



A Clinical Study on effect of Strong Antioxidant Astashine silver capsules on sperm function and fertility.

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ABSTRACT

Aim: A single-blinded clinical trial on effect of strong natural antioxidant Astashine silver supplement on sperm parameters in infertile male.

Objective of research

The objective of the present trial was to assess the effects of strong lipophilic antioxidant (Astashine silver) on sperm function and fertility of sub fertile men.

Materials and methods

The present research was a single-blinded clinical trial. The research population comprised infertile oligospermic and asthenospermic men visiting OPD of India IVF Centre, Fortis Hospital vasant kunj Newdelhi. In the first phase, in advance to the study, all participants were asked for informed consent to take part in the research. This was done through an interview. All patients had at least one year experience of inability to conceive. The inclusion criteria were asthenospermia/oligospermia, more than a year of infertility, no history of surgery in genitals or pelvis such as vasectomy, varicocele, hernia, etc., no alcohol consumption or drug addiction, no chronic physical/mental disease including cardiac, renal, immunological, cancer, hepatic and AIDS, no consumption of vitamin complements within the past 2 months, no exposure to radiation during work or routine activities. The main exclusion criteria were azoospermia or reports of sexual problems, use of any unscheduled vitamin complement, and ICSI candidate for intense spermographic disorders and unwillingness to take part in the research. The initial inclusion information was obtained via a checklist developed by the researcher. In the second phase, the subjects were visited by an urologist. Their seminal fluid test results were examined. Eventually, 30 asthenospermic and oligospermic subjects were selected. They were informed of the need for a seminal fluid test so as not to have an intercourse for 3–4 days. Upon arrival at the lab, a sample was taken through masturbation. Once taken, the sample was stored in an incubator at 37 degrees for 20 minutes to liquefy. Computerized seminal fluid analysis was done in vitro based on WHO standards. For all subjects, color, volume, viscosity, count, motion, morphology and pH were analyzed.

Upon receiving the test results, each patient visited the same physician and followed the prescribed medical diet in proper dosage and time. This procedure took 3 months. The prescribed medicine contained Astashine silver in BD dose. To control the complements and prevent attrition, every two weeks the subjects were contacted through phone calls. At the end of the third month, all subjects were informed to come for a seminal fluid test after 3 days of refraining from sexual intercourse. They referred to the same lab as for the first test. The same full list of information obtained for the first test was again obtained for this second test. Mean and standard deviation were used to describe quantitative data. Frequency and percentage were used to describe qualitative data. To test the research hypotheses, a test of normality was run as well as a test of variance equality. One-way ANOVA was run to compare quantitative data. Chi-squared test was used to compare qualitative data. Paired-sample T-test was used to compare the means cores of quantitative data before and after the intervention. The significance level was set at $p \leq 0.05$.

Result

The mean age of the patients was 32.24 ± 6.87 years; the length of their infertility was 4.16 ± 2.82 years. Sperm parameters were divided in two groups of qualitative and quantitative. Each had a certain statistical analysis. The mean scores for sperm parameters can be observed before the intervention and after 3 months of receiving Astashine Silver capsules.

Comparison of mean sperm parameters before and after intervention showed that the mean volume of sperm changed from 3.48 ± 1.44 to 3.71 ± 1.42 ; sperm motion changed from 27.22 ± 13.69 to 31.85 ± 5.82 ; sperm morphology changed from 23.22 ± 23.28 to 33.60 ± 20.01 ; sperm count turned from 21.76 ± 23.02 to 23.22 ± 23.28 ; progressive motility was increased from 9.82 ± 9.10 to 11.57 ± 10.18 .

All sperm parameters including total motility, morphology, count and progressive motility were significantly increased after the intervention ($p \geq 0.005$).

Conclusion: The present study suggests a positive effect of Astashine silver on sperm parameters and fertility.

Keywords: male infertility; antioxidant; astashine silver; ROS; treatment; pregnancy

INTRODUCTION

A couple is considered infertile if they are unable to get pregnant for more than one year. About one third of infertility cases are attributed to the man. Infertility is caused by many different factors, including irregular development of the testicles, low mobility of the sperm, irregular growth of veins around the testicles, and lack of sperm development among others.

In 2010, an estimated 48.5 million couples worldwide were infertile according to the World Health Organization (WHO). Infertility is defined as the inability of a sexually active, non-contracepting couple to achieve spontaneous pregnancy within one year. Other surveys have shown that 15% of couples do not achieve pregnancy within one year and seek medical treatment for infertility. Eventually close to 5% will remain unwillingly childless. One in eight couples encounters problems when attempting to conceive a

first child and one in six when attempting to conceive a subsequent child.

Infertility affects many couples of child-bearing age. A couple is considered infertile if they are unable to get pregnant for more than one year. About one third of infertility cases are attributed to the man. Infertility is caused by many different factors, including irregular development of the testicles, low mobility of the sperm, irregular growth of veins around the testicles, and lack of sperm development among others. However, research suggests a potential new factor affecting male fertility. Damage caused by reactive oxygen species, could play a very large factors in male fertility. When ROS levels exceed your body's normal antioxidant levels it may lead to increased cellular damage. Oxygen species, free radicals, and peroxides are grouped together under the general term reactive oxygen species. And, over half of the infertile men, according to research, showed higher than normal levels of ROS. (Figure 1)

Table 1 : Semen analysis : normal values for men	
Parameter	Normal Values
Ejaculate (semen) volume	≥ 1.5 ml
Sperm Concentration	≥ 20 million/ml
Total sperm count	≥ 40 million
Sperm motility	$\geq 50\%$ with forward progression
Sperm with rapid progression	$\geq 25\%$
Morphology (Shape)	$> 30\%$ normal form

Figure 1

Male Factor Infertility Accounts For up to half of All Cases of Infertility.

Infertility affects both men and women. A WHO survey of 7,273 couples with infertility revealed that in 24% of the cases the infertility was attributable to male factors alone. A further 24% was attributable to both male and female factors. Therefore, the male factor is at least partly responsible in about 50% of infertile couples. Another study indicates infertility affects one man in 20 in the general population.

Oxidative Stress Contributes to Male Infertility

Though about half of all infertility cases are at least partially attributable to men, most of the established therapies, such as artificial insemination or *in vitro* fertilization, are aimed at women. Recently, there has been a spate of study results which indicate the possibility that intratesticular oxidative stress may contribute to male infertility. Supporting this theory is a study which reported that men who showed evidence of oxidative stress in their semen also had poor results in tests of basic semen quality and low pregnancy rates. Other evidence suggests that damage from oxidative stress exists in between 30 to 80 % of male infertility patients.

Oxidative stress and Infertility

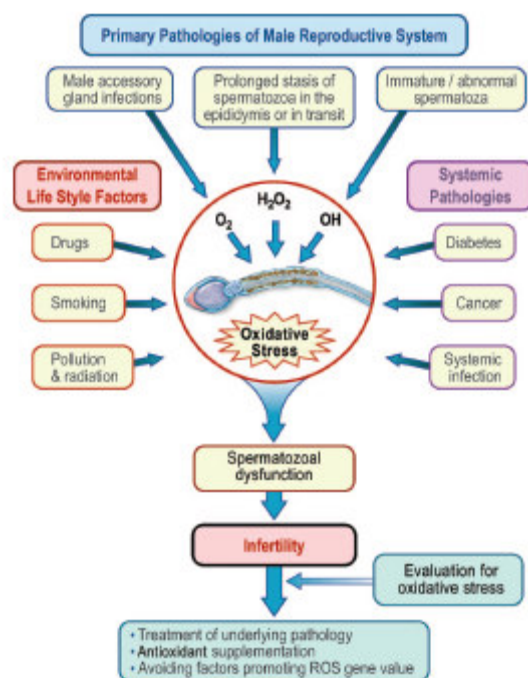


Figure 2

Oxidative stress affects the sperm of men in two different ways

1. Oxidative stress damages the cell membrane of sperm, which could decrease sperm motility and its ability to connect with an oocyte.
2. Oxidative stress causes damage to the DNA of sperm. This could increase the chance of passing along damaged DNA from the man.

According to clinical research, albumin found in sperm has the potential to block free radicals, which prevents them from reaching the sperm. Also, sperm DNA is tightly covered by a protective protein. And this layer can protect the DNA in your sperm, suggests research, which could prevent damage from occurring to your sperms DNA. However, infertile men could be deficient in this protein, possibly leaving the DNA exposed to reactive oxygen species.

Composition of Astashine silver capsules

Astaxanthin - 2mg (Naturally derived from *Haematococcus pulvialis* algae extract, which is microencapsulated) & L-Carnitine L-Tartrate 368 mg.

Patho- Physiology of Male Infertility

Male infertility refers to a male's inability to cause pregnancy in a fertile female.¹ In humans it accounts for 40–50% of infertility.^{2, 3, 4} It affects approximately 7% of all men.⁵ Male infertility is commonly due to deficiencies in the semen, and semen quality is used as a surrogate measure of male fecundity.⁶

Causes

Factors relating to male infertility include:⁷

Immune infertility

Antisperm antibodies (ASA) have been considered as infertility cause in around 10–30% of infertile couples.^[8] ASA production are directed against surface antigens on sperm, which can interfere with sperm motility and transport through the female reproductive tract, inhibiting capacitation and acrosome reaction, impaired fertilization, influence on the implantation process, and impaired growth and development of the embryo. Risk factors for the formation of antisperm antibodies in men include the breakdown of the blood-testis barrier, trauma and surgery, orchitis, varicocele, infections, prostatitis, testicular cancer, failure of immuno suppression and unprotected receptive anal or oral sex with men.^{8, 9}

Genetics

Chromosomal anomalies and genetic mutations account for nearly 10–15% of all male infertility cases.¹⁰

Kline felter syndrome

One of the most commonly known causes of infertility is Klinefelter syndrome, affecting 1 out of 500–1000 newborn males.¹¹ Klinefelter syndrome is a chromosomal defect that occurs during gamete formation due to a non-disjunction error during cell division. Resulting in males having smaller testes, reducing the amount of testosterone and sperm production.¹² Males with this syndrome carry an extra X chromosome (XXY), meaning they have 47 chromosomes compared to the normal 46 in each cell. This extra chromosome directly affects sexual development before birth and during puberty (links to learning disabilities and speech development have also been shown to be affected). There are varieties in Klinefelter syndrome, where some cases may have the extra X chromosome in some cells but not others, referred to as mosaic Klinefelter syndrome,

or where individuals have the extra X chromosome in all cells. The reduction of testosterone in the male body normally results in an overall decrease in the production of viable sperm for these individuals thereby forcing them to turn to fertility treatments to father children.^[11]

Y chromosome deletions

Y chromosomal infertility is a direct cause of male infertility due to its effects on sperm production, occurring in 1 out of every 2000 males.^[13] Usually affected men show no sign of symptoms other than at times can exhibit smaller testis size. Men with this condition can exhibit azoospermia (no sperm production), oligozoospermia (small number of sperm production), or they will produce abnormally shaped sperm (teratozoospermia).¹³ This case of infertility occurs during the development of gametes in the male, where a normal healthy male will produce both X and a Y chromosome, affected males have genetic deletions in the Y chromosome. These deletions affect protein production that is vital for spermatogenesis. Studies have shown that this is an inherited trait; if a male is fathered by a man who also exhibited y chromosome deletions then this trait will be passed down. These individuals are thereby “Y-linked”, although daughters are not affected due to the lack of the Y chromosome.

Other

- Age group 12-49
- Abnormal set of chromosomes
- Centriole¹⁴
- Neoplasm, e.g. seminoma
- Idiopathic failure
- Cryptorchidism
- Trauma
- Hydrocele
- Hypopituitarism in adults, and hypopituitarism untreated in children (resulting in growth hormone deficiency and proportionate dwarfism.)
- Mumps¹⁵
- Malaria
- Testicular cancer
- Defects in USP26 in some cases¹⁶
- Acrosomal defects affecting egg penetration
- Idiopathic oligospermia - unexplained sperm deficiencies account for 30% of male infertility.¹⁷

Pre-testicular causes

Pre-testicular factors refer to conditions that impede adequate support of the testes and include situations of poor hormonal support and poor general health including:

Varicocele

Varicocele is a condition of swollen testicle veins.¹⁸

It is present in 15% of normal men and in about 40% of infertile men.

It is present in up to 35% of cases of primary infertility and 69–81% of secondary infertility.¹⁹

- Hypogonadotropic hypogonadism due to various causes
 - Obesity increases the risk of hypogonadotropic hypogonadism.²⁰ Animal models indicate that obesity causes leptin insensitivity in the hypothalamus, leading to decreased Kiss1 expression, which, in turn, alters the release of gonadotropin-releasing hormone (GnRH).²⁰
- Undiagnosed and untreated coeliac disease (CD). Coeliac men may have reversible infertility. Nevertheless, CD can present with several non-

gastrointestinal symptoms that can involve nearly any organ system, even in the absence of gastrointestinal symptoms. Thus, the diagnosis may be missed, leading to a risk of long-term complications.²¹ In men, CD can reduce semen quality and cause immature secondary sex characteristics, hypogonadism and hyperprolactinaemia, which causes impotence and loss of libido.²² The giving of gluten free diet and correction of deficient dietary elements can lead to a return of fertility.^{21,22} It is likely that an effective evaluation for infertility would best include assessment for underlying coeliac disease, both in men and women.²³

- Drugs, alcohol
- Strenuous riding (bicycle riding,²⁴ horseback riding)
- Medications, including those that affect spermatogenesis such as chemotherapy, anabolic steroids, cimetidine, spironolactone; those that decrease FSH levels such as phenytoin; those that decrease sperm motility such as sulfasalazine and nitrofurantoin
- Genetic abnormalities such as a Robertsonian translocation

Tobacco smoking

There is increasing evidence that the harmful products of tobacco smoking may damage the testicles²⁵ and kill sperm,^{26,27} but their effect on male fertility is not clear.²⁸ Some governments require manufacturers to put warnings on packets. Smoking tobacco increases intake of cadmium, because the tobacco plant absorbs the metal. Cadmium, being chemically similar to zinc, may replace zinc in the DNA polymerase, which plays a critical role in sperm production. Zinc replaced by cadmium in DNA polymerase can be particularly damaging to the testes.²⁹

DNA damage

Common inherited variants in genes that encode enzymes employed in DNA mismatch repair are associated with increased risk of sperm DNA damage and male infertility.³⁰ As men age there is a consistent decline in semen quality, and this decline appears to be due to DNA damage.³¹ The damage manifests by DNA fragmentation and by the increased susceptibility to denaturation upon exposure to heat or acid, the features characteristic of apoptosis of somatic cells.³² These findings suggest that DNA damage is an important factor in male infertility.

Epigenetic

An increasing amount of recent evidence has been recorded documenting abnormal sperm DNA methylation in association with abnormal semen parameters and male infertility.^{33,34} Until recently, scientists have thought that epigenetic markers only affect the individual and are not passed down due to not changing the DNA.³⁵ New studies suggest that environmental factors that changed an individual's epigenetic markers can be seen in their grandchildren, one such study demonstrating this through rats and fertility disruptors.^[35] Another study bred rats exposed to an endocrine disruptor, observing effects up to generation F5 including decreased sperm motility and decreased sperm count.³⁶ These studies suggest that environmental factors that influence fertility can be felt for generations even without changing the DNA.

Post-testicular causes

Post-testicular factors decrease male fertility due to conditions that affect the male genital system after testicular sperm production and include defects of the genital tract as well as problems in ejaculation:

- Vas deferens obstruction
- Lack of Vas deferens, often related to genetic markers for cystic fibrosis
- Infection, e.g. prostatitis
- Retrograde ejaculation
- Ejaculatory duct obstruction
- Hypospadias
- Impotence

Review Literature; Astaxanthin and Fertility

However, when levels of reactive oxygen species are too great, and there are not enough antioxidants, this could potentially lead to damage to cells, Research suggests that powerful antioxidants could reduce damage associated with ROS's by destroying them. One powerful antioxidant, Astaxanthin, has been shown in research to reduce free radical damage associated with male infertility and could help improve sperm motility.

In a clinical study it has been shown that Astaxanthin has the ability to reduce damage associated with free radicals. Thirty infertile men who had suffered infertility for 12 or more months. They administered 16mg/day of Astaxanthin for three months. The researchers noted, the Astaxanthin group showed a significant reduction in reactive oxygen species. Also noted in the Astaxanthin group, was a significant increase in sperm velocity which was different than the placebo group.

Total pregnancies and pregnancies per cycle increased in the **Astaxanthin group (54.3% and 23.17%)** than in the placebo group (10.5% and 3.6%).

(Ref: *Asian J Androl.* 2005 Sep;7 (3):25762).

The researchers concluded that the Astaxanthin could potentially be a new method of treatment for male infertility. The latest research shows damage from reactive oxygen species could be a cause of male infertility. And, according to research, increasing total antioxidant levels could reduce damage to sperm membranes and its DNA. Powerful antioxidants like Astaxanthin could be potent nutrients that could reduce reactive oxygen species and research suggests this could improve the function of male sperm count and motility.

Astaxanthin silver capsules for Sperm Health

Around 40% of infertile men have high levels of free radicals in their semen. This may be due to exposure to environmental toxins, poor diet and unhealthy lifestyle habits such as smoking cigarettes. Sperm also produce high quantities of free radicals as they work hard to traverse the many challenges along their journey to the awaiting egg. These challenges can be anything from simply having to move through the uterus itself, cervical mucus and the thick gelatinous outer layer that surrounds an egg called the cumulus oophorus (it takes a lot of energy to break through this layer of cells).

Objective of research

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Materials and methods

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Result

The mean age of the patients was 32.24 ± 6.87 years; the length of their infertility was 4.16 ± 2.82 years. Sperm parameters were divided in two groups of qualitative and

quantitative. Each had a certain statistical analysis. The mean scores for sperm parameters can be observed before the intervention and after 3 months of receiving Astashine Silver capsules.

Comparison of mean scores for sperm parameters before and after intervention.

Sperm Parameter	Group	F.	Mean	Sd	T-Value	P-Value
Volume	Pre-test	30	3.48	1.44	2.20	0.032
	Post-test	30	3.71	1.42		
Ph	Pre-test	30	7.31	0.29	1.85	0.070
	Post-test	30	7.27	0.18		
Total Motility	Pre-test	30	27.22	13.69	3.96	0.001
	Post-test	30	31.85	15.82		
Morphology	Pre-test	30	23.22	23.28	3.14	0.003
	Post-test	30	33.60	20.01		
Count	Pre-test	30	21.76	23.02	4.01	0.001
	Post-test	30	23.22	23.28		
Motility	Pre-test	30	9.82	9.10	5.87	0.001
	Post-test	30	11.57	10.18		

Quantitative parameters after intervention:

To compare the mean scores of sperm parameters before and after intervention, paired-sample T-test was run, as can be observed in Table.

Comparison of mean sperm parameters before and after intervention showed that the mean volume of sperm changed from 3.48 ± 1.44 to 3.71 ± 1.42 ; sperm motion changed from 27.22 ± 13.69 to 31.85 ± 5.82 ; sperm morphology changed from 23.22 ± 23.28 to 33.60 ± 20.01 ; sperm count turned from 21.76 ± 23.02 to 23.22 ± 23.28 ; progressive motility was increased from 9.82 ± 9.10 to 11.57 ± 10.18 .

All sperm parameters including total motility, morphology, count and progressive motility were significantly increased after the intervention ($p \geq 0.005$).

Qualitative parameters after intervention

To better compare the effectiveness of therapeutic methods in sperm pH, the pH of patients' sperm was classified as either normal or abnormal. pH at or above 7.2 was taken as normal and below that degree was taken as abnormal.

To compare the quality of pH before and after the intervention, McNamara's test was run. The results showed that from among 14 subjects with abnormal pH = 5 (10%) ($p = 0.001$) had a return to a normal extent of pH. This change was statistically significant and showed a significant improvement.

In terms of sperm concentration, the subjects were divided in 3 groups (below normal, normal and above normal). The test results revealed that 2 of 16 subjects had an above-normal sperm concentration (12.2%) ($p = 0.001$). Their sperm concentration returned to a normal state which was statistically significant ($p = 0.001$).

DISCUSSION

Comparison of patients' sperm parameters before and after the interventions showed that consuming Astashine silver capsules can significantly increase sperm volume, total motility, morphology, count and progressive motility. Moreover, sperm pH and concentration were improved.

Because of the powerful antioxidant actions astaxanthin provides, potential fertility benefits to-

- Enhance reproductive health
- Stabilize blood sugar
- Boost immune system function
- Reduce inflammation of all causes; it is a powerful anti-inflammatory agent
- Improve male fertility by increasing sperm strength, quality, motility and sperm count
- Improve endurance
- Reduce oxidative damage to DNA
- Reduce pain – astaxanthin blocks COX 2 enzymes, which may be potentially supportive for reproductive organ pain

The present research was a single-blinded clinical trial on both semen parameters and the effect of antioxidant Astashine silver capsules.

CONCLUSION

Consuming Astashine silver capsules showed to positively affect qualitative parameters (concentration and pH) as well as quantitative parameters (volume, total motility, and morphology, count and progressive motility). Yet, there is a need for further research with more subjects and research at molecular level.

SAFETY OF ASTASHINE SILVER CAPSULES

Astaxanthin has demonstrated safety in numerous human clinical trials. In one open-label clinical study on subjects with metabolic syndrome (n=17). Astaxanthin (16 mg/day, for three months) significantly raised blood bilirubin ($p \leq 0.05$), potassium ($p \leq 0.05$), and creatine kinase ($p \leq 0.01$), although all three values remained within normal range. Also, astaxanthin significantly lowered the liver enzyme gamma-glutamyl transpeptidase (GGTP; $p \leq 0.05$). Since the researchers noted this enzyme was abnormally elevated in 11 of the 17 subjects at baseline, this astaxanthin effect may have been beneficial. Animal experiments have investigated astaxanthin at levels well over 120 mg/day in human equivalents, without causing apparent harm. Hoffman-La Roche confirmed its safety with extensive tests, including acute toxicity, mutagenicity, teratogenicity, embryotoxicity, and reproductive toxicity. L-carnitine is listed as pregnancy category B; indicating animal studies have revealed no harm to the fetus but that no adequate studies in pregnant women have been conducted. L-carnitine has been given to pregnant women late in pregnancy with resulting positive outcomes. The racemic mixture (D, L-carnitine) should be avoided. D-carnitine is not biologically active and might interfere with the proper utilization of the L isomer. In uremic patients, use of the racemic mixture has been correlated with myasthenia-like symptoms in some individuals.

Supplement Facts

Presentation: 60 capsules

Usage: As a food supplement combination of antioxidants to improve health and vitality.

Contra-indications: Product is contra-indicated in persons with Known hypersensitivity to any component of the product hypersensitivity to any component of the product.

Recommended usage: *Adults:* two capsules per day along with food.

“Do not exceed the recommended daily dose”

Administration: Taken by oral route at anytime with food.

Precautions: Food Supplements must not be used as a substitute for a varied and balanced diet and a healthy lifestyle. This Product is not intended to diagnose, treat, cure or prevent any diseases. Do not exceed the recommended daily dose.

Warnings: If you are taking any prescribed medication or has any medical conditions or have any medical conditions (seizures) under age group 17 year always consults doctor or healthcare practitioner before taking supplements.

Side Effects: Mild side effects like nausea, headache and vomiting in some individuals have been reported.

Storage: Store in a cool, dry and dark place. Keep out of reach of children.

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ABOUT THE AUTHOR

Dr. Richika Sahay Shukla is leading infertility and IVF Specialist in NCR Delhi & Gurgaon. She has a wide experience of over 20 years and has done extensive trainings in the field of IVF-ICSI & Gynaecological Endoscopy. She has worked with some of the best in class institutes in India such as AIIMS New Delhi and Sir Ganga Ram Hospital New Delhi. Her expertise lies in- Vitro fertilization (IVF)/ICSI by various protocols and in difficult cases involving postmenopausal, poor ovarian responders, surrogacy, and donor eggs conception and managing difficult Embryo transfers. She is also skilled doing difficult oocyte retrieval (adhered ovaries, high ovaries, ovaries with endometrioma). Hundreds of her patients have conceived through her fertility enhancing surgeries by Laparoscopy and Hysteroscopy (like septal resection, intrauterine adhesiolysis, myomectomy, tubal cannulation).

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