Indian Journal of Urology, 2001, Vol. 18, No. 1

Management of Idiopathic Oligoasthenospermia with Lycopene

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ABSTRACT

Idiopathic oligoasthenospermia accounts for almost 24% of all male infertility. The role of free radicals as a cause of such male infertility has been established recently. We undertook a study to establish the role of Lycopene (antioxidant) in management of such infertile males due to free radicals.

A total number of 50 patients having no obvious cause for their infertility with normal hormone profile and antisperm antibody titre but showing oligoasthenospermia were given Lycopene (Lycored) 8 mg daily till their sperm analysis improved to optimal level or pregnancy was achieved. Regular follow-up for one year with sperm analysis was done.

Result showed a 36% pregnancy rate with improvement of sperm count and functional sperm concentration in 70% and 60% respectively, sperm motility and sperm motility index improved in 54% and 46% while 38% showed improvement in sperm morphology. There were no side effects with good patient compliance.

***Conclusion**: Lycopene supplementation has a definite role in management of idiopathic oligoasthenospermia.*

INTRODUCTION

Impaired sperm function is an obvious and general cause of male idiopathic infertility.[1] Idiopathic male infertility accounts for almost 24% of all male infertility cases. Though their antisperm antibody titre and hormone profile are well within normal values but their seminalogram shows either oligospermia, asthenospermia or tetraspermia.

One of the most common abnormalities associated with male infertility is the presence of free radicals in their ejaculate. These free radicals damage the sperm's structure and DNA material. (Brit Scientific & Med; Nov 1998)

Oxidative stress status (OSS) resulting in production of excessive reactive oxygen species (ROS) is now considered to be the causative factor for sperm damage, low sperm count and sluggish motility leading to idiopathic male infertility. Uncontrolled and excessive production of free radicals have a significant role as one of the major factors leading to infertile males.[2-6] Studies have shown that 40-80% of non selected infertile patients have high levels of seminal free oxygen radical.[7] Infertile men have higher free radicals than fertile men. (Centre for Male Reprod Med)

Human spermatozoa are rich in poly unsaturated fatty acid (PUFA) and therefore are susceptible to free radical attack mediated by lipid peroxidation.[8,9]

Free radicals can be detected in the semen of 40% of infertile men, whereas none is detected in semen from fertile men. (Ind Jr of Androl; 1993)

Excessive free radicals are related to an increase in lipid peroxidation of sperm cell. Lipid peroxides damage proteins by oxidation of critical — SH group in proteins and DNA which alter the structure and function of spermatozoa.

To counteract the harmful effects of ROS, sperm and seminal plasma possess a number of antioxidant systems that scavenges ROS and prevents internal cellular damage.[10,12,13]

A prospective study has demonstrated that men with high levels of free radical (FR) generation have sevenfold less chance of initiating a pregnancy as compared with those with low free radicals.[10] Free radicals causing male infertility by affecting the process of conception at various stages like damage to sperm membrane, DNA and protein resulting in decreased sperm count, mortility, viability and increased mid piece defect that impairs sperm capacitation and acrosome reaction.[14-16]

Studies have shown infertile males have elevated levels of free radical induced DNA damage in their ejaculated spermatozoa[17] and also 8-hydroxydeoxyguanosine.[18] Recent research have shown OSS results in sperm DNA fragmentation.[19] Li-

pid peroxides are highly toxic to spermatozoa and causes reversible arrest of motility[20,21,8] resulting in tetraspermia.

High levels of FR block the sperm motility though the inhibition of ATP synthesis by the mitochondria enzyme and cell membrane compounds injury.[22,23] Research have shown high levels of free radicals induce reversible anxonemal damage and sperm immobilisation[24] mostly due to depletion of ATP and insufficient axonemal protein phospherylation and decreased capacity for sperm oocyte fusion.[25-27] A negative correlation is observed in sperm oocyte fusion due to FR.[25-27, 20]

Infection of male genitalia like prostatitis, epididymorchitis and seminal vesiculitis result in production of more free radicals resulting in harmful effects on spermatozoa.[28] The level of Lycopene was significantly decreased in seminal plasma of infertile males.

Therefore free radicals cause infertility by affecting the process of spermatogenesis at different levels like sperm membrane damage, sperm protein damage and sperm DNA damage through lipid peroxidation.[29]

The role of FR as a cause of idiopathic male infertility is getting a lot of attention and more and more studies today confirm this hypothesis. Depressed seminal antioxidant capacity have been implicated in male infertility. Both total antioxidant capacity (TAC) and individual antioxidant levels have been shown to be lower in the serum of infertile males.[4,10,11]

Studies have shown that pre treatment with antioxidants that dispose, scavenge and suppress this formation of free radicals can reduce DNA damage.[30]

Among well known biological antioxidants, super oxide dismutase (SOD), catalase (CAT) and glutathione peroxidase (GSH) have a significant role in protecting the sperm against peroxidase damage.[31,32] Therefore antioxidant therapy can be considered for idiopathic infertile males.[33,34] Another study[35] has shown that restoration of antioxidants defence might prove useful for invigorating the physiological function of sperm.

Furthermore studies on infertile males empirically treated with antioxidant have demonstrated improved semen characteristics[36-39] with higher rate of pregnancy.

Lycopene is one of the 650 different carotenoids naturally synthesised and found in fruits and vegetables. Lycopene is the most potent quencher of FR in our redox defence against FR.[39,40] It plays a major role in management of male infertility due to oligoasthenospermia.

The aim of our study is to assess the role of Lycopene supplementation in treating patients with idiopathic male infertility due to oligoasthenospermia.

MATERIALS AND METHODS

50 infertile males having normal hormone profile, antisperm antibody titre, but oligoasthenospermic were included in our study with the following inclusion criteria.

- Age between 21 to 50 years.
- Sperm count less than 50 million/cu.mm.
- Sperm motility less than 50%.
- Sperm morphology (normal) less that 50%.
- Sperm motility index less than 80.
- Functional sperm count less than 3 million/cu.mm.
- No history of taking any therapy for their infertility.
- No history of obstructive azoospermia.
- Normal female partner.
- A written consent.

TABLE I

Optimal Seminal Fluid Analysis

Volume	2-5 ml
pH	Alkaline
Sperm Motility	50-90%
Sperm Normal Morphology	50-90%
Sperm Concentration	60-150 million/cu.mm
Functional Sperm Concentration	0.3 million/ml - Poor 3-13 million/ml - Medium Above 13 million/ml - Good
Sperm Motility Index	0-80 - Poor 80-160 - Medium Above 160 - Good
Fructose	+ve

With the above inclusion criteria all these 50 males were subjected to a thorough history, sexual habit and clinical examination. A routine haemogram, Liver Function Test, Kidney Function Test, hormone profile and antisperm antibody titre was conducted. Seminal fluid examination was done within 2 hours of ejaculation at three different centres with a 3 days period of abstinence before each test.

All these 50 patients were then treated with daily dose of 8 mg of Lycopene (Lycored) till their sperm analysis showed optimal level (Table I) or pregnancy was achieved. Patients were regularly followed up with sperm analysis. Results was then analysed.

We present our result after a twelve months follow-up as follows:

RESULTS

All 50 patients completed the trial with very good patients compliance and no adverse reaction noted in a 12 months follow-up.

TABLE II

Seminal Fluid Analysis

Parameter	Baseline	Follow-up	Improvement	
			Cases	%
Sperm Concentration	20 ± 25 million (5-45)	↑60-90 million (40-65)	35	70
Sperm Motility	28 ± 30% (10-40)	↑68-80% (40-50)	27	54
Sperm Morphology	35 ± 40% (20-50)	↑60-70% (25-30)	19	38
FSC	2 ± 5 million (1-3)	↑10-18 million (8-13)	30	60
SM Index	40 ± 80 (10-20)	↑110 ± 170 (70-90)	23	46

Seminal fluid analysis showed improvement in sperm count in 35 patients (70%) and improvement in functional sperm concentration (FSC) in 30 patients (60%). Sperm motility improved to optimal level in 27 patients (54%) while sperm motility index (SMI) improved in 23 patients (46%), and improvement in sperm morphology was seen in 19 patients (38%) though much more was expected. (Table II)

In total in 18 patients (36%) all the parameter of sperm analysis showed improvement to optimal level (Table I) making them proud fathers. The pregnancy rate (36%) was mostly seen at the end of 3 months of therapy followed by end of 6 months of therapy and thereafter reduced. (Table III)

TABLE III

Pregnancy Rate

8	At the end of 3rd month
6	At the end of 6th month
4	At the end of 12th month

DISCUSSION

Controlled generation of ROS has a physiological role in spermatozoal function such as hyperactivation, capacitation acrosome reaction[42,14] but increased levels of ROS has been found in the semen of infertile males[15,16] and this results in DNA fragmentation.[8] Defective sperm function is the most common cause of idiopathic male infertility and until recently it was difficult to evaluate and treat. This was partly due to our incomplete understanding of the factors constituting normal and abnormal sperm function leading to male infertility. The excessive generation of reactive oxygen species (ROS) by abnormal spermatozoa contaminated leukocytes (Leukocytospermia) has been identified as one of the few defined etiologies for idiopathic male infertility (Sikka SC 1996). Lycopene is present in high concentration in testis, prostate and adrenals. Epidemiological studies suggest that people living in the Mediterranean region who consume more tomatoes, watermelon and other fruits and vegetable rich in Lycopene have reduced risk of developing infertility (both males/females). The result of these studies consider Lycopene as being responsible for these beneficial effects.

Recent data published show that Lycopene supplementation offer promise of increased sperm production as well as survival in idiopathic oligoasthenospermia.

Lycored, an extract from Lycopene rich tomatoes is 100% natural, commercially available Lycopene.

Genitourinary infection/inflammation, ageing and environmental toxicants create oxidative stress status resulting in oligoasthenospermia.

Lenzi Geva and Sulciman SA in their respective studies[9,43,44] have shown that idiopathic infertile males treated with Lycopene demonstrated improved semen characteristic, fertilisation in vitro and higher pregnancy rate.

In our study we found that maximum beneficial effect was observed in improvement of sperm count and functional sperm concentration followed by improvement in sperm motility percentage and sperm motility index. Though improvement in sperm morphology was observed much more was expected. No adverse effects were observed and patients compliance was good. A total pregnancy rate of 36% was observed in our study at the end of 12 month follow-up.

We attribute our good pregnancy rate of 36% due to use of high dose of lycopene (8 mg) once daily and meticulous screening of only those patients who had no other definite cause for their infertility with normal hormone profile and antisperm antibody titre.

Our study clearly justifies the role of Lycopene (Lycored) in management of idiopathic male infertility due to oligoasthenospermia but a long term study is desired to establish its credentials.

CONCLUSION

Lycopene (Lycored) supplementation improved sperm count, motility and morphology to optimum level in oligoasthenospermia infertile males, making them proud fathers.

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Key Words: Lycopene; Antioxidant; Oligoasthenospermia; Motility; Idiopathic.

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