Singapore Journal of Obstetrics and Gynaecology
2009; 40(1): 13-21

Role of Micro Nutrients in Enhancing Fertility Potential in Male Having Oligospermia, Asthenospermia and Oligoasthenospermia

Mosammat Rashida Begum, David Miller, M.A Salam, Ehsan Quadir, Mosammat Sahina Begum, Farzana Khan, Zahid Hassan Bhuiyan

ABSTRACT

Objective: Objective of this study was to explore the effect of empirical micro nutritional blends in infertile men having idiopathic oligospermia, asthenospermia and oligoasthenospermia

Materials and methods: This prospective cross sectional study was undertaken in a tertiary level infertility care unit of Dhaka between September 2005 and August 2006. Forty-six oligo, astheno and oligoasthenospermic patients were the target population for this study. Thorough infertility evaluation was done to identify idiopathic oligo, astheno and oligoasthenospermia. Female partners were also evaluated to exclude bilateral tubal blockage, pelvic inflammatory diseases, endometriosis, uterine pathology and resistant PCOS. Male partners were divided into two groups for I) micronutrients, and II) no intervention as control. Treatment was continued for three months. Semen analysis was repeated at the end of two and three months. Main outcome measures were improvement of semen parameters and pregnancy rate.

Results: Before treatment all patients' characteristics were comparable. After treatment there was significant improvement both in count and motility in group I ($p < 0.05$). In group II where there was no intervention, there was no significant change of semen parameters ($p > 0.05$). Four patients (17.39%) from group I got pregnant within three months observation period. There were no pregnancy in group II.

Conclusion: Empirical use of micronutrients in idiopathic oligo, astheno and oligoasthenospemia appeared to improve sperm quantity and quality and aid a couple in achieving pregnancy. Further studies are required.

Key words: Micronutrients, Oligospermia, Asthenospermia

Mosammat Rashida Begum
FCPS (OB/GYN), MS (MED EDU, UK),
MSc, Assisted Reproductive Technology (UK)
Assistant Professor
Dhaka Medical College

David Miller.
Andrologist,
University of Leeds, UK.

M.A Salam,
Urologist, BSMMU, Dhaka, Bangladesh.

Ehsan Quadir
Assistant Professor (Paediatrics)
Sir Salimullah Medical College

Mosammat Sahina Begum
Embryologist Infertility Care and Research Centre (ICRC)
Dhaka

Farzana Khan
Medical Officer Infertility Care and Research Centre (ICRC)
Dhaka

Zahid Hassan Bhuiyan
Urologist Bangladesh Medical College

Corresponding Author:
Dr. Mosammat Rashida Begum
2/4 Block "F", Monjuri, Flat A-1,
Lalmatia, Dhaka-1207
e-mail: rashida_icrc@yahoo.com

INTRODUCTION

Infertility is disability to procreate. Male and female are equally responsible for infertility. Nearly 90% of male factor infertility is idiopathic with no identifiable cause for the infertility or abnormal semen parameters. Only a minority of affected males has a definite detectable abnormality related to infertility. Up to 1-3% may have endocrine disease [1]. Antisperm antibodies are present in 3-13% [2]. An increased incidence of varicocele is reported in infertile males in 30% [3] versus an incidence of 10-23% in fertile males' [4]. Genetic cause affects 10-15%. In 10% cases of low sperm count, the cause can be identified and treated medically. In other 90% cases of oligospermia no cause is identified and is called idiopathic oligospermia.

The total sperm count as well as sperm quality of the general male population has been deteriorating over the past few decades. Environmental, dietary or lifestyle changes in recent decades may be interfering with a man's ability to manufacture sperm. Idiopathic male infertility may be due to exposure (s) to environmental toxicants that alter the reproductive hormones, spermatogenesis or sperm function. The most widely studied evidence of potential environmental reproductive hazards is that sperm counts have declined in certain industrialized countries [5-8]. Various chemicals have been implicated as reproductive toxicants. A number of these chemicals categorized as air pollutants are present in the blood, urine and semen of exposed men and many affect sperm quality. Air pollution may adversely affect semen quality [9-13].

The idiopathic oligospermia and asthenospermia is often treatable. Nutritional and lifestyle changes can improve semen parameters. Reproductive organs are highly susceptible to free radicals or oxidative damage from environmental toxins like pesticides, insecticides and heavy metals. Reduction of these enhances sperm production. A balanced nutritional diet and nutritional supplements with high antioxidants content can help reverse some of the oxidative damage from environmental toxins and natural aging.

Medical treatment of oligospermia can be quite effective if cause is known. But when cause is not identified approach of treatment for oligoasthenospermia is to focus on enhancing those factors, which promote sperm formation. In addition to life style changes consumption of a healthful diet and different micronutrients can increase both count and motility of sperm. Among micronutrients Vit C, Vit B12, Vit E, Arginine, Carnitine, Zinc and Selenium play important role in increasing count and motility of sperm. Each has specific role to increase sperm count and improve function [14-17].

Considering the positive effects of micronutrients on sperm motility and count a mixture of micronutrients can be applied to reverse sperm parameters. On the basis of published scientific literature on individual nutritional components that benefit fertility, we want to use the different component of fertility blend for oligoasthenospermia to explore the effect of micro nutritional blends in infertile men having idiopathic oligospermia, asthenospermia and oligoasthenospermia.

MATERIALS AND METHODS

This prospective experimental study was undertaken in Infertility Care and Research Centre, a tertiary level infertility care unit, Dhaka, Bangladesh between September 2005 and August 2006. Forty-six infertile male patients who attended in the mentioned private clinic were the target population. Semen analysis performed on two occasions at 8 weeks interval and at least one of analysis was at Infertility Care and Research Center. Detailed personal history was taken regarding occupation, lifestyle, and personal habit of smoking, alcoholism and drug history. Genital tract infection was evaluated by semen culture and sensitivity and chlamydial antibody testing. Antisperm antibody was tested both in sera and sperm surface. Clinical examination, hormone analysis, CBC, blood sugar and VRDL testing identified general and endocrinological diseases. Thorough physical examination was done by andrologist. If any specific cause of oligospermia, asthenospermia or oligoasthenospermia was identified it was excluded from the study. Smokers and patients having history of taking any drugs or alcohol were excluded. Female partner's fertility assessment was done. Uterine pathology, endometriosis, bilateral tubal block, history of pelvic inflammatory diseases, resistant PCOS or any patient who fails to ovulate even with controlled ovarian hyperstimulation were excluded.

All patients were advised to avoid hot environment, diary products, non-organically grown products and to consume organic fruits and vegetables during study period.
The seminological inclusion criteria were normal appearance, consistency, liquefaction, volume and pH, sperm concentration $<20x10^6$/ml, total motility <40%, forward motility<20% and abnormal sperm <70%. Selected patients were divided into two groups by lottery.

GroupI (Study):
Group I was treated by following micronutrients for 3 months.
Vit C-1 gm daily
Vit E- 800 IU daily
Vit B12-1000 mg daily
Zinc-120 mg daily
Carnitine-2.6 gm daily

Group II (Control)
Group II was advised for only life style changes and no medication even placebo, as vitamins are usually used for placebo.

All were advised to repeat semen analysis for two occasions, one at the end of 2nd month and other at the end of 3rd month. Analysis was done by neuber counting chamber. All analysis were done by same observer. Motility was assessed as percentage of
a) Rapid forward progression
b) Slow forward progression
c) Non progressive
d) Non-motile.

After improvement of semen parameters anovulatory female partners were treated by ovulation inducing agents with monitoring of ovulation.
Final outcome measures were improvement in sperm count and motility and pregnancy rate.

Data analysis:
Data were analyzed by SPSS software. Mean ± SD, students t tests were performed for test of significance. A value of <0.05 was considered significant

RESULTS

Forty six patients were recruited for two management options. Patients were selected on the basis of exclusion of all patients having any specific cause of oligoasthenospermia. All recruited patients were free from any medical diseases.

All the patients of two groups were with similar characteristics regarding age, duration of infertility, basal hormone levels, pretreatment count and motility (Table I). Table II elaborately showed the pretreatment and post-treatment difference in individual group. In group I (study group) there is significant difference in count with treatment, $p<0.001$. There is 108% increment of count in group I. But group II, which was taken as control was without intervention did not show any change in count, $p>0.05$. When it was analyzed in individual group it shows significant change in motility among treatment groups. In treatment group both total and fast forward motility was increased significantly, $p<0.001$. Total motility increment was 52% and fast forward motility was 49% in group I. But in group II there was no change in motility percentage, $p>0.05$.

Table III shows that count was increased much more in study group $p<0.05$. Motility increment was significant in study group in comparison to control group for both total ($p<0.001$) and fast forward motility ($p<0.05$).

Table IV shows the improvement of semen parameters after treatment or after just passing of time. In study group 69.55% improvement after treatment in terms of count and motility. In control group though there was no intervention, 8.70% shows change of seminal parameters. Four patients (17.29%) from study group got pregnant within 3 months of observation. No one got pregnant from control group.

DISCUSSION

Infertility affects one in 25 men. Most cases of male infertility are due to an abnormal sperm count or low sperm motility. Low sperm count or motility dramatically reduces the chance of sperm reaching the egg. In about 10% of the cases of low sperm count the cause can be identified and treated medically. In the other 90%, the cause of low sperm count can not be identified and is called “idiopathic oligospermia”.

The cause of infertility is often treatable. Nutritional and life style changes increase chances of conception. In known case avoidance of smoking, caffeine, drugs, alcohol consumption and stress, which are related to infertility, can improve fertility potential. Reproductive organs are highly susceptible to free radicals or oxidative damage from environmental toxicants like pesticides, insecticides lead, radiation and heavy metals and natural aging. In idiopathic oligospermia and asthenospermia where there is no specific reason for life style changes, a simple balanced nutritional diet and nutritional supplements with antioxidants can help reverse some of the oxidative damage from environmental toxins and natural aging.

There is no role of hormonal treatment in idiopathic oligospermia when men are normogonadotrophic. In men certain nutrients are essential for formation of healthy sperm. Micronutrients like vitamin C, vitamin E, L carnitine, zinc, vitamin B complex improve overall reproductive health, which help improve sperm count and motility. They are critical nutrients in the male reproductive system for proper hormone metabolism, sperm formation and motility. An improvement in nutrition or supplementation is necessary to reverse damage to the reproductive system increased by the stress and post-abuse. High intake of fruits, vegetables, whole grains and nuts are important but supplements are also needed to get sufficient amounts of these nutrients for noticeable effects on sperm quality. In this study oligospermic, asthenospermic and oligoasthenospermic patients were evaluated thoroughly to identify the specific cause.

Table I. Patient Characteristics

Parameters	Group I Mean ±SD	Group II Mean ±SD	Significance p
Age (yr)	35.00 ±3.55	35.17 ±4.07	0.875
Duration of Infertility (yr)	4.38 ±3.02	4.22 ±2.58	0.848
Hormones			
FSH mU/ml	5.70 ±1.3	5.72 ±1.7	0.953
LH mU/ml	5.74 ±0.88	5.15 ±1.3	0.166
Prolactin ng/ml	16.74 ±1.13	17.00 ±1.17	0.492
Testosterone ng/ml	382.78 ±101.40	524.09 ±660.03	0.311
Pretreatment count (mill/ml)	15.67 ±15.15	18.00 ±15.32	0.629
Pre-treatment motility (%)			
Total motility	39.65 ±22.33	38.04 ±20.13	0.726
F.F motility	18.09 ±9.87	19.04 ±9.30	0.673

Student's t test

F.F- Fast forward

Table II. Pretreatment and post treatment difference in count and motility in study and control group

Groups	Pre treatment		Post treatment		Significance
	Mean	±SD	Mean	±SD	p
Count					
Group I	15.67	±15.15	32.63	±21.18	0.000
Group II	18.00	±15.32	19.41	±16.66	0.215
Motility					
Group I	39.65	±22.34	60.30	±11.29	0.000
Total motility (%)	18.09	±9.87	27.00	±6.13	0.000
F.F motility (%)					
Group II					
Total motility (%)	38.04	±20.13	33.39	±14.77	0.296
F.F motility (%)	19.04	±9.30	19.48	±10.08	0.894

Student's t test

F. F - Fast forward

Table III. Difference in post treatment count and motility between study and control group

Count & Motility	Study	Control	Significance
Count (million/ml)	32.63 ±21.18	19.41 ±16.66	0.017
Motility			
Total motility (%)	60.30 ±11.29	33.39 ±14.77	0.000
F.F motility (%)	27.00 ±6.13	19.48 ±10.08	0.014

Student's t test

F.F- Fast forward

Table IV. Outcome of the treatment

Groups	Total patients	Improvement		Pregnancy	
		N	%	N	%
Group I	23	16	69.55	4	17.39
Group II	23	2	8.70%	0	00

Where no definite cause is identified it referred to as idiopathic oligospermia asthenospermia and oligoasthenospermia. Free radical or oxidative damage to sperm is thought to be responsible for many cases of idiopathic oligospermia. A great deal of evidence has accumulated in recent years to suggest that there has been gradual increase in male reproductive pathology over last 30-40 years. This is causally related to the ability of male germ cells to generate reactive oxygen metabolites. When produced in low levels such metabolites are thought to enhance sperm function by DNA compaction and promoting the induction of sperm capacitation. When produced in excessive amounts, the same metabolites stimulate DNA fragmentation and a loss of sperm function associated with peroxidative damage to the sperm plasma membrane. Use of antioxidants has been shown to be very important in protecting the sperm against damage. Different studies showed the positive effect of direct antioxidants in improving sperm count and motility [18-26]. In a double blind placebo controlled study of 110 men with subnormal sperm activity, treatment with 100IU of vitamin E daily resulted in improved sperm activity [20]. However, a small double blind trial found no benefit from high dose of vitamin E and C [27]. Some study showed positive effect by using vitamin E in high doses (600 and 800 IU daily) [28,29]. In our study we found profound positive effect but we can not say the isolated effect of drug as we used in combination.

Vitamin B_{12} deficiency in men can lead to reduced sperm counts and lowered sperm mobility. For this reason B_{12} supplements have been triad for improving fertility in men with abnormal sperm production. In one double blind study of 375 infertile men B_{12} supplementation produced no benefit as a whole [30]. However weak evidence suggests that B_{12} supplements may improve sperm count and motility in poor semen parameters [21].

A number of clinical trials have demonstrated the efficacy of oral administration of carnitine for men with various forms of sperm dysfunction [31-33]. Different double blind placebo controlled trials suggest that various forms of the supplement of L-carnitine may improve sperm function [22-24, 31-33]. In a double blind placebo controlled study showed significant improvement in sperm function in treated group. Double blind placebo controlled study showed the significant improvement of sperm count and motility by administration of zinc in infertile men [34]. In present study zinc and carnitine are also used along with vitamins and the effect of combination drug is significant (Table II and Table III).

In the treated group by micronutrients, increment of count and motility is significant in comparison to untreated group (Table II and Table III). As individual micronutrient has positive effect in sperm count and motility this combined effect should be more beneficial. A number of studies have evaluated the benefits of antioxidants for male infertility, which is consistent with present study also [18-26].

In-study group 69.55% patients showed improvement whereas no improvement shown in control group. In study group there was not only improvement of semen parameters but also a satisfactory (17.39%) pregnancy occurred.

Microdeletion of the section of the Y chromosome may be detected in 3% to 10% of oligospermic men with normal karyotype [35,36], which can be identified with sequenced –tagged site probes along entire length of the Y chromosome. The limitation of the present study is that we could not do the genetic testing and we may miss chromosomal defects if there is any. Few patients in this study did not response to treatment at all; genetic problem can not be ignored in those cases.

Treatment of male infertility is a challenge for fertility specialists. Various nutritional strategies have been presented, which have a beneficial impact on sperm count, motility and ultimately fertility. For males with idiopathic infertility, dietary supplementation with a combination of well tolerated, clinically efficacious and non-invasive vitamins and vitamin-like agents vitamin C, E, B_{12}, carnitine and zinc provides an alternative pharmacological therapy, which can improve sperm quantity and quality and aid a couple in achieving pregnancy.

REFERENCES

1. *Vertoppen GR, Steeno OP. Varicocele and the pathogenesis of associated sub-fertility: a review of various theories II: results of surgery. Andrologia 1977;9:293.*

2. *Bowie, W, Pollock, H. M., Forsyth, P. S., Floyd, J. F., Alexander E. R., Wang S. P and Holms, K. K.. Bacteriology of the urethra in normal men and in men with nongonococcal urethrities. J. Clin. Microbiol. 1977;6:482-488.*

3. *Comhaire, F.H., Vermeulen, I and Verschraegen, G. Relation between bactericidal capacity, concentration of murimidase and other biochemical substances in semen*

plasma. In Salvadori, S., Semm, K. and Vadora F. (eds). Fertil Steril., p. 47-49. (Edizione International Gruppo Editoriale Medico).

4. *Rusk, j., Tallgren, L. G., Alfthan, O. S. and Johanson, C-J. The antibacterial activity of semen and its relation to semen proteins. Scand. J. urol. Nephrol. 1973; 7:23 29*

5. *CarlsE, et al: Evidence for decreasing quality of semen during past 50 years. British Med J 1992;305:609-613.*

6. *Moline J, Golden A, Bar-Chama N, Smith E, Rauch ME, Chapin RE, et al.. Exposure to hazardous substances and male reproductive health: a research framework. Environ Health Perspect. 2000;108:803-813.*

7. *Safe S. Endocrine Disrupters and Human Health. Is there a problem? An update. Environ Health Perspect. 2000;108:487-493.*

8. *Sharpe RM, Skakkebaek NE. Are oestrogens involved in falling sperm counts and disorders of the male reproductive tract? Lancet. 1993;341:1392-1395.*

9. *Fredricsson B, Moller L, Pousette A, Westerholm R. Human sperm motility is affected by plasticizers and diesel particle extracts. Pharmacol Toxicol. 1993;72: 128-133.*

10. *Samet JM, Dominici F, Curriero FC, Coursac I, Zeger SL. Fine particulate air pollution and mortality in 20 U.S. cities, 2000. N Engl J Med. 2000;343:1742-1749.*

11. *Selevan SG, Borkovec L, Slott VL, Zudova Z, Rubes J, Evenson DP, et al. Semen quality and reproductive health of young Czech men exposed to seasonal air pollution. Environ Health Perspect. 2000;108:887-894.*

12. *Sram RJ, Binkova B, Rossner P, Rubes J, Topinka J, Dejmek J. Adverse reproductive outcomes from exposure to environmental mutagens. Mutat Res. 1999;428: 203-215.*

13. *Telisman S, Cvitkovic P, Jurasovic J, Pizent A, Gavella M, Rocic B. Semen quality and reproductive endocrine function in relation to biomarkers of lead, cadmium, zinc, and copper in men. Environ Health Perspect. 2001;108:45-53.*

14. *Goa KL, Brodgen RN. L-carnitinea preliminary review of its pharmacokinetics and its therapeutic use in ischemic cardiac disease and primary and secondary carnitine deficiencies in relationship to its role in fatty acid metabolism. Drugs 1987;34:1-24.*

15. *Prasad AS: Zinc in growth and development and spectrum of human zinc deficiency. J Am Coll Nutr 1988;7:377-384.*

16. *Ursini F, Heim S, Kiess M, et al. Dual function of the selenoprotein PHGPx during sperm maturation. Science 1999;285:1393-1396.*

17. *Hansen JC, Deguchi Y. Selenium and fertility in animals and man a review. Acta Vet Scand 1996;37:19-30.*

18. *Dawson EB, et al: Effect of ascorbic acid on male fertility. Ann NY Acad Sci 1987;498:312-23.*

19. *Moilanen J, Hovatta O and Lindroth L: Vitamin E levels in seminal plasmacan be elevated by oral administration of vitamin E in infertile men. Int J Androl. 1993;16: 165-6.*

20. *Suleiman SA, Ali ME, Zaki ZM, et al. Lipid peroxidation and human sperm motility: protective role of vitamin E. J Androl. 1996;17:530-537.*

21. *Sender B and Faragher B: Treatment of oligospermia with vitamin B12. Infertility.1984;7:133-8.*

22. *Loumbakis P, Anezinis P, Russo A et al. Effect of L-Carnitine in patients with asthenospermia. Eur Urol. 1996;30(suppl 2):255.*

23. *Muller-Tyl E, Lohninger A, Fishchl F, et al. The effect of carnitine on sperm count and sperm motility. Fertilitat. [translated from Jerman]. 1988;4:1-4.*

24. *Micic S, Lalic N, Nale DJ, et al. Effects of L-carnitine on sperm motility and number in infertile men. Fertil Steril. 1998;70 (3 suppl 1):S12.*

25. *Lenzi A, Lombardo F, Agro P, et al. Use of carnitine therapy in selected cases of male factor infertility: a double-blind cross over trial. Fertil Steril. 2003;79: 292-300.*

26. *Lenzi A, Sgro P, Salacone P, et al. A placebo-controlled double-blind randomized trial of the use of combined L-carnitine and L-acetyl-carnitine treatment in men with asthenozoospermia. Fertil Steril. 2004;81:1578-84.*

27. *Rolf C, Cooper TG, Yeung CH, et al. Antioxidant treatment of patients with asthenospermia or moderate oligoasthenospermia with high-dose vitamin C and vitamin E: a randomized, placebo-controlled, double-blind study. Hum Reprod. 1999;14:1028-1033.*

28. *Kessopoulou E, Powers HJ, Sharma KK, et al. A double-blind randomized placebo cross-over controlled trial using the antioxidant vitamin E to treat reactive oxygen species associated with male infertility. Fertil Steril 1995;64:825-831.*

29. *Vezina D, Mauffette F, Roberts KD, Bleau G. Selenium-vitamin E supplementation in infertile men. Effects on semen parameters and micronutrient levels and distribution. Biol Trace Elem Res 1996;53:65-83.*

30. *Kumamoto Y et al: Clinical efficacy of mecobalamin in treatment of oligospermia. Results of a bouble blind comparative clinical study. Acta Urol Japan. 1988;34:1109-1132.*

31. *Campaniello E, Petrarolo N, Mariggiola MC, Valdiserri A, Pareschi A, Ucci N, Flamigni C, Filicori M. Carnitine*

administration in asthenospermia [abstract] In: IV Int Congress Andrology;1989 May;Firenze. P.14-18.

32. *Vitali G, Parente R, Melotti C. Carnitine supplementation in human idiopathic asthenospermia:clinical results. Drugs Exp Clin Res. 1995;21(4):157-9.*

33. *Costa M, Canale D, Filicori MD, Iddio S, Lenzi A. L-carnitine in iriopathic asthenospermia a multicentre study. Andrologia. 1994;26(3):155-9.*

34. *Wong WY, Merkus HM, Thomas CM et al. Effects of folic acid and zinc sulfate on male factor subfertility: a double blind, randomized, placebo-controlled trial. Fertil Steril. 2002;77:491-498.*

35. *Pryor JL, Kent-First M, Muallem A. Van Bergen AH, Nolten WE, Meisner l, et al. Microdeletions in the Y chromosome of infertile men. N Engl J Med 1997;336:534-9.*

36. *Kent-First MG, Kol S, Muallem A, ofir R, manor D, Blazer S, et al. The incidence and possible relevance of Y-linked microdeletions in babies born after intracytoplasmic sperm injection and their infertile fathers. Mol Hum Reprod 1996;2:943-50*