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RESEARCH PAPER

Role of Micronutrients on the improvements of sperm count & motility in Idiopathic Oligospermia, Asthenospermia and Oligoasthenospermia

Mahbuba Khan Eusuf Zai[1*], Md. Habibullah[2], Sharmin Ali Tithy[3], Rashida Khanom[4]

[1]Sir Salimullah Medical College Mitford Hospital, Dhaka, Bangladesh, [2]Department of Critical Care Medicine, Dhaka Medical College, Dhaka, Bangladesh, [3]Department of Surgery outdoor, Rangpur Medical College Hospital, Rangpur, Bangladesh, [4]Department of Obstetrics and Gynaecoloy, Dhaka Medical College, Dhaka, Bangladesh

Abstract

Background: The management approach to infertility has changed remarkably in this age of assisted reproductive techniques (ART) with the aim of bringing hope for previously untreatable cases.

Objective: To assess the effectiveness of micronutrients on sperm count and motility in treating patients with idiopathic oligospermia, asthenospermia and oligoasthenospermia.

Methods: This prospective observational study was carried out at Reproductive Endocrinology and Infertility OPD and IVF center of Dhaka Medical College Hospital (DMCH) for the period of two years from July 2017 to June 2019 over 100 patients. All infertile men aged between 25-45 years with idiopathic oligospermia, asthenospermia or oligoasthenospermia attending Reproductive Endocrinology and Infertility OPD and IVF center of DMCH during the study period were assigned for the study. After obtaining informed written consent selection of the patient was done by using inclusion and exclusion criteria with the help of attending physicians.Semen analysis was performed at day zero (during inclusion date) and after 1 month of initial report at the center. Those patients with confirmed abnormal semen parameters in terms of oligospermia, asthenospermia or oligoasthenospermia were treated with micronutrients (Capsule Sperm Care, 1 capsule twice daily after meal for 3 months) by the attending physicians at Reproductive Endocrinology and Infertility OPD and IVF center of department of obstetrics and gynaecology, DMCH as per treatment protocol. Semen analysis was again performed at the end of three months of micronutrient treatment in the same center. Then information was collected from semen analysis reports and attending physicians. Comparison of the result of these two semen analysis reports in terms of sperm count and motility was observed after three months of micronutrient treatment.

Results: Of total 100 patients, mean age was 34.40±5.40 SD (years). Among them, 63% were suffering from primary subfertility and 37% had secondary subfertility. Overall frequency of oligospermia, oligoasthenospermia and asthenospermia were 28%, 60% and 12%, respectively. Base line sperm count was 12.13±8.03 million/ml, mean progressive motility (PR) was 27.31±9.81% and mean total motility (PR+NP) was 38.76±12.27% . Significant improvement was noted in sperm count, progressive motility (PR) and total motility (PR+NP) of patients after three months of therapy ($p<0.001$).

Conclusion: Significant improvement was noticed in sperm count and motility after providing three months of micronutrient therapy.

Keywords: Idiopathic Oligospermia, Asthenospermia, Oligoasthenospermia, Micronutrients.

Introduction

Failure of couple to conceive after twelve months of regular intercourse without contraception in women below 35 years; and after six months of regular intercourse without contraception in women more or equal 35 years is called infertility.[1] It is categorized as primary infertility who have never conceived and secondary infertility who have conceived in the past.[2] One in every four eligible couples in developing countries has been found infertile according to WHO. Globally it is a health issue, affecting approximately 15% of couple worldwide.[3] Rate of infertility in Bangladesh is 4% .[2]

Female is responsible for about 50% of cases of infertility, males account for 20-30% of cases and rest are unexplained.[1] Global male infertility rate is actually

***Correspondence:** Mahbuba Khan Eusuf Zai, Sir Salimullah Medical College Mitford Hospital, Dhaka, Bangladesh*

Res. Address: Flat No. 17D, Building No. 29, Azimpur Government Residential Area (Zone-A), Azimpur, Dhaka-1205

Email:mkeusufzai61@gmail.com

ORCID ID:0009-0004-0125-0535

lacking and under reported.[1,2]One of the commonest cause of male infertility is sperm dysfunction which can be due to many risk factors like varicocele, obstructive lesions, cryptorchidism, cystic fibrosis, trauma, genitourinary infection and environmental factors leading to defective spermatogenesis.[4,5] Normal spermatogenesis process requires an intact hypothalamic-pituitary-testicular axis. Hypothalamus releases GNRH in a pulsatile fashion, which controls gonadotropin synthesis, storage and release in/from the pituitary. The action of gonadotropins (FSH, LH) are fundamental for normal spermatogenesis. Spermatogenesis takes place inside the seminiferous tubules and the process takes about 74± 4 days as determined by means of autoradiograph.[6]

Almost ninety percent of male infertility is idiopathic. The total sperm count as well as sperm quality has been worsen over last few decades. This downward shift has led to speculation that recent environmental, dietary or lifestyle changes may be interfering with a man's ability to manufacture sperm.[6]

Oxidative stress is the result of imbalance between reactive oxygen (ROS) and nitrogen species (NOS) and responsible for the pathogenesis of idiopathic sperm dysfunction as primary cause.[7,8] There is low amount of antioxidants within the cytoplasm of spermatozoa and in seminal plasma, and hence, could be highly susceptible to oxidative stress. Decreased sperm viability and motility and damage to sperm nuclear DNA are associated with high ROS in semen and subsequently decline men fertility.[9,10]

Semen analysis is the cornerstone investigation for male infertility. Medical treatment of oligospermia, asthenospermia or oligoasthenospermia can be quite effective when the causes are known. But when cause is not identified approach of treatment is to focus on enhancing those factors, which promote sperm formation. Micronutrients are essential elements required for normal physiology of male reproductive system and play important role in spermatogenesis.

In recent years, the use of micronutrients, vitamins and antioxidants treatment in men with infertility has been strongly recommended. However, several studies have shown weak evidence or no benefit at all from micronutrients supplementation on semen parameters.[11,12]

Micronutrients like vitamin C, vitamin E, L carnitine, zinc, vitamin B complex are crucial in male reproductive system for proper hormone metabolism, sperm formation and motility and improvement of sperm quality. [6, 13-15] All parameters like Median ejaculatory volume, sperm cell density, sperm motility (progressive and total) and normal morphology rate evaluated by semen analysis significantly increased after three months of treatment with micronutrients.[13]

High or low dose antioxidants in combination with antibiotic for two months significantly increased both sperm count and motility in Idiopathic oligospermia, asthenospermia and oligoasthenospermia and the effect was more notable with high dose.[16] Use of multiple antioxidants for 3–6 months improved at least one semen parameter (motility, concentration, normal morphology and antioxidant capacity).[15]

Supplementation of micronutrients can improve sperm quality and quantity in idiopathic oligospermia, asthenospermia and oligoasthenospermia. Therefore, this study was conducted to evaluate the effectiveness of micronutrients in treating idiopathic oligospermia and asthenospermia so that it can be utilized by the infertility specialists in future in an attempt to reduce the overall burden of male infertility.

Materials and Methods

This prospective observational study was carried out at Reproductive Endocrinology and Infertility OPD and IVF center of department of obstetrics and gynaecology, DMCH for the period of two years from July 2017 to June 2019.

Inclusion criteria:

Inclusion criteria for the study are the following:

1. Infertile men attending Reproductive Endocrinology and Infertility OPD and IVF center of department of obstetrics and gynaecology, DMCH with primary or secondary infertility exhibiting idiopathic oligospermia, asthenospermia or oligoasthenospermia.
2. Patient who gives consent voluntarily.
3. Who didn't receive any course of micronutrient treatment within 3 months.

Exclusion criteria:

1. Infertile men with azoospermia and aspermia.
2. Patient having varicocele and recent urological infection.
3. Who have already received any micronutrient treatment.

4. Patient having any other known cause for oligospermia, asthenospermia or oligoasthenospermia.

Study variables:

Demographic variable: Age

Clinical variable: Type of subfertility, duration of subfertility

Outcome variable: Sperm count (mill/ml), sperm total motility (%), sperm Progressive motility (PR) (%)

All infertile men aged between 25-45 years with idiopathic oligospermia, asthenospermia or oligoasthenospermia attending Reproductive Endocrinology and Infertility OPD and IVF center of department of obstetrics and gynaecology, DMCH during the study period who did not receiveany course of micronutrient treatment within 3 months were assigned for the study. After obtaining informed written consent , detailed personal history was taken. Patients having any known cause of abnormal semen parameters eg. Diabetes mellitus, hypertension, genitourinary infection, drugs, genital surgery, hormonal problem (abnormalities in serum FSH, LH, Testosterone, Prolactin) were identified & excluded from the study. Smokers and patients having history of any drug or alcohol were excluded from the study. The study was not randomized. Sampling was purposive.

After selection of the patient by using inclusion and exclusion criteria with the help of attending physicians at Reproductive Endocrinology and Infertility OPD and IVF center of department of obstetrics and gynaecology, DMCH initial semen analysis was done. Then reports were reviewed after 1 months of initial report. If any parameter either count, motility or both motility and count found below the normal level of WHO 2010 criteria was considered as abnormal semen parameter. Though abnormal morphology is also included in abnormal semen parameter, teratospermia cases were not included in this study. In case of abnormal semen parameter patient was examined thoroughly by the help of the department of urology to exclude any abnormality in genital system. Following investigations were done to diagnose the cause of abnormal semen: hormone analysis FSH, LH testosterone and prolactin, RBS and anti-chlamydial antibody. Testicular, prostatic and seminal vesicle ultrasonography was done to detect any abnormality. If any specific cause of abnormal semen parameter was identified, it was excluded from the study. Smokers and patients having history of any drug or alcohol were excluded. These patients were prescribed with micronutrients from Reproductive Endocrinology and Infertility OPD and IVF center of department of obstetrics and gynaecology, DMCH by the attending physicians for the patients at that department and were followed up over telephone.

Total of 100 patients were enrolled for the study. They were treated with single Sperm Care capsule containing Coenzyme Q (6 mg), Riboflavin (1.4 mg), L-Arginine (24 mg), L-Carnitine (40 mg), Omega 3 fatty acids (50 mg),Vitamin A (30000 IU),Vitamin D3 (400 IU), Vitamin C (100 mg),Vitamin E (30 IU), Vitamin K (50 mcg),Vitamin B6 (2 mg),Vitamin B12 (20 mcg), Thiamine (1.5 mg), Niacin (12 mg), Pyridoxine (10 mg), Elemental Zinc (20 mg), Elemental Iron (10 mg), Elemental Manganese (2 mg), Folic Acid (6 mg), Elemental Copper (2 mg), Elemental Chromium (80 mcg), Elemental Selenium (200 mcg), Elemental Iodine (100 mcg) twice daily after meal for three months.

At the end of 3 months of micronutrient treatment, further semen analysis was done. Then information was collected from semen analysis reports and improvement of semen parameters in terms of appearance, consistency, liquefaction, volume and pH, sperm concentration, total motility and forward motility were analyzed in comparison to the initial report. All data were collected by using a preformed data sheet.

Data were checked, verified for consistency and edited for final result. Data cleaning validation and analysis were performed using the SPSS software version 23 where required and chart by MS excel. Data analysis was carried out to describe the study population where categorical variables were summarized using frequency tables while continuous variables were summarized using measures of central tendency and dispersion such as mean and standard deviation. Comparison of Semen analysis report of patients before and after treatment was performed by paired t-test & at 95% confidence interval (CI). Improvement of semen analysis reports of patients after treatment was compaired by Mc Nemar's test (X^2 Test). A *p*-value of less than 0.05 was considered significant.

Results

Total 100 male patients attending in the Reproductive Endocrinology and Infertility OPD and IVF center were included for analysis.

Table I: Baseline characteristics of the study subjects (N=100)

Characteristic	Mean ± SD or Number (%)
Age (years)	34.40 ± 5.40 (25-45)
Hormone analysis	
FSH (IU/L)	5.99 ± 1.17
LH (IU/L)	4.55 ± 0.83
Prolactin (ng/ml)	9.74 ± 2.64
Testosterone (ng/ml)	5.48 ± 1.18
Type of subfertility	
Primary	63 (63)
Secondary	37 (37)
Duration of subfertility (years)	4.62 ± 2.88
Semen analysis report before treatment	
Sperm count (million/ml)	12.13 ± 8.03
Progressive motility PR (%)	27.31 ± 9.81
Total motility (PR+NP) (%)	38.76 ± 12.27

Their mean age was 34.40±5.40 years ranged from 25 years to 45 years. The most prevalent age group was 25 – 30 years constituting 33% of the study population. Mean level of FSH, LH, prolactin and testosterone were within normal range. Among 100 participants 63% were suffering from primary subfertility and 37% had secondary subfertility and mean duration of infertility was 4.62 ± 2.88 years.

Before initiating treatment, baseline mean sperm count was 12.13 ± 8.03 million/ml, mean progressive motility (PR) was 27.31 ± 9.81% and mean total motility (PR+NP) was 38.76 ± 12.27% (Table II).

The most common study diagnosis was oligoasthenopermia (60%), followed in second by oligospermia (28%), and third by asthenospermia (12%) (Figure-1).

All of the patients were given micronutrient as a treatment. Significant improvement was noted in sperm count, progressive motility (PR) and total motility (PR+NP) after three months of therapy (Table II and Table III).

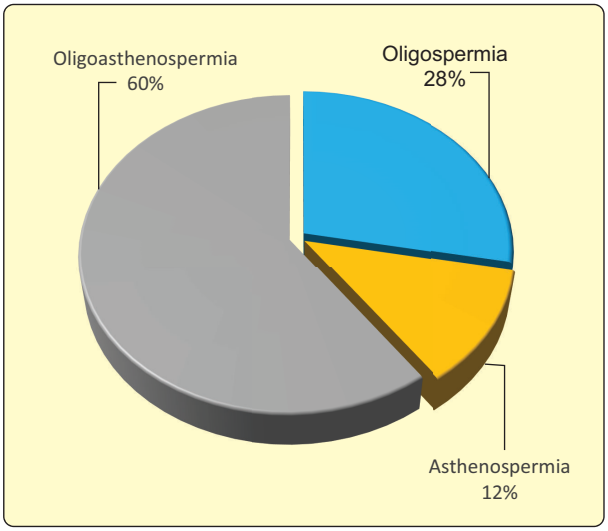

Figure-1: Frequency of study population according to diagnosis (n=100)

Table II: Comparison of Semen analysis report before and after treatment (N=100)

Variables	Before treatment Mean ± SD	After treatment Mean ± SD	p-value*	Mean Improvement (95%CI)
Sperm count (million/ml)	12.13 ± 8.03	14.11 ± 7.92	<0.001	1.97(1.39 – 2.55)
Progressive motility (PR) (%)	27.31 ± 9.81	30.21 ± 9.37	<0.001	2.90(2.15 – 3.65)
Total motility (PR+NP) (%)	38.76 ±12.27	43.36 ± 12.67	<0.001	4.65(3.03 – 6.26)

*p-values were determined by paired samples t-test

*PR- Progressive motility

*NP- Non Progressive motility

Table III: Improvement of Semen analysis report of patients after treatment (N=100)

Variables	Before treatment (%)	After treatment (%)	p-value
Sperm Count (million/ml)			
<15	88	53	p<0.001
≥15	12	47	
Progressive motility (PR) (%)			
<32 %	72	51	p<0.001
≥32%	28	49	
Total motility (PR+NP) (%)			
<40%	52	30	p<0.001
≥40%	48	70	

*p-values were determined by McNemar's test

Discussion

Total 100 male patients of infertility were included in this study to find the role of micronutrients on sperm count and motility in idiopathic Oligospermia, Asthenospermia and Oligoasthenospermia in context of Bangladesh.

Mean age of the patients was 34.40 ± 5.40 years which is concordant with other studies conducted on male infertility in Bangladesh.[6,17,18]

In this study 63% patients were found to have primary infertility and 37% had secondary infertility. This is different than the overall estimates in South Asian region which may be due to delayed presentation for infertility treatment in developing countries.[3]

The present study found 28% cases of oligospermia, 60% cases of oligoasthenospermia and 12% cases of asthenospermia. Severe oligoasthenospermia, azoospermia and aspermia patients were excluded from the study. Mean duration of infertility was 4.62 ± 2.88 years. These are compatible with the findings of a previous study .[6]

The present study found a mean sperm count of 12.13 ± 8.03 million/ml, mean progressive motility (PR) of 27.31 ± 9.81%, and mean total motility (PR+NP) of 38.76 ± 12.27%. After treatment with micronutrients significant improvement was noted in sperm count, progressive motility (PR) and total motility (PR+NP) of patients after three months of therapy. Zinc supplementation causes significant improvement in sperm count, motility and morphology after 3 months of treatment.[18]

In a previous study the effect of micronutrients blend in addition to the effect of antibiotic and lifestyle change in sperm count and quality of male infertility patients was observed. The patients were divided in three groups: I, II and III. Group I was treated by antibiotic Doxicycline 100 mg twice daily for 1 month followed by micronutrients for 3 months, Group II was treated with the same micronutrients only for 3 months and Group III were advised about life style changes only. After treatment there was significant improvement both in sperm count and motility in groups I and II. In group III where there was no intervention there was no improvement of semen parameters.[6] This is similar to the findings of the present study. The effect of high dose and low dose antioxidants along with antibiotics in idiopathic oligospermia, asthenospermia and oligoasthenospermia was noted in another previous study and found a significant improvement ($p<0.01$) in both count and motility of sperm after two months of treatment which is comparable with the present study.[16]

The interventional studies involving different micronutrients in the therapy of infertility in male was reviewed and noted that since there is no linear correlation between sperm quality and pregnancy rates, an improvement in semen parameters should not be the sole outcome considered in studies of micronutrients therapies.[19]

Although the present study found improvement in sperm count and motility after treatment with micronutrients, a definitive conclusion cannot be obtained. Even if beneficial effects were reported in a few cases of male infertility, more multicenter, double-blind studies performed with the same criteria are necessary for an increased understanding of the effects of various micronutrients on fertility.

Role of specific micronutrients and pregnancy outcome has not evaluated.

There is a need for further investigation with randomized controlled studies to confirm the efficacy and safety of micronutrient supplementation in the medical treatment of idiopathic male infertility as well as the need to determine the dosage required to improve semen parameters, fertilization rates and pregnancy outcomes.

Conclusion:

Micronutrient has improved the quality of sperm in terms of count & motility in idiopathic oligospermia, asthenospermia and oligoasthenospermia.

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Conflict of interest: There is no conflict of interest to any of the authors of the article.

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Ethical Clearance: Ethical clearance for the study was taken from the Institutional Review Board and concerned authority, Dhaka Medical College.

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