A Qualitative Analysis of Efficacy of Multivitamin and Micronutrient Supplementation on Semen Parameters in Patients with Primary Infertility: A Prospective Randomized Control Study

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Research Article

Abstract: **Background**: Studies have shown that seminal antioxidant capacity is suppressed in infertile men with high reactive oxygen species (ROS) levels as compared to men with normal levels of ROS. Controversy exists, as to whether the high ROS levels detected in semen of infertile men are due to increased ROS production or decreased ROS scavenging or both. **Aim:** The study was undertaken to evaluate the efficacy of antioxidants multivitamin and micronutrient supplementation on semen parameters in patients with primary infertility. **Methods:** n =30 patients, between 25 - 35 years, with primary infertility were enrolled for the study. Standard doses of multivitamin and micronutrient supplements were given twice daily for 6 months. Semen parameters including sperm count, motility and morphology were studied before and after the therapy. Paired't' test was used for statistical analysis. **Results:** The sperm count, and motility improved significantly (P< 0.05) after multivitamin and micronutrient therapy. **Conclusion:** Multivitamin and micronutrient supplementation improves the seminal parameters and might have a place as an additional supplement in the treatment of male infertility.

Key Words: antioxidant, micronutrient, multivitamin, oxidative stress, Primary infertility.

Introduction

Infertility is a major clinical concern, affecting 15% of all reproductive age couples of which male factors account for 25%.[1] 10-15% of infertile men suffer from azoospermia.[2] The etiology of diminished seminal quality in primary infertility is poorly understood and many physiological, environmental, and genetic factors, including oxidative stress have been implicated.[3]Oxidative stress is believed to be one of the main factors in the pathogenesis of sperm dysfunction and sperm DNA damage in male infertility.[4] A number of studies have shown that seminal antioxidant capacity is suppressed in infertile men with high reactive oxygen species (ROS) levels as compared to men with normal levels of ROS.[5] It is not clear whether reduced semen antioxidant capacity causes sperm dysfunction.[6,7,8] There is some controversy as to whether the high ROS levels detected in semen of infertile men are due to increased ROS production, decreased ROS scavenging or both.[9,10] If the high semen ROS levels are due to a decreased ROS scavenging capacity of semen, it would support the use of dietary antioxidant supplementation. Various studies have been done regarding the mechanism of antioxidant on male infertility, but they failed to reach at firm conclusions.[11] Therefore, this study was undertaken to evaluate the efficacy of multivitamins and micronutrients as antioxidants in azoospermic patients with primary infertility.

Material and Methods

The Study was carried out in the Reproductive Biology Unit of Department of Physiology, Government Medical College, Aurangabad. The study was approved by the Institutional Ethical Committee (IEC-GMCH).

Source of patients:

The patients of primaryinfertility,referredfor semen analysis form the outpatient department ofobstetrics and Gynaecology(OBGY), were enrolled for the studyafter obtaining informed written consent.

Methodology:

A total of n=30 patients with primary infertility were enrolled for the study.

Patients received multivitamins and micronutrients supplementation as a FDC (fixed dose combination) tablet. Tablet A to Z (brand name; contents: Vitamin C – 40mg, Vitamin B_3- 16mg, Vitamin E - 15mg, Vitamin B_5- 5mg, Vitamin B6 - 2mg ,Vitamin B2 - 1.4mg, Vitamin B1- 1.2mg,Vitamin A - 600mcg, Folic acid- 100mcg , Methylcobalamine- 1mcg ,Zinc- 10mg ,Manganese- 2 mg, Copper- 0.9mg and Selenium- 55mcg) ***Dose***: one tablet twice dailyfor 6 months. (Free of cost). All the patients were advised for monthly follow up.

Inclusion criteria:

Diagnosed cases of Primary infertility referred to the reproductive unit of department of Physiology.

Exclusion criteria:

Patients with the following conditions known to influence oxidative stress were excluded by the referred department.

1. Patients with history of smoking since last 5 years, alcohol consumption and tobacco chewing.
2. Patients suffering from diabetes mellitus, hypertension, tuberculosis, COPD, arthritis, infections and AIDS.
3. Patients taking drugs like vitamin E, vitamin C or glutathione supplementation.
4. Patients with abnormalities like cryptorchidism (undescended testes), atrophic testes or varicocele.
5. Patients having genitourinary infection.
6. All those not ready to give informed written consent.

Collection of semen sample:

The semen samples were collected in a wide mouthed sterile container by masturbation after an abstinence of 3-4 days**.**

Semen analysisas per WHO criteria:[12]

The semen samples after collection were kept at room temperature. The liquefaction was confirmed at every 5 min till the time of liquefaction. Then the volume and pH was measured.Microscopic examination of the semen sample was done using the sperm meter. If no spermatozoa wasobserved, the sample was centrifuged and then the pellet was examined for spermatozoa. After treatment with multivitamin and micronutrients, again asemen analysis was done after 6 months**.**

Statistical analysis:

Seminal values determined before and after treatment were compared by the paired 't' test. $p < 0.05$ was considered for statistical significance.

Observations and Results

The mean age of the patients was 33.23 ± 4.4 years. The sperm count before treatment was 10.5 ± 25.0 million/ml and after treatment it was found to be 50 ± 4.1millions/ml The sperm motility% before treatment was 18.4 ± 9.62%and after treatment it was found to be 48.72 ± 14.2%.

Table 1: Seminal parameters in the study group before and after treatment with multivitamin andmicronutrients

Parameters	Before Treatment	After Treatment
Sperm count(millions/ml)	10.5±25.0	50 ±4.1
Sperm motility(%)	18.4± 9.62%	48.72± 14.2%.

The values are expressed as ± SEM

Discussion

The study was undertaken to ascertain the beneficial effect of multivitamin and micronutrients supplementation in azoospermic patients with primary male infertility. There was asignificant improvement in the seminal parameters in these patients after the therapy. The rationale for treating infertile men with oral antioxidants is based on the hypothesis that seminal oxidative stress in infertile men is due in part to a deficiency of seminal antioxidants.[13] Many small uncontrolled studies have shown a significant improvement in semen parameters following antioxidant therapy.[14] Spermatozoa are particularly susceptible to oxidative injury due to abundance of plasma membrane polyunsaturated fatty acids (PUFA).The unsaturated nature of these molecules predisposes them to free radical attack and ongoing lipid peroxidation throughout the sperm plasma membrane.Accumulation of lipid peroxides occurs on the sperm surface which results in loss of sperm motility and oxidative damage to the sperm DNA.Oxidative damage is common for spermatozoa during epididymalmaturation and storage . Human spermatozoa are highly susceptible to oxidative injury but are naturally protected from such injury by the oxidant properties of seminal plasma. ROS plays a central role for sperm physiology such as sperm maturation and capacitation. Abnormal ROS production is associated with defective sperm function. A fine balance between ROS production and recycling is essential for spermatogenesis.Asthenozoospermiais probably the best surrogate marker of oxidative stress in a routine semen analysis.[15] The multivitamins and micronutrients act as antioxidant and neutralize the preformed free radicals.[16]

Conclusion

Routine estimation of antioxidant status while evaluating infertility should be done. Use of dietary antioxidant supplementation must be recommended in such patients. More studies with case control design should be undertaken. These biological antioxidants and their associated mechanisms is an important area for further investigation in the treatment of infertility

References

1. Rowe PJ, Comhaire FH, Hargreave TB, Mahmoud AMA. WHO Manual for the Standardized Investigation, Diagnosis and Management of the Infertile Male. Cambridge (UK): Cambridge University Press; 2000.
2. Jarow JP, Espeland MA, Lipshultz LI. Evaluation of the azoospermic patient. J Urol1989; 142: 62–65.
3. Ursini F, Heim S, Kiess M, et al. Dual function of the selenoproteinPHGPx during sperm maturation. Science. 1999;285(5432):1393–1396.
4. Iwasaki A, Gagnon C. Formation of reactive oxygen species in spermatozoa of infertile patients. FertilSteril1992; 57: 409–16.

5. Hampl JS, Taylor CA, Johnston CS. Vitamin C deficiency and depletion in the United States: the Third National Health and Nutrition Examination Survey, 1988 to 1994. Am J Public Health 2004; 94: 870–5.
6. Smith R, Vantman D, Ponce J, Escobar J, Lissi E. Total antioxidant capacity of human seminal plasma. Hum Reprod1996; 11: 1655–60.
7. Lewis SE, Sterling ES, Young IS, Thompson W. Comparison of individual antioxidants of sperm and seminal plasma in fertile and infertile men. FertilSteril1997; 67: 142–7.
8. Sanocka D, Miesel R, Jedrzejczak P, Kurpisz MK. Oxidative stress and male infertility. J Androl1996; 17: 449–54.
9. Zini A, de Lamirande E, Gagnon C. Reactive oxygen species in semen of infertile patients: levels of superoxide dismutase- and catalase-like activities in seminal plasma and spermatozoa. Int J Androl1993; 16: 183–8.
10. Lewis SE, Boyle PM, McKinney KA, Young IS, Thompson W. Total antioxidant capacity of seminal plasma is different in fertile and infertile men. FertilSteril1995; 64: 868–70.
11. Zini A, San Gabriel M, Baazeem A. Antioxidants and sperm DNA damage: a clinical perspective. J Assist Reprod Genet 2009; 26: 427–32.
12. WHO laboratory manual for the Examination and processing of human semen fifth edition 2010.
13. Agarwal A, Nallella KP, Allamaneni SS, Said TM. Role of antioxidants in treatment of male infertility: an overview of the literature. Reprod Biomed Online 2004; 8: 616– 27.
14. deLamirande E, Gagnon C. Reactive oxygen species and human spermatozoa. I. Effects on the motility of intact spermatozoa and on sperm axonemes. J Androl1992; 13: 368–78.
15. Alvarez JG, Touchstone JC, Blasco L, Storey BT. Spontaneous lipid peroxidation andproduction of hydrogen peroxide and superoxide in human spermatozoa. Superoxidedismutase as major enzyme protectant against oxygen toxicity. J Androl1987; 8: 338–48.
16. Twigg J, Fulton N, Gomez E, Irvine DS, Aitken RJ. Analysis of the impact of intracellular reactive oxygen species generation on the structural and functional integrity of human spermatozoa: lipid peroxidation, DNA fragmentation and effectiveness of antioxidants. Hum Reprod1998; 13: 1429–36.