, *52*(2), 255-260.
10. López-Burillo, S., Tan, D. X., Mayo, J. C., Sainz, R. M., Manchester, L. C., & Reiter, R. J. (2003). Melatonin, xanthurenic acid, resveratrol, EGCG, vitamin C and α-lipoic acid differentially reduce oxidative DNA damage induced by Fenton reagents: a study of their individual and synergistic actions. *Journal of pineal research*, *34*(4), 269-277.
11. Fabris, S., Momo, F., Ravagnan, G., & Stevanato, R. (2008). Antioxidant properties of resveratrol and piceid on lipid peroxidation in micelles and monolamellar liposomes. *Biophysical chemistry*, *135*(1-3), 76-83.