

A MULTICENTRIC RETROSPECTIVE INTERVENTIONAL STUDY TO ASSESS THE EFFICACY OF ANTIOXIDANT FORMULA (TRAZER M FORTE™) IN MALE FERTILITY IN INDIA (SMART TRIAL)

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Abstract

Background: The SMART trial, a single-arm prospective interventional study, investigated the impact of Trazer M Forte™, an antioxidant formula, on sperm parameters and male fertility outcomes in individuals with suboptimal sperm parameters. **Materials and Methods:** A diverse cohort of males (n=84), aged 18 to 45 years, diagnosed with suboptimal sperm parameters, was enrolled in 10 fertility clinics in India. Informed consent was obtained, and participants received Trazer M Forte™ twice daily for a standardized duration. Sperm parameters were assessed at baseline and the final visit following World Health Organization guidelines. Compliance was monitored through regular follow-ups and self-reporting. **Result:** The enrolled cohort exhibited various characteristics with a mean age of 32.87±4.84 years and infertility duration ranging from 1 to 6 years. Primary infertility was prevalent in [54 (64.3%)], secondary fertility in 28 (33.3%), and 2 (2.4%) had a varicocele. High compliance [82 (97.6%)] with Trazer M Forte™ was observed. Significant improvements in sperm motility (32.43±17.62%, p < 0.001), sperm concentration (52.33%, p < 0.001), and sperm morphology (12.67%, p = 0.001) were noted at the last visit. Despite a non-significant decrease in ejaculated volume, a substantial increase in sperm parameters (52.33%, 32.43%, and 12.67% increase in sperm concentration, sperm motility, and sperm morphology, respectively) was observed. Clinical pregnancies were achieved by 34 (40.5%) of couples during the study. **Conclusion:** The SMART trial reveals the potential efficacy of Trazer M Forte™ in enhancing sperm parameters, with significant percentage improvements observed. These findings highlight the role of antioxidant interventions in male fertility management, necessitating further research to validate and extend these outcomes.

INTRODUCTION

Couple infertility, as defined by the World Health Organization (WHO), refers to the inability to achieve pregnancy despite engaging in frequent unprotected sexual intercourse for 12 months or more.^[1] Globally, infertility affects 15% of couples, where 50% have a male factor involved.^[2]

Male infertility is a complex problem with multiple causes, including genetic, environmental, and

behavioral factors.^[3] Out of these factors, oxidative stress has been identified as a crucial factor that negatively affects sperm function and reduces fertility. Reactive oxygen species (ROS) produced during regular cellular activities can cause oxidative stress, which can negatively affect the shape, movement, and genetic material of sperm.^[4] Antioxidants have a crucial function in reducing oxidative harm and, as a result, enhancing sperm quality.^[5]

The SMART study aims to examine the effectiveness of Trazer M Forte™, a specialized antioxidant mixture developed to target male reproductive problems in the Indian population. This study is distinctive because it focuses on 'Ubiquinol,' a reduced version of Coenzyme Q10 (CoQ10) with potent antioxidant effects. CoQ10 is necessary for energy synthesis and has significant antioxidant characteristics. It is frequently utilized to promote spermatogenesis in cases of idiopathic male infertility.^[2]

Trazer M Forte™ is a combination of antioxidant supplements, including lycopene, zinc, astaxanthin, L-carnitine, and Ubiquinol, providing enhanced benefits. Lycopene helps improve lipid peroxidation and deoxyribonucleic acid damage, whereas zinc is linked to improvements in sperm motility and shape.^[6] Astaxanthin has a beneficial effect on the concentration, movement, and shape of sperm.^[7] Additionally, in this formulation, including L-carnitine and Ubiquinol enhances sperm motility.^[6] Research on the effect of Ubiquinol on male fertility, particularly among the Indian population, is limited despite its potential importance. Despite a thorough literature search, there has been very little evidence of reduced CoQ10 (Ubiquinol) in Indian patients. This is the first of a kind study in Indian patients to evaluate the role of Ubiquinol in an Indian scenario. This forthcoming interventional study was carried out at various centers in India, encompassing a heterogeneous group of male participants who have been identified with suboptimal sperm parameters. The main objective was to evaluate the influence of Trazer M Forte™ on sperm parameters such as sperm volume, concentration, motility, and morphology by WHO Manual 2021 parameters, widely acknowledged as a crucial factor in male fertility. The study also seeks to investigate the correlation between antioxidant supplementation and clinical pregnancy rates, offering valuable insights into the broader implications of such interventions in assisted reproductive technologies.

MATERIALS AND METHODS

The SMART trial is a single-arm prospective interventional study. The study adheres to the principles of the Declaration of Helsinki and has obtained ethical approval from the institutional review boards of all participating centers.

A diverse cohort of male participants aged 18 to 45 years were diagnosed with suboptimal sperm parameters and were recruited from 10 fertility clinics in India. Informed consent was obtained from all participants after providing detailed information about the study objectives, procedures, and potential risks.

Males diagnosed with suboptimal sperm parameters, including reduced sperm motility, and couples with a history of infertility for a duration ranging from 1 to 6 years were included. Individuals with a history of

known genetic abnormalities affecting fertility, participants undergoing concurrent treatments for male infertility, and the presence of systemic illnesses known to impact fertility were excluded.

Intervention

Participants received Trazer M Forte™, an antioxidant formula comprising lycopene, zinc, astaxanthin, L-carnitine, and Ubiquinol as the intervention. The recommended dosage (two times daily) and duration of supplementation (approx. 90 days) were standardized across all participating centers. Compliance with the intervention was monitored through regular follow-up appointments and participant self-reporting.

Outcome Measures

Major sperm parameters, including ejaculated volume, sperm concentration, sperm motility, and sperm morphology, were assessed at baseline (first treatment day) and during the final visit (last treatment day as decided by the treating physician or the occurrence of pregnancy). Semen analysis was conducted according to WHO guidelines. Mean and percentage changes in these parameters were evaluated to determine the impact of Trazer M Forte™ on male fertility outcomes. Data were collected using standardized case report forms and entered into a secure electronic database. Regular monitoring visits were conducted at each study site to ensure data accuracy, participant safety, and protocol adherence.

Statistical Analysis: Data analysis was performed using IBM SPSS ver. 25. Descriptive statistics were used to summarize participant characteristics. Continuous variables were compared using paired t-tests. A p-value of <0.05 was considered significant.

RESULTS

Participant Characteristics: A total of 84 male participants with suboptimal sperm parameters were enrolled in the SMART trial across eight participating fertility clinics in India. The mean age of the participants was 32.87±4.84 years, ranging from 18 to 45 years. Mean height and weight were 170.32±6.94 cm (range 152-188) and 73.77±10.47 kg (range 47-100) respectively. The duration of infertility in the enrolled couples ranged from 1 to 6 (mean 2.19±1.47 years) years.

The majority had primary infertility [54 (64.3%)], 28 (33.3%) were diagnosed with secondary fertility and 2 (2.4%) had varicocele. 24 (28.6%) were smokers and 31 (36.9%) were alcoholics.

Intervention Compliance

Eighty-six patients' data were collected; 2 were excluded due to non-compliance. The compliance rate with Trazer M Forte™ was high, with 97.6% of participants completing the recommended duration of antioxidant supplementation. Regular follow-up appointments and participant self-reports indicated consistent adherence to the intervention protocol.

Changes in Sperm Parameters

Following the intervention with Trazer M Forte™, a statistically significant improvement in sperm motility was observed. The mean sperm motility increased to 42.55±17.62 at the last visit ($p < 0.001$). Changes in Sperm Concentration ($p < 0.001$) and sperm morphology ($p = 0.001$) were also analyzed, showing significant improvement at the last visit [Table 1, Figure 1]. Ejaculated volume was decreased

by 0.14%, though insignificant, whereas sperm concentration, sperm mortality, and sperm morphology were significantly increased by 52.33%, 32.43%, and 12.67%, respectively (Figure 2).

Clinical Pregnancy Rates

During the study period, 34 couples achieved clinical pregnancy. The clinical pregnancy rate was 40.5%.

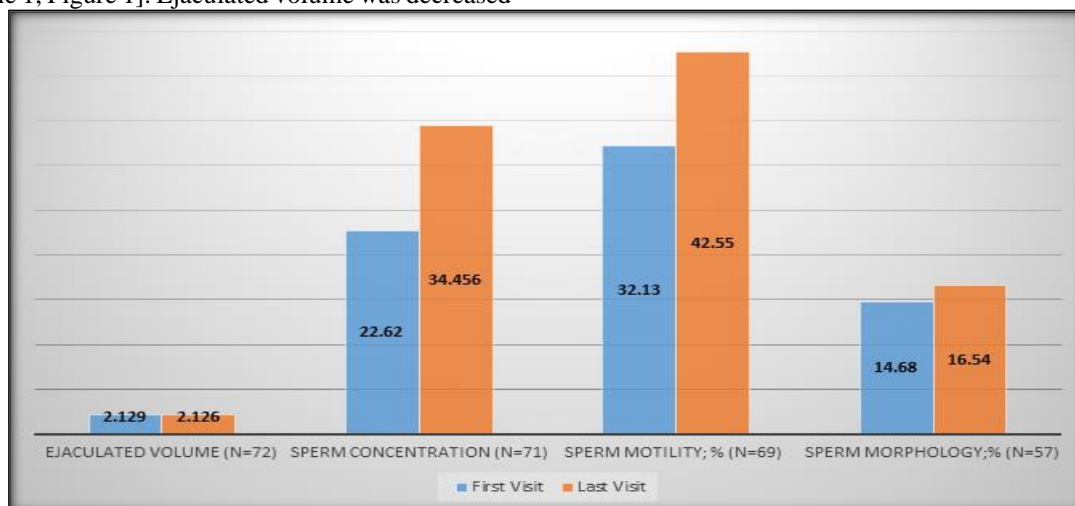


Figure 1: Change in sperm parameters from first to last visit in study participants

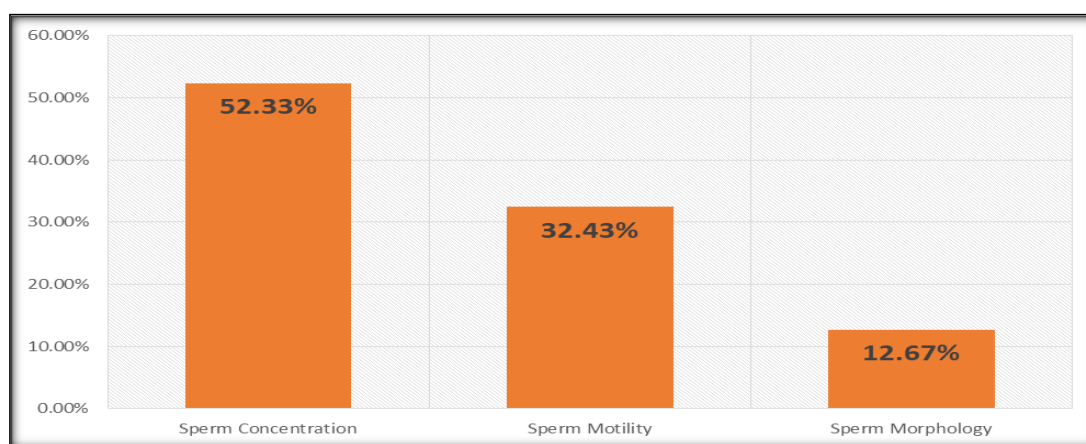


Figure 2: Showing percentage increase in significant sperm parameters at last visit from the baseline

Table 1: Comparing sperm parameters between the first and last visit of study participants

Parameters	First Visit	Last Visit	Percentage change	P value
Ejaculated volume (n=72)	2.129±0.860	2.126±0.863	0.14% decrease	0.975
Sperm Concentration (n=71)	22.620±24.36	34.456±24.03	52.33% increase	<0.001
Sperm Motility; % (n=69)	32.13±20.08	42.55±17.62	32.43% increase	<0.001
Sperm Morphology; % (n=57)	14.68±7.91	16.54±9.10	12.67% increase	0.001

DISCUSSION

CoQ10 is a necessary co-factor that possesses potent antioxidant qualities. It plays a crucial role in the production of energy in mitochondria. This energy production is vital for maintaining the efficient energy system of spermatozoa. Additionally, CoQ10 helps preserve the membranes of spermatozoa from lipid peroxidation.^[8] Low levels of CoQ10 have been

linked to many disorders that contribute to infertility, including varicocele and oligozoospermia. CoQ10 is a commonly used antioxidant in the treatment of idiopathic male infertility.^[9]

The diverse participant characteristics revealed in the SMART trial shed light on the intricate clinical and demographic profiles of males grappling with suboptimal sperm parameters, reflecting the complex landscape of infertility. The mean age of 32.87±4.84

years is consistent with the age range typically associated with male fertility concerns, underscoring the relevance of the study cohort to real-world fertility issues.^[10-12] Notably, the duration of infertility at 2.19±1.47 years highlights the persistent nature of reproductive challenges faced by participating couples.

The prevalence of primary infertility (64.3%), secondary fertility (33.3%), and varicocele (2.4%) contributes to the heterogeneity of the study population, providing valuable context to the multifaceted nature of male reproductive health addressed in this study. Additionally, lifestyle factors such as smoking (28.6%) and alcohol consumption (36.9%) highlight the importance of considering environmental influences on male fertility.

The exceptionally high compliance rate of 97.7% among participants, with only two exclusions due to non-compliance, underscores the feasibility and acceptability of Trazer M Forte™ antioxidant supplementation. Such robust compliance is essential for maintaining the study's internal validity, aligning with findings from similar studies emphasizing the practicality of integrating antioxidant interventions into male fertility management.^[13,14]

The observed improvements in sperm parameters following Trazer M Forte™ supplementation align with and extend findings from existing literature on antioxidant interventions in male infertility.^[13,14] Notably, the substantial enhancement in sperm motility echoes outcomes reported by Alahmar et al.^[10] and Safarinejad et al.^[11] highlighting the consistent potential of antioxidant interventions to positively influence this critical aspect of male fertility. The improvements in sperm concentration and morphology observed in our study are consistent with previous findings emphasizing the multifaceted benefits of antioxidant supplementation. Alahmar et al. studied 50 patients with idiopathic OA who received CoQ10 (300 mg/day) orally once daily for three months. Treatment resulted in increased sperm progressive motility ($p < 0.01$) compared to baseline, highlighting promising therapy for patients with idiopathic infertility and may improve their fertility potential.^[10] In a Randomized, double-blind, placebo-controlled study by Safarinejad et al., 228 patients with idiopathic oligoasthenoteratospermia (aged 24-44 years) who received Ubiquinol 200 mg/day Once daily orally for 26 weeks reported significant improvement in sperm density ($p = 0.005$), motility ($p = 0.008$) and morphology ($p = 0.01$) after ubiquinol treatment. Another study by Thakur et al. (60 patients with oligospermia aged 20-40 years) investigated the role of Ubiquinol 150 mg/day Once daily orally for six months reported increase in total sperm count and total sperm motility ($p < 0.05$) and reduction of number of immobile and sluggish motile sperm ($p < 0.05$).^[15] In a recent prospective, randomized study by Alahmar et al, (70 patients with idiopathic oligoasthenoteratospermia aged 25 years) receiving CoQ10 200 mg/day compared with Selenium 200 mcg/day Once daily

orally for three months reported an increase in sperm density total sperm motility and progressive sperm motility ($p < 0.01$) after CoQ10 administration.^[16] These collective results substantiate the contention that Trazer M Forte™, with its unique formulation, including Ubiquinol, holds promise as an effective intervention for ameliorating suboptimal sperm parameters, aligning with the encouraging outcomes reported in the literature.

The attainment of clinical pregnancy in 40.5% of couples during the study period adds a compelling dimension to our findings. While further exploration is needed to establish a direct causative link between improved sperm parameters and increased clinical pregnancy rates, the correlation observed between enhanced sperm motility and clinical pregnancy aligns with previous findings.^[10,15,16]

The SMART trial has limitations, including the absence of a control group, a relatively modest sample size, and a short follow-up duration. Self-reported lifestyle data may introduce bias, and unexplored confounding factors, such as dietary habits, could influence the observed outcomes. Despite these constraints, the study provides valuable preliminary insights into the potential efficacy of Trazer M Forte™, underscoring the need for further research with more extensive cohorts and refined methodologies. Further research with larger cohorts and extended follow-up periods is essential to validate and build upon these findings, advancing our knowledge of antioxidant interventions in addressing male infertility.

CONCLUSION

In conclusion, the SMART trial highlights the potential effectiveness of Trazer M Forte™ in ameliorating suboptimal sperm parameters among males with fertility concerns. The observed significant improvements in sperm motility, concentration, and morphology, coupled with a high compliance rate, provide promising initial evidence.

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