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Original Article

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Impact of antioxidants in improving semen parameters like count, motility and DNA fragmentation in sub-fertile males: a randomized, double-blind, placebo-controlled clinical trial

Ameet Patki [1,*], Rohit Shelatkar [2], Monica Singh [3], Sweta Agarwal [4], Venugopal M [5], Shashikant Umbardand [6], Apoorva Reddy [7], Priya Kannan [8], Srilatha Gorthi [9], Gautam Khastgir [10], Anita Kulshreshtha [11], and Gayatri Ganu [12]

[1]Fertility Associates, Mumbai 400052, India
[2]Vitabiotics Ltd., London, NW2 7HF, UK
[3]Bhopal Test-Tube Baby Centre, Bhopal 462016, India
[4]Southern Gem Hospital, Hyderabad 500063, India
[5]ARMC IVF Fertility Centre, Thrissur 680003, India
[6]Mangalya Nursing Home & Atharva Fertility Center, Solapur 413002, India
[7]Phoenix Speciality Clinic, Bengaluru 560009, India
[8]Garbba Rakshambigai Fertility Centre, Chennai 600024, India
[9]Revive Clinic, Hyderabad 500019, India
[10]Bengal Infertility & Reproductive Therapy Hospital (BIRTH), Kolkata 700020, India
[11]Yashlok Hospital, Prayagraj 211001, India
[12]Mprex Healthcare Pvt. Ltd., Pune 411057, India

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***Correspondence to**
Ameet Patki
Fertility Associates, 4th Floor Gupte House, Near Khar Police Station, 81 S V Road, Khar West, Mumbai 400052, India.
Email: ameetpatki@fertilityassociates.in

ORCID iDs
Ameet Patki
https://orcid.org/0000-0002-8712-4991
Rohit Shelatkar
https://orcid.org/0009-0002-5596-2592
Monica Singh
https://orcid.org/0009-0006-5613-3699
Sweta Agarwal
https://orcid.org/0009-0009-7587-9113
Venugopal M
https://orcid.org/0009-0004-0926-240X
Shashikant Umbardand
https://orcid.org/0009-0007-4539-6327
Apoorva Reddy
https://orcid.org/0009-0005-4114-4865
Priya Kannan
https://orcid.org/0009-0002-5780-8302
Srilatha Gorthi
https://orcid.org/0009-0000-9573-1188
Gautam Khastgir
https://orcid.org/0009-0002-6749-4191
Anita Kulshreshtha
https://orcid.org/0009-0005-6820-4717
Gayatri Ganu
https://orcid.org/0000-0001-7812-3738

ABSTRACT

Male infertility is solely responsible for 20–30% of infertility cases. Oxidative damage of sperm DNA is positively linked with oligoasthenoteratozoospermia (OAT), and male infertility. The antioxidants are being explored worldwide to combat OAT, sperm DNA fragmentation and reactive oxygen species. The objective of the study was to assess the effectiveness of an antioxidant blend in improving sperm count, semen parameters and reducing DNA fragmentation index (DFI) in sub-fertile males. A prospective, double-blind, randomized, placebo-controlled trial was conducted in 300 sub-fertile males (25–45 years) from ten study sites in India. Subjects were randomized in either the antioxidant blend treatment group or placebo group. We assessed changes in sperm count, motility, normal morphology, semen volume, and percent DFI before and after treatment (90 days). To further stratify data on different criteria *post hoc* analysis was performed. Statistical analysis was performed using SPSS 10.0 software. There were improvements in sperm count, semen volume, sperm motility, and sperm normal morphology in the treatment group. There was improvement in sperm count in severe oligospermia subjects (sperm count < 5 million/mL, 5–10 million/mL, 10.1–15 million/mL), and high-extremely higher baseline DFI (20–30%, 31–40% and above 40%), as per *post hoc* analysis. There was no premature discontinuation and adverse events were reported during the study, indicating safety and well-tolerability of treatment. Study results confirmed the well-researched fact of antioxidants being effective to reduce oxidative stress and thus improve sperm DNA integrity and also improved semen parameters in males aged 40 and above.

Trial Registration
Clinical Trials Registry-India Identifier: CTRI/2020/12/029590

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Keywords: Subfertility; Antioxidant; Asthenoteratozoospermia; DNA Fragmentation; Oligospermia

INTRODUCTION

Infertility is a serious concern worldwide. An estimated 60–80 million couples experience infertility each year, affecting 8–10% of couples· [1]. According to the World Health Organization (WHO), one in every 4 couples in developing countries is prone to infertility. India counts between 15–20 million (25%) infertile couples per year [2]. The magnitude of the problem calls for urgent action.

Male infertility is solely responsible for 20–30% of infertility cases [3]. Abnormalities in semen such as oligospermia, asthenozoospermia, and teratozoospermia are always best correlated with infertility in males [4]. Following factors contribute to male fertility: pre-testicular factors include gonadotrophin deficiency, pituitary insufficiency, hyperprolactinemia, glucocorticoid excess, and hyper- or hypo-thyroidism. Testicular factors include klinefelter syndrome, cryptorchidism, injury, varicocele, and testicular tumors. Post-testicular factor includes congenital absence of the vas deferens, infection, iatrogenic vasal injury, sperm function or motility disorders, and erectile or ejaculatory dysfunction. In about 30% of infertile men, where no causative factor is found for deranged semen parameters by common clinical, instrumental, and or laboratory means, the condition is termed idiopathic (unexplained) [5].

Oligospermia/oligozoospermia is defined as presence of low sperm count, according to WHO, < 15 million per milliliter of semen [6]. Asthenozoospermia is defined as < 40% sperm motility or < 32% with progressive motility [7]. Teratozoospermia represents a heterogeneous group of abnormal sperm phenotypes affecting, solely or simultaneously, the head, neck, midpiece and tail. oligoasthenoteratozoospermia (OAT) is one of the most common phenotypes of male infertility, characterized by combination of qualitative and quantitative sperm defects [8].

Surgical procedures, hormonal and drug therapy, intrauterine insemination (IUI), assisted reproductive technologies (ART), *in vitro* fertilization (IVF), and intracytoplasmic sperm injection (ICSI) are available treatment options for male infertility [9] but these methods also have special concerns like higher cost, uncertain clinical effectiveness and side effects. This calls for a convenient, less costly and yet clinically effective therapeutic agent to be used as foremost therapeutic option. Oxidative damage of sperm DNA is positively linked with OAT and male infertility [10]. Sperm DNA damage is associated with reduced fertility, an increased frequency of spontaneous abortions, and affects embryo quality [11]. DNA fragmentation index (DFI) is a measure of the proportion of damaged sperm within an ejaculate [9,12]. Antioxidants have acquired increasing interest amongst clinicians and researchers for the treatment of male subfertility owing to their cost, convenience, benefits, and long-term safety advantages. The frequently prescribed compounds include vitamins E & C, carnitine, N-acetyl cysteine, selenium, and zinc [9,12]. The experiential use of antioxidants for oligospermia is aimed at improving semen parameters and DFI, enhancing the probability of conception. While the credibility of such a concept has been reported in clinical practice,

scientifically acceptable evidence in controlled human studies is needed [12]. The present study is an attempt to generate evidence around the effectiveness of an antioxidant blend in improving semen parameters in oligospermia.

METHODS

A prospective randomized controlled trial was conducted involving patients with oligospermia recruited from ten study sites nationwide in India. The details of the sites are listed on Clinical Trials Registry of India (CTRI) with registry number CTRI/2020/12/029590. The Royal Pune Independent Ethics Committee approved the study, in Pune, Maharashtra. The Consolidated Standards of Reporting Trials flow of the entire study are depicted in **Fig. 1**.

Inclusion criteria

Male subjects of age between 25–45 years, with oligospermia, asthenozoospermia, and teratozoospermia, and willing to provide written informed consent to participate and willing to follow up were enrolled in the study. The female partner with no reported infertility was considered. As per the WHO guidelines for OAT, the subjects indicating any 2 of the following semen analysis criteria were enrolled in the study: semen volume < 1.5 mL, sperm count < 15 × 10^6/mL, motile count < 25%, morphology < 4% normal form, DNA fragmentation > 20%.

Exclusion criteria

Subjects having a history of hypogonadism, vasectomy, undescended testis, prostate cancer, varicocele, and hydrocele were excluded. Subjects having a history of chemotherapy or radiation for malignant conditions and a history of azoospermia were excluded.

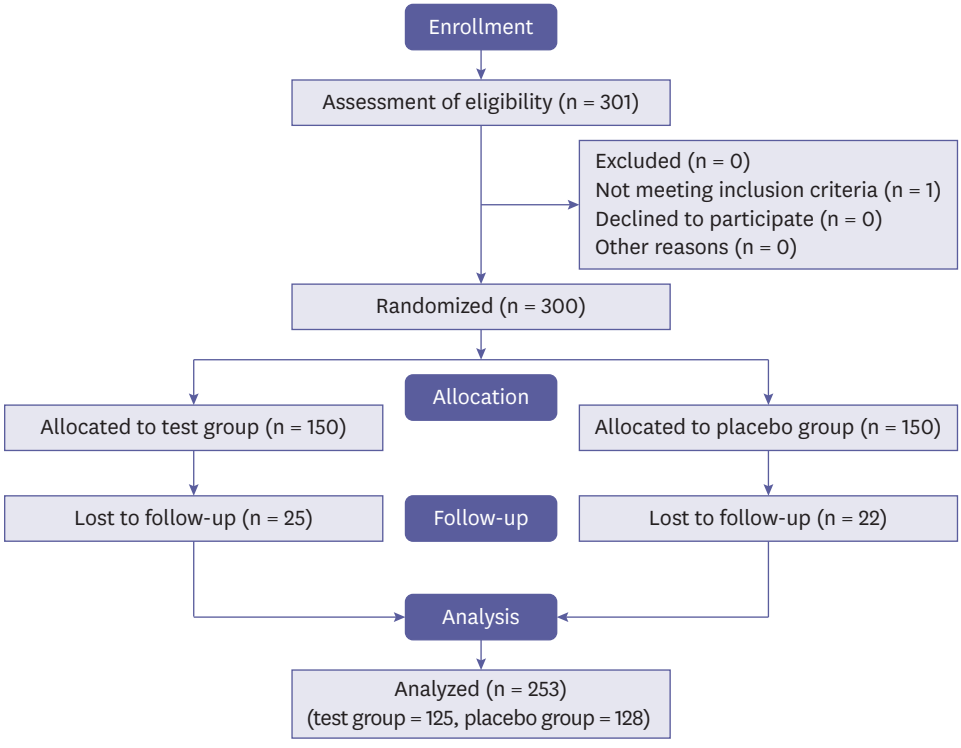

Figure 1. Consolidated Standards of Reporting Trials flow diagram.

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Study groups

Three hundred participants were found suitable for inclusion in the study. They were randomized using computer-generated randomization in a placebo or treatment (antioxidant blend tablets).

Sample size

We have considered a 25% difference in sperm count between groups at a sample size of 300 total (150 subjects in each group) to assess the study objective at 90% power and a 5% level of significance https://clincalc.com/stats/samplesize.aspx.

Intervention details

The intervention was an antioxidant blend in tablet form having a combination of micronutrients, essential amino acids, antioxidants, and vitamins such as coenzyme Q10, L-carnitine, L-arginine, L-glutathione, vitamins like C, E, B6, B12, B1, A, D, ginseng extract, lycopene, folic acid along with elemental zinc, iron, copper selenium, manganese having beneficial effects in improving male fertility outcomes (**Table 1**).

Therapeutic rationale

Male factor infertility is a clinical challenge. As per the earlier published comprehensive review of human studies over 2 decades from PubMed, Google Scholar, Cochrane Central Register of Controlled Trials, Cochrane Database of Systematic Reviews, and Embase in accordance with the guidelines of the Preferred Reporting Items for Systematic Reviews and Meta-Analyses, it is reinforced that there is vital role of diet and antioxidant supplementation in male factor infertility [11].

In male infertility, OAT describes a combination of qualitative and quantitative sperm defects leading to idiopathic infertility. Several published studies demonstrate the benefits of antioxidant treatment, especially for idiopathic or unexplained infertility. The use of antioxidants for OAT is explored worldwide as a safe and effective therapeutic option.

Table 1. Ingredients of the antioxidant blend tablet

Ingredients	Label claim (per tablet)
Coenzyme Q10	50 mg
L-carnitine	50 mg
Vitamin C	40 mg
Vitamin E	10 mg
Ginseng extract	10 mg
L-arginine	10 mg
Elemental zinc (as zinc sulphate)	7.5 mg (20.588 mg)
Elemental iron (as ferrous fumarate)	5 mg (15.21 mg)
L-glutathione	2.5 mg
Vitamin B6	2 mg
Elemental manganese (as manganese sulphate)	2 mg (6.152 mg)
Lycopene	2 mg
Vitamin B1	1.4 mg
Elemental copper (as cupric sulphate)	1 mg (2.795 mg)
Vitamin A	375 mcg (1,250 IU)
Folic acid	100 mcg
Elemental selenium (as sodium selenate)	40 mcg (95.716 mcg)
Vitamin D	10 mcg (400 IU)
Vitamin B12	1 mcg

Under normal physiological conditions, reactive oxygen species (ROS) are vital for sperm maturation, hyperactivation, capacitation, acrosome reaction, as well as fertilization. However, a number of endogenous and exogenous factors may induce supra-physiological levels of ROS resulting in lipid peroxidation, sperm DNA fragmentation and apoptosis, and consequently infertility. Therefore, administering antioxidant supplements to reduce ROS is thought to be helpful to combat sperm DNA fragmentation [11,13].

Considering the gaining interest of fraternity in antioxidant therapy in male fertility and the need for systematic scientific pieces of evidence, the present study was proposed to evaluate the efficacy of antioxidant blend in sub-fertile male.

Dosage and administration

The antioxidant blend in tablet form and identical placebo tablet were advised to be consumed once daily after the main meal with water for 3 months from trial initiation in respective group subjects (treatment and placebo). The tablet dosage form is licensed by the concerned authority, designed as per available references and well within recommended dietary allowance requirement of each ingredient (**Table 1**).

Outcome measures

The primary study outcomes of the present study were to evaluate changes in total sperm count and DFI in sub-fertile males after treatment of 90 days. The secondary outcomes were to evaluate changes in total semen volume, sperm motility, and sperm morphology after treatment of 90 days.

Study schedule

This was a randomized, multicentric, double-blind, placebo-controlled interventional, prospective, comparative clinical study conducted in 300 sub-fertile male subjects across ten study sites in India.

On the screening visit, written informed consent was obtained from the subject for their participation in the study and then demographic details were recorded. The subject's clinical status was assessed on every visit, and semen analysis (sperm count, morphology, motility, semen volume, color, pH, liquefaction, DFI, and so on) was performed at baseline and day 90. We conducted DFI testing at The Andrology Center, Coimbatore, India 641018 by the Sperm Chromatin Structure Assay. Each participant was advised to observe sexual abstinence for 3 days prior to the semen collection. The enrollment of subjects was done based on the inclusion and exclusion criteria. Enrolled subjects were randomized to either the treatment or placebo group in a 1:1 ratio as per the computer-generated randomization schedule. The investigational products (IPs) were masked to make their appearance identical. The blinded IPs in high-density polyethylene containers containing 35 tablets of either treatment or placebo were dispensed to the enrolled subjects on each visit for 3 months. The subjects were instructed to take the given medication as one tablet once a day after their main meal with water for 90 days. Any other antioxidant agents, vitamins, nutraceuticals, ayurvedic, or herbal medications were prohibited. Subjects were called for follow-up visits once a month. The pregnancy incidences were recorded. The subject further continued the treatment even after conception by a female partner to complete the study. The investigator assessed compliance to intervention on every follow-up visit by counting the leftover unadministered tablets returned by the subject. If a subject continuously missed dosing for > 3 consecutive days or total missed doses > 6 every thirty days of the trial period, the subject was treated as a dropout from the study.

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Statistical analysis

We analysed per protocol study population. Statistical analysis was performed using SPSS 10.0 software (SPSS, Chicago, IL, USA). Statistical methods included mean and standard deviation for normal distribution and median and interquartile range for abnormal distribution. Shapiro-Wilk's test was used to verify normality. Statistical comparisons between groups were made by a *t*-test, or Mann-Whitney *U* test (nonparametric test). A value of $p \leq 0.05$ was considered significant.

RESULTS

The mean age for the subjects randomized in treatment and placebo groups were comparable statistically (35 ± 5.1 years and 34 ± 5 years respectively).

Assessment of change in total sperm count in sub-fertile male subjects

The mean total sperm count in the treatment group was 27.56 ± 20.69 million/ml and in the placebo group was 27.15 ± 18.55 million/mL which was comparable at baseline. There was 42.41% (39.25 ± 80.32 million/mL) and an 11.04% (30.15 ± 19.38 million/mL) increase in total sperm count in treatment and placebo groups respectively. There was a significant increase in sperm counts in both groups compared to their respective baseline analyzed by dependent Student's *t*-test for the treatment and placebo group respectively). There was no significant difference observed between groups in sperm count at end of the study (**Table 2**).

When we further stratified the data *post hoc*, in subjects with a baseline sperm count less than 5, between 5 to 10, and between 10–15 million/mL, interesting results were observed. In subjects with baseline sperm counts less than 5 million/mL, antioxidant treatment increased total sperm counts by 76.75% compared to the placebo group's 5.57% increase. With baseline sperm counts less than 5–10 million/mL and 10–15 million/mL in the treatment group, there was a significant increase in sperm count of 73.62% and 43.72%, respectively, which was higher as compared to the placebo group (**Fig. 2**).

There was a significant increase in sperm count in the treatment group than placebo (31.33% and 4.52%, respectively) analyzed *post hoc* for subjects (n = 20 and 25 in placebo and treatment group, respectively) aged above 40 years (**Table 2**).

Table 2. Mean improvement in semen parameters

Parameters	Baseline		*p*-value (b/w group)	Day 90 (*p*-value within group)		*p*-value (b/w group)
	Treatment	Placebo		Treatment	Placebo	
Average sperm count (million/mL)	27.56 ± 20.69	27.15 ± 18.55	0.8690	39.25 ± 80.32 (0.0800)	30.15 ± 19.38 (0.7700)	0.1639
Average sperm motility (%)	17.18 ± 11.95	17.84 ± 11.70	0.6603	21.88 ± 14.21 (0.0010)	23.03 ± 22.09 (0.0043)	0.7878
Average DFI (%)	32.59 ± 12.67	31.38 ± 10.71	0.8219	26.81 ± 11.61 (0.0073)	28.45 ± 14.35 (0.0688)	0.6218
Average semen volume (mL)	1.77 ± 0.92	1.82 ± 0.91	0.6805	2.00 ± 0.89 (0.0032)	2.00 ± 1.90 (0.2412)	0.8617
Average sperm morphology (%)	3.46 ± 1.84	4.07 ± 3.46	0.0873	4.28 ± 1.91 (0.0010)	4.31 ± 2.28 (0.2859)	0.0199
Data analyzed for subjects over age of 40 yr						
Average sperm count (million/mL)	25.85 ± 23.89	24.32 ± 14.54	0.8111	33.95 ± 29.04 (0.0015)	25.42 ± 14.20 (0.5777)	0.0500
Average sperm motility (%)	16.78 ± 8.70	18.06 ± 11.57	0.3880	23.83 ± 15.33 (0.0018)	21.83 ± 15.65 (0.17303)	0.6224
Average DFI (%)	29.55 ± 12.40	25.15 ± 10.97	0.6912	24.90 ± 9.25 (0.8040)	23.90 ± 8.46 (0.6934)	0.8906
Average semen volume (mL)	1.58 ± 0.75	1.83 ± 0.71	0.7451	1.78 ± 0.58 (0.0032)	1.73 ± 0.56 (0.2755)	0.8440
Average sperm morphology (%)	4.40 ± 2.69	2.95 ± 0.40	0.0249	4.80 ± 2.38 (0.4222)	5.11 ± 2.23 (0.0008)	0.0212

Values are presented as mean ± standard deviation. Data analyzed by Student's *t*-test. Significant at $p < 0.05$. For semen analysis, n = 125 (treatment) and n = 128 (placebo). For DFI analysis, n = 66 (treatment) and n = 75 (placebo). In age group 40 years and above n = 20 for placebo and n = 25 for treatment group.
DFI, DNA fragmentation index.

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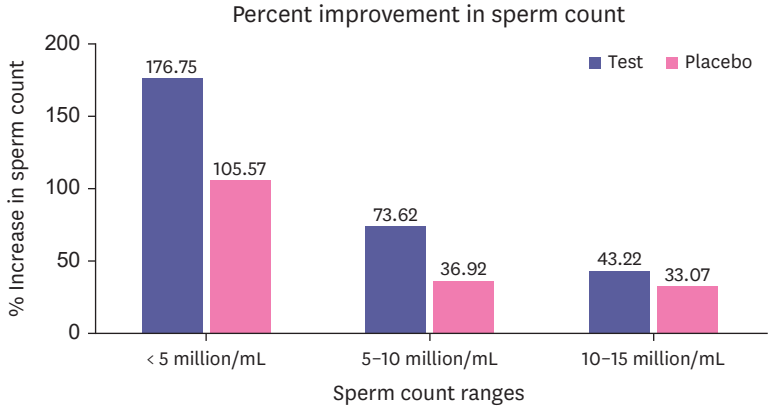

Figure 2. Percent improvement in sperm count with different baseline ranges.

Assessment of change in sperm motility in sub-fertile male subjects

The mean sperm motility was significantly increased by 27.35% (from 17.18% to 21.88%) in the antioxidant blend treated group and by 28.41% in placebo group. When the data involving subjects with age 40 and above was considered there was a significant increase in sperm motility of 42.01% in the treatment group and 20.87% (not significant) in the placebo group as compared to baseline (**Table 2**).

Assessment of change in % DFI in sub-fertile male subjects

Amongst subjects having DFI of more than 20%, the antioxidant blend treated group significantly reduced DFI from 32.59 ± 12.67% to 26.81 ± 11.61%. In subjects with age 40 years and above, there was more reduction in DFI in the antioxidant blend treated group than placebo (15.74% compared to 4.97%) (**Table 2**). For evaluating the effectiveness of intervention by an antioxidant blend we further stratified the subjects in a population with baseline DFI 20–30%, 31–40% and above 40%. The stratified data denoted in **Table 3** indicated that there is significant DFI reduction after treatment of antioxidant blend in subjects with high and extremely high baseline DFI (31–40% and above 40% DFI at baseline respectively).

Table 3. Changes in % reduction of DFI in population with different DFI slabs

Duration	Treatment (n = 42)	Placebo (n = 43)	*p*-value
DFI 20–30%			
Screening	24.03 ± 2.56	25.05 ± 2.87	0.1057
Day 90	26.08 ± 10.97	27.03 ± 10.90	
Mean diff. (Screening – Day 90)	−2.05 ± 11.60	−1.97 ± 11.59	0.9763
p-value	0.2824	0.3073	
DFI 31–40%			
Screening	35.56 ± 2.83	33.89 ± 2.03	0.1328
Day 90	27.25 ± 13.23	24.44 ± 8.55	
Mean diff. (Screening – Day 90)	8.31 ± 15.05	9.44 ± 8.34	0.8376
p-value	0.0431	0.0093	
DFI above 40%			
Screening	51.13 ± 13.26	49.00 ± 9.25	0.6409
Day 90	28.20 ± 12.06	35.83 ± 23.36	
Mean diff. (Screening – Day 90)	22.93 ± 19.55	13.17 ± 19.39	0.2073
p-value	0.0004	0.0383	

Values are presented as mean ± standard deviation. Data analyzed by Student's *t*-test. Significant at $p < 0.05$.
DFI, DNA fragmentation index.

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Assessment of change in total semen volume in sub-fertile male subjects

In the treatment group, the mean semen volume was significantly increased from 1.77 mL to 2.00 mL (12.99%). In placebo group, the mean semen volume was significantly increased by 9.89%. When the data involving subjects with age 40 and above were considered there was significant increase by 12.65% in the treatment group compared to a reduction of semen volume in the placebo group was observed (**Table 2**).

Assessment of change in sperm morphology in sub-fertile male subjects

The mean percent of sperm presenting normal morphology was increased in the antioxidant blend treated group from 3.46% to 4.28% and from 4.07% to 4.31%. There was a significant increase in normal sperm morphology in the treatment group compared to the placebo. Improvement in the morphology of sperms in subjects with age 40 years and more was also observed (**Table 2**).

DISCUSSION

There were improvements in sperm count, semen volume, sperm motility and sperm normal morphology in the treatment group. We studied the subject population, which included subjects aged 40 years and above, and found that antioxidant blend treatment significantly improved semen parameters compared to the placebo. There were improvements in semen parameters like sperm count (sperm count < 5 million/mL, 5–10 million/mL, 10.1–15 million/mL), i.e., severe oligospermia subjects, and in high to extremely higher baseline DFI (20–30%, 31–40% and above 40%) when the data was further stratified *post hoc*. There was no premature discontinuation of the subjects, no adverse events were reported during the study, indicating treatment is safe and well tolerated.

Interventional antioxidant blend tablet is a combination of micronutrients, essential amino acids, antioxidants, and vitamins that are essential for the male reproductive system.

As per clinical experience and published articles, after adjusting for female age, conception during a 12-month period was 30% less likely for men over age of 40 years as compared with men younger than age 30 years. A significant detrimental effect of advanced paternal age on sperm chromatin integrity (DFI > 10%) was also observed in the group of subjects with age 40 years and above. The sexual ability, as well as semen parameters, get compromised after 40 years in aging males [14]. We have performed *post hoc* treatment to the data collected stratifying it according to the age of subjects 40 years and above and observed improvement in semen parameters.

Studies worldwide have ascertained the important role of nutrients, vitamins and minerals in sperm health [15]. Sperm DNA fragmentation is correlated clinically with infertility. The sperm DNA damage is correlated with an increased frequency of spontaneous abortions, and diminished embryo quality. When DFI is above 25%, current literature suggests that therapeutic interventions like antioxidants, medical intervention, and change of lifestyle need to be employed [16].

The interventional antioxidant blend contains a blend of vitamins such as A, D, E, C, B12, and B6. Literature reports that clinical trials have shown the potential of these vitamins in reducing DNA fragmentation worldwide [17]. In some studies, the combination of vitamins with micronutrients like zinc, selenium, manganese, copper and iron as an antioxidant

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combination has achieved DFI% reduction at around 15–17% [18]. Antioxidants in the form of essential amino acids, vitamins and minerals are essential for energy metabolism and spermatozoa maturation and possess the potential of keeping sperm DNA integrity. In past literature, incorporation of the ginseng as a supplementation has demonstrated a reduction in DFI% in sub-fertile males [14,19].

Our study results confirmed that the antioxidant blend established clinical superiority over the placebo by significantly reducing the DFI% in a subset of subjects having a DFI of above 30–40% as well as having around a 15% reduction in DFI for subjects aged 40 years and above. The same is having clinical implication that the antioxidant blend studied in this trial can be a good treatment option in males with age 40 years and above with sub fertility.

There are many published researches available depicting the benefits of antioxidant treatment, especially for idiopathic or unexplained infertility [20-23]. Many pieces of evidence suggest that vitamin C protects sperm from oxidative damage. Supplementing vitamin C improves the quality of sperm in smokers by reducing sperm agglutination and has proved to increase fertility [23].

Research has ascertained that zinc deficiency leads to reduce sperm count and impotence in men. Supplementation with zinc improves sperm count [24]. Supplementation with selenium has also been shown to improve sperm motility. L-arginine, an amino acid is needed to produce sperm. Research worldwide has shown that quite a few nutrients, especially vitamin A, vitamin E, zinc and selenium are favorably related to androgen deficiency and sperm production [25]. It is well-researched fact that supplementation with vitamin B12 has increased sperm counts. Coenzyme Q10 is an antioxidant useful in the improvement in sperm function and has proven role in the treatment of asthenozoospermia [26]. Vitamin E supplementation may enhance fertility by decreasing free-radical damage to sperm cells. This possesses spermatogenetic activity also help increase the secretion of androgens, reduce free radicals, nourish sperm, decrease stress and promotes overall well-being [27].

According to the literature available, around 30% to 80% of male sub-fertility may be linked with oxidative stress damaging spermatozoa and decreasing the success of IVF techniques. Interventions of oral antioxidants like mayo-inositol, alpha-lipoic acid, folic acid, coenzyme Q10, zinc, selenium, and vitamins have shown improvement in semen reproductive potential and ICSI clinical outcome. From past research, it was observed that, sperm competence was improved after antioxidant supplementation evident by significantly better embryo quality in the cycles performed at T90, in terms of a higher proportion of good-morphology embryos with respect to baseline cycles [28].

In a previous Cochrane Data Base Systemic Review by Showell et al. [29], which included randomized controlled studies in a total of 2,876 couples using various antioxidant compounds, a positive impact on live birth and pregnancy rate in sub-fertile couples undergoing ART cycles has been shown. Only a part of the studies reported on pregnancy rates while others were restricted to sperm parameters. In this present study, the data obtained is in the agreement with the fact that antioxidant treatment could improve DFI and other semen parameters [29]. The present study is a scientific evidence for using antioxidant therapy in the treatment of male infertility to expect a good prognosis for IUI, ART, or IVF. Treatment with the present intervention is a very assertive option to aging sub-fertile males to improve semen parameters for better fertility outcomes.

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Our data is first-hand evidence of the safety of the use of tablets with the antioxidant blend to be administered for 3 months with no adverse effects were observed in any participants. We believe that the strength of this study is that it displayed the effectiveness of antioxidants in improving semen parameters, especially in men with severe oligospermia, extremely high DFI, and with age 40 years and above.

From our study, we confirm that the antioxidant blend tablet was effective in reducing sperm DNA fragmentation which is a major attribute of the study. In our study, we have processed all samples for DFI analysis at a centralized laboratory which removes bias and subjectivity and thus the effectiveness of interventional product can hold promise for reproducibility and robustness. We are aware of the limitation of the study as male age was used as a confounder but nutritional status, body mass index, partner age etc. To assess pregnancy outcomes after treatment of antioxidant blend tablet, a clinical trial with longer duration is warranted in future.

In conclusion, there is improvement in sperm count, semen volume, DFI, sperm motility, and sperm normal morphology in the treatment group. Study results confirmed the well-researched fact of antioxidants being effective to reduce oxidative stress and thus improve sperm DNA integrity. The study results indicate that the antioxidant blend tablet treatment improved semen parameters in males aged 40 and above. There were no adverse events during the study suggesting the safety and tolerability of the interventional antioxidant blend tablet.

Oligospermia is the most common cause of infertility in males. Many nutraceuticals have traditional claims which improve fertility in such cases. Antioxidant blend as an interventional tablet has shown promising effects in clinical trials. We propose the use of an antioxidant blend will improve the quality and quantity of sperm in sub-fertile males even in aging males with age 40 years and above.

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