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Original Research Article

Comparative effects of pentoxifylline and coenzyme Q10 on sperm motility in subfertile men with asthenozoospermia: a randomized controlled trial

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ABSTRACT

Background: Asthenozoospermia, characterized by reduced sperm motility, is a leading cause of male subfertility. While both pentoxifylline and coenzyme Q10 have demonstrated beneficial effects on semen parameters, comparative evidence regarding their efficacy remains limited. This study aimed to assess and compare the effects of pentoxifylline and coenzyme Q10 on sperm motility and other seminal parameters in sub fertile men with asthenozoospermia.
Methods: This randomized controlled trial was conducted at the Department of Reproductive Endocrinology and Infertility, Bangladesh Medical University, from April 2022 to March 2023. A total of 104 subfertile men diagnosed with asthenozoospermia were randomly assigned to receive either pentoxifylline (400 mg twice daily) or Coenzyme Q10 (100 mg twice daily) for three months. Semen parameters, including ejaculate volume, sperm concentration, total and progressive motility, total motile sperm count, and morphology, were evaluated before and after treatment. Statistical analysis was performed via SPSS v26.0, with $p<0.05$ considered significant.
Results: Baseline demographic characteristics were comparable between the two groups. Both treatments resulted in significant improvements in sperm motility and total motile sperm count after three months. However, the pentoxifylline group demonstrated significantly greater improvements in total sperm motility (41.28±12.38% vs. 36.15±11.84%), progressive motility (32.30±10.26% vs. 24.95±10.40%), total motile sperm count (55.04±41.18 vs. 32.85±25.62 million), and ejaculate volume (2.83± 0.96 ml vs. 2.32 ± 0.96 ml) than did the CoQ10 group ($p<0.05$). No significant differences in the sperm concentration or morphology were detected between the groups.
Conclusions: Both pentoxifylline and Coenzyme Q10 effectively improve semen quality in men with asthenozoospermia, but pentoxifylline appears to be more effective in enhancing motility-related parameters and the ejaculate volume. Pentoxifylline may be considered a preferred first-line option in the pharmacologic management of asthenozoospermia.

Keywords: Asthenozoospermia, Subfertility, Sperm motility, Pentoxifylline, Coenzyme Q10, Randomized controlled trial, Male infertility

INTRODUCTION

Male fertility is a growing public health concern worldwide.[1] Approximately 15% of couples worldwide face fertility issues, and males account for approximately half of these cases.[2] Semen analysis is the primary method for evaluating male fertility and focuses on both the quantity (azoospermia, oligospermia) and quality (asthenozoospermia, teratozoospermia) of sperm.[3] Their reduction leads a man to become subfertile.[4] Male subfertility refers to a man's reduced ability to become pregnant after one year of regular unprotected intercourse due to poor sperm quality.[5] It can be subdivided into primary and secondary subfertility. Primary subfertility refers to a delay before taking a first child, whereas secondary subfertility refers to a delay in taking a subsequent child with a previous experience.[6] Some lifestyle practices, such as poor diet, lack of physical activity, smoking, excessive alcohol consumption, psychological stress, exposure to low-level electromagnetic fields from devices such as mobile phones and laptops, obesity, and aging, lead men to become subfertile.[7] A global meta-analysis revealed that human semen quality has significantly declined over the past 75 years from 1938-2013, and particularly in Western countries, semen quality decreased by more than 50% between 1973 and 2011.[8,9]

Asthenozoospermia is a common cause of male fertility, where the progressive motility rate and total motility rate of sperm are less than 30% and 40%, respectively.[10] This condition is characterized by a reduced or total lack of sperm motility in a fresh semen sample.[11] It can be caused by various factors, including urogenital infections, varicocele, flagellar defects, metabolic diseases, and genetic conditions.[11]

Several drugs, surgeries, and synthetic reproductive technologies are often applied as treatments for male fertility problems, and empirical drugs are still the most commonly used treatments for asthenozoospermia due to their long-standing history.[12] Pentoxifylline is a derivative of methylxanthine, which is a commonly used drug to prevent fertility problems, increasing cAMP levels, increasing oxygen consumption and metabolic activity, and generating energy that enhances sperm motility and compatibility.[13,14] The drug has been used in low-fertility treatments since 1979.[15]

A previous study reported the significant effectiveness of asthenozoospermia treatment by increasing the motility of sperm immediately, after one hour and after 2 hours of activation compared with the control group.[16] It is generally well tolerated with few side effects, contraindications, or drug interactions. However, it should be avoided in individuals with a history of cerebral or retinal hemorrhage; intolerance to theobromine, theophylline, or caffeine; and pregnant or breastfeeding women. Caution is advised when warfarin is used, as it may prolong the prothrombin time.[17]

Another compound, coenzyme Q10 (CoQ10), was also used for the same reason. It simulates the structure and function of the sperm.[18] It was discovered by Frederick Crane and colleagues in 1957. It is ubiquitously found in nature because it is also known as ubiquinone.[19] It is the third most consumed dietary supplement worldwide.[20] It is a vitamin-like, fat-soluble compound ubiquitously present in all cells that functions in essential energy-producing enzymatic reactions and prevents reactive oxygen.[18-21] Endogenous CoQ10 is closely linked to sperm count and motility and is a key antioxidant in seminal plasma. Supplementing with exogenous CoQ10 improves sperm motility due to its ability to support mitochondria and to its antioxidant properties.[21] A study was conducted to determine the efficacy of the coenzyme in treating asthenozoospermia and was found to be significantly effective in increasing sperm motility.[22] Another study compared CoQ10 and a placebo, in which the enzyme was found to be significantly effective in increasing sperm motility.[23]

Numerous clinical and experimental studies have consistently shown that CoQ10 is very safe, well tolerated, and has minimal side effects (insomnia, digestive problems) or drug interactions (with insulin, warfarin).[24] Previous studies have shown the effectiveness of both substances in treating asthenozoospermia. However, which of these methods performs better in the treatment of sub fertile males with asthenozoospermia has not been explored. This lack of evidence led us to conduct this study to assess the comparative effects of pentoxifylline and coenzyme Q10 on sperm motility in sub fertile men with asthenozoospermia.

METHODS

Study design, setting and period

This randomized controlled trial was conducted at the Department of Reproductive Endocrinology and Infertility, Bangladesh Medical University (BMU) (formerly Bangabandhu Sheikh Mujib Medical University), Dhaka, Bangladesh, from April 2022 to March 2023.

Study population and selection criteria

A total of 104 sub fertile men diagnosed with asthenozoospermia were enrolled in the study. Men aged 25-45 years, with a history of infertility for ≥12 months, and with abnormal sperm motility (total motility <40% or progressive motility <32%) according to the 2010 WHO criteria were included. Patients with azoospermia, varicocele, genital tract infections, hormonal disorders, systemic illnesses, a history of smoking or recent antioxidant therapy, and those whose partners had identifiable female factor infertility were excluded.

A detailed clinical history, physical examination, and relevant investigations were performed to exclude known causes of infertility.

Study procedure

Eligible participants were enrolled after informed written consent was obtained. Patients were randomly allocated into two treatment groups. One group received oral pentoxifylline 400 mg twice daily, whereas the other group received oral Coenzyme Q10 100 mg twice daily, both for a duration of three months. The participants were advised to maintain their usual diet and lifestyle and to avoid any additional medications, supplements, or fertility-enhancing agents during the study period. Compliance was assessed during follow-up visits.

Semen analysis

Semen samples were collected by masturbation after 3-5 days of sexual abstinence at baseline and again after three months of treatment. The samples were allowed to liquefy at 37°C for up to 30 minutes before analysis. Semen parameters, including ejaculate volume, sperm concentration, total motility, progressive motility, total motile sperm count, and normal morphology, were assessed following the WHO Laboratory Manual for the Examination and Processing of Human Semen (5th edition). All analyses were performed in the same laboratory by experienced personnel to ensure consistency.

Outcome measures

The primary outcome measure was the change in total and progressive sperm motility from baseline to three months of treatment. The secondary outcomes included changes in the sperm concentration, sperm morphology, ejaculate volume, and total motile sperm count.

Ethical approval

Ethical approval: Ethical approval was obtained from the institutional review board of BMU (previously known as Bangabandhu Sheikh Mujib Medical University (Approval number: BSMMU/2022/5/56)) before the commencement of this study.

Statistical analysis

The data were analyzed via SPSS version 26.0 (IBM Corp., Armonk, NY, USA). Continuous variables are expressed as the mean ± standard deviation (SD). Paired T tests were used to compare pre- and posttreatment values within each group, while independent sample T tests were applied for between-group comparisons. A P value <0.05 was considered to indicate statistical significance.

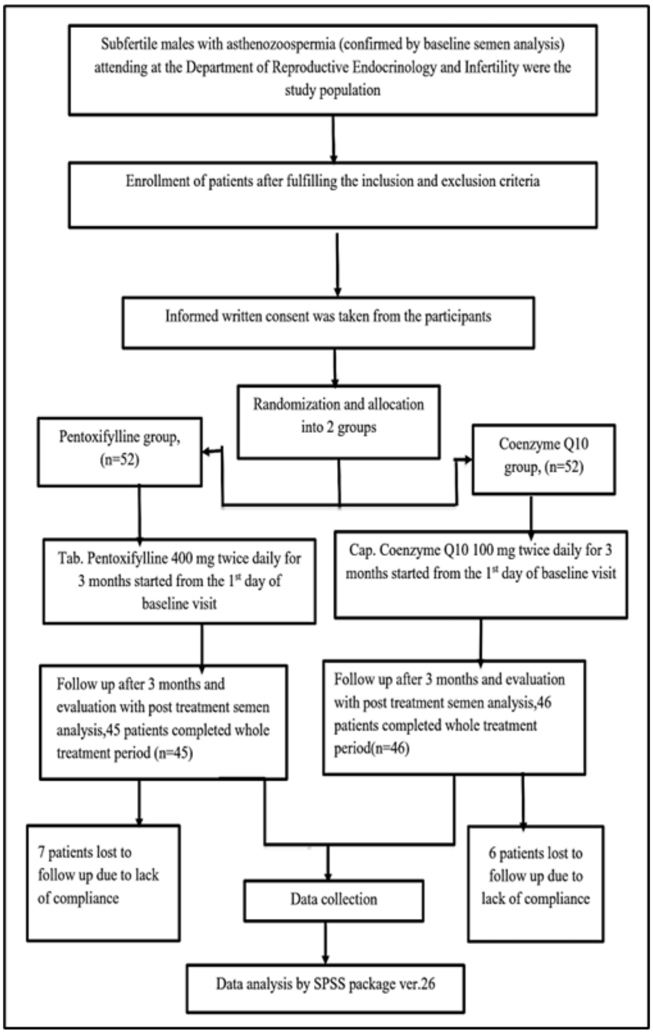

Figure 1: Data collection and processing flow chart.

RESULTS

Baseline demographic characteristics were comparable between the two groups. The mean age was 34.0±3.8 years in the pentoxifylline group and 33.5±4.0 years in the Coenzyme Q10 group (p=0.452). The mean BMIs were 26.3±2.2 kg/m² and 27.0±2.2 kg/m², respectively (p= 0.149), with most participants being overweight. Educational status and residence distribution were similar across groups (p> 0.05) (Table 1).

Total sperm motility increased substantially from 25.23±6.31% to 41.28±12.38% (p<0.001), whereas progressive motility improved markedly from 15.82±6.21% to 32.30±10.26% (p<0.001), reflecting a notable increase in sperm functional dynamics. The total motile sperm count rose significantly from 18.36±12.09 to 55.04±41.18 million (p<0.001), and the sperm concentration increased from 34.58±16.37 to 43.59±17.37 million/ml (p<0.001). Additionally, the ejaculate volume improved from 2.05±0.81 mL to 2.83±0.96 mL (p<0.001), and normal sperm morphology increased from 24.44±9.83% to 32.71±15.36% (p<0.001) (Table 2).

Table 1: Baseline demographic characteristics of the study participants in the pentoxifylline and coenzyme Q10 groups (n=104).

Variables	Category	Pentoxifylline group (n=52), N (%)	Coenzyme Q10 group (n=52), N (%)	P value
Age (years)	Mean ± SD	34.0±3.8	33.5±4.0	0.452
BMI	Mean ± SD	26.3±2.2	27.0±2.2	0.149
	Normal BMI (18.5-24.9)	13 (25.0)	9 (17.3)	
	Overweight (25.0-29.9)	39 (75.0)	43 (82.7)	
Education				
	Primary	8 (15.4)	8 (15.4)	0.895
	Secondary	8 (15.4)	11 (21.2)	
	Higher secondary	21 (40.4)	19 (36.5)	
	Graduate	15 (28.8)	14 (26.9)	
Residence				
	Rural	16 (30.8)	15 (28.8)	0.830
	Urban	36 (69.2)	37 (71.2)	

The data are expressed as the means ± SDs or numbers (%); independent T tests and chi-square tests were applied as appropriate; p< 0.05 was considered statistically significant.

Table 2: Semen parameters in sub fertile men with asthenozoospermia before and after the administration of pentoxifylline treatment.

Parameter	Pentoxifylline group		P value
	Pretreatment (52)	Post treatment (45)	
Ejaculate volume (ml)	2.05±0.81	2.83±0.96	<0.001**
Sperm count (million/ml)	34.58±16.37	43.59±17.37	<0.001**
Sperm motility (%)	25.23±6.31	41.28±12.38	<0.001**
Progressive motility (%)	15.82±6.21	32.30±10.26	<0.001**
Total motile sperm count (mil)	18.36±12.09	55.04±41.18	<0.001**
Sperm morphology (%)	24.44±9.83	32.71±15.36	<0.001**

*Significance level 0.05; **Significance level 0.001

Table 3: Semen parameters in sub fertile men with asthenozoospermia before and after administration of coenzyme Q10.

Parameter	Coenzyme Q10 group		P value
	Pretreatment (52)	Post treatment (46)	
Ejaculate volume (ml)	2.04±0.68	2.32±0.96	0.087
Sperm count (million/ml)	36.37±20.74	42.38±26.73	0.007*
Sperm motility (%)	24.83±8.50	36.15±11.84	<0.001**
Progressive motility (%)	14.13±5.87	24.95±10.40	<0.001**
Total motile sperm count (mil)	18.06±12.65	32.85±25.62	<0.001**
Sperm morphology (%)	27.0±11.85	30.51±17.22	0.060

*Significance level 0.05; **Significance level 0.001

Table 3 shows that three months of treatment with Coenzyme Q10 therapy significantly improved multiple seminal parameters among sub fertile men. Total sperm motility increased markedly from 24.83±8.50% to 36.15±11.84% (p<0.001), whereas progressive motility improved from 14.13±5.87% to 24.95±10.40% (p<0.001), indicating a robust increase in the functional potential of the sperm. The total motile sperm count also increased significantly (18.06±12.65 to 32.85±25.62 million; p<0.001), and the sperm concentration showed a modest but statistically significant increase (36.37±20.74 to 42.38±26.73 million/mL; p=0.007). Although there was an increase in ejaculate volume and sperm morphology posttreatment, these changes were not statistically significant (p=0.087 and p=0.060, respectively). Posttreatment comparisons between the pentoxifylline and Coenzyme Q10 groups revealed significant differences in several key semen parameters.

Compared with the Coenzyme Q10 group, the pentoxifylline group presented significantly greater ejaculate volume (2.83±0.96 mL vs. 2.32±0.96 mL; p=0.013), sperm motility (41.24±12.38% vs. 36.15±11.84%; p=0.046), progressive motility (32.30±10.26% vs. 24.95±10.40%; p<0.001), and total motile sperm count (55.04±41.18 million vs. 32.85±25.62 million; p=0.002). However, no significant differences were observed in the sperm count (p=0.798) or morphology (p=0.516) between the two groups (Table 4).

Table 4: Comparison of posttreatment semen parameters between the pentoxifylline and coenzyme Q10 groups in sub fertile men with asthenozoospermia.

Parameter	Posttreatment comparison		P value
	Pentoxifylline (45)	Coenzyme Q10 (46)	
Ejaculate volume (ml)	2.83±0.96	2.32±0.96	0.013*
Sperm count (million/ml)	43.59±17.37	42.38±26.73	0.798
Sperm motility (%)	41.24±12.38	36.15±11.84	0.046*
Progressive motility (%)	32.30±10.26	24.95±10.40	<0.001**
Total motile sperm count (mil)	55.04±41.18	32.85±25.62	0.002*
Sperm morphology (%)	32.17±15.36	30.51±17.22	0.516

*Significance level 0.05; **Significance level 0.001

DISCUSSION

This randomized controlled trial was conducted at a tertiary care center in Bangladesh to compare the efficacy of pentoxifylline and coenzyme Q10 in improving seminal parameters, especially sperm motility, among sub fertile men with asthenozoospermia. This study revealed that both treatments significantly enhanced sperm quality. Notably, compared with Coenzyme Q10, pentoxifylline resulted in superior improvements in sperm motility, progressive motility, and total motile sperm count.

The present study revealed that three months of pentoxifylline administration led to significant improvements in all evaluated semen parameters in sub fertile men with idiopathic asthenozoospermia. Improvements in sperm motility, progressive motility, concentration, morphology, total motile sperm count, and ejaculate volume were observed, indicating a broad enhancement in both functional and structural sperm quality. These results are consistent with findings of Moein et al, who reported increased progressive motility in asthenozoospermic men treated with oral pentoxifylline for three months, regardless of the presence of mild varicocele.[25] Similarly, Nabi et al demonstrated that post thaw incubation with pentoxifylline significantly enhanced sperm motility in vitrified samples without compromising chromatin or DNA integrity.[26] The current findings also align with those of Çetintaş et al, who reported significant improvements in both sperm concentration and morphology in asthenozoospermic and oligoasthenozoospermic males treated with pentoxifylline.[27] Moreover, Amer et al reported that the use of pentoxifylline during semen preparation improved fertilization outcomes in ICSI procedures, further supporting its clinical utility.[28] From a mechanistic standpoint, the effects of pentoxifylline can be attributed to its inhibition of phosphodiesterase activity, which increases the level of intracellular cyclic AMP and enhances sperm motility. Its antioxidant and hemorheological properties also reduce oxidative stress and improve testicular blood flow, creating a more favorable environment for spermatogenesis.[26] Additionally, Ghasemzadeh et al noted that pentoxifylline preserved sperm viability more effectively than control treatments did in in vitro studies.[29] These findings may be due to the ability of pentoxifylline to increase intracellular cAMP levels by inhibiting phosphodiesterase, which may stimulate sperm motility. Its antioxidant effects likely reduce oxidative damage to sperm cells, whereas improved microcirculation may support spermatogenesis.

This study also demonstrated that three months of Coenzyme Q10 (CoQ10) therapy led to significant improvements in several seminal parameters among sub fertile men. Specifically, total sperm motility increased from 24.83% to 36.15%, and progressive motility increased from 14.13% to 24.95% (both $p<0.001$), reflecting a substantial increase in sperm function. Additionally, the total motile sperm count and sperm concentration significantly increased, whereas the ejaculate volume and morphology improved non significantly. These findings indicate that CoQ10, a potent mitochondrial antioxidant, may increase sperm bioenergetics and reduce oxidative stress, a major contributor to male subfertility. The observed improvements in motility and count align with previous studies reporting similar benefits. For example, Alahmar et al (2021) reported that treatment with 200 mg/day CoQ10 for 3 months improved total and progressive motility in men with idiopathic oligoasthenozoospermia.[30] Another study confirmed that CoQ10 supplementation enhanced seminal antioxidant status and reduced reactive oxygen species (ROS).[30] Moreover, Hasoon (2019) reported improved sperm volume and activity following combination therapy with CoQ10 and L-arginine.[31] Alahmar et al also reported that CoQ10 decreased sperm DNA fragmentation and increased the activity of antioxidant enzymes, supporting our hypothesis that CoQ10 counters oxidative stress.[32] However, not all of the findings were consistent. Tiseo et al (2017) noted no significant associations between dietary CoQ10 intake and sperm quality, likely because of lower bioavailability from food sources.[33] Furthermore, a comparative study revealed that multivitamin therapy yielded greater improvements than did CoQ10 alone, suggesting synergistic effects of combined antioxidants.[34] These findings may be due to the role of CoQ10 as a mitochondrial antioxidant that enhances ATP production, thereby increasing sperm motility and function. Its ability to neutralize reactive oxygen species likely reduces oxidative damage to spermatozoa. Additionally, improved seminal antioxidant status may support spermatogenesis and overall sperm quality.

Our study also revealed that compared with Coenzyme Q10, pentoxifylline significantly improved ejaculate volume, total motility, progressive motility, and total motile sperm count in men with asthenozoospermia. These results indicate that while both agents positively influence semen quality, pentoxifylline has a more pronounced effect on motility-related parameters and seminal fluid production. This outcome supports earlier clinical findings. Cetintaş et al demonstrated enhanced motility and acrosomal integrity following pentoxifylline treatment in asthenozoospermic samples.[27] Similarly, Nassar et al reported that pentoxifylline increased hyperactivated motility and cervical mucus penetration capacity.[29] A prospective study by Amer et al revealed improved fertilization and embryo quality after pentoxifylline use during sperm preparation for ICSI.[28] Coenzyme Q10 was less effective than pentoxifylline in this study; however, it has shown numerous beneficial effects. An RCT conducted by Debnath et al reported significant increases in motility and total motile sperm count after 12 weeks of CoQ10 therapy.[35] Additionally, Balercia et al demonstrated improved motility through enhanced mitochondrial activity.[36]

Although it has beneficial effects, its outcomes tend to be slower and more dose dependent, often requiring longer durations or higher concentrations for maximal benefit.[35] These findings may be due to the rapid pharmacologic action of pentoxifylline as a phosphodiesterase inhibitor, which swiftly elevates cAMP levels and stimulates sperm motility. Its hemorheological and antioxidant effects may also enhance seminal fluid production more effectively than CoQ10. In contrast, the benefits of CoQ10 are more gradual and dose dependent, potentially requiring prolonged supplementation to match the efficacy of pentoxifylline.

CONCLUSION

Both pentoxifylline and coenzyme Q10 improved seminal parameters, including sperm motility, sperm count, and total motile sperm count, in sub fertile men with asthenozoospermia. In particular, compared with Coenzyme Q10, pentoxifylline demonstrated superior outcomes in increasing sperm motility. Therefore, the use of pentoxifylline as a first-line agent might increase treatment success compared with the use of coenzyme Q10 in men with asthenozoospermia.

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Ethical approval: Ethical approval was obtained from the institutional review board of BMU (previously known as Bangabandhu Sheikh Mujib Medical University (Approval number: BSMMU/2022/5/56)) before the commencement of this study

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