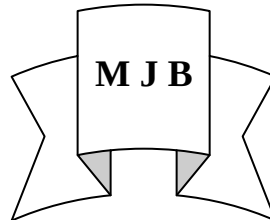


The Effect of Selenium and Vitamin E on Male Infertility

Mohammad Ridha Judi Abbood

Dept. of Surgery, College of Medicine, University of Babylon, Hilla, Iraq.



Abstract

100 male patient complain from primary or secondary male infertility with asthenospermia and teratospermia submitted to this prospective study attained to the privet clinic from June /2010-june/2011 with normal or mild subnormal sperm count, received antioxidant selenium and vitamin E for 90 days, and result show good percentage improvement in shape and motility, also these drugs are safe if given in the recommended does. It is difficult to asses the rate of pregnancy exactly because difficult to follow the patient when his wife become pregnant.

الخلاصة

شملت هذه الدراسة التوقعية مائة رجل مريض يشكون من عقم ذكري اولي او ثانوي مع وهن النطف وامساخ نطفي، وهم من مرضى عيادتي الخاصة للفترة من حزيران ٢٠١٠ الى حزيران ٢٠١١ اضافة الى مجموعة من الاصحاء او معتدلي عدد النطف تناولوا عقاري السلينيوم وفيتامين E لمدة ٩٠ يوما.

اظهرت النتائج نسبة جيدة من التحسن في شكل وحركة النطف. وتعد هذه الادوية امنة اذا ما اخذت بالجرع الموصى بها. ومن الصعب تقييم نسبة الحمل بالضبط بسبب صعوبة متابعة المرضى عندما تصبح زوجاتهم حوامل.

Introduction

The World Health Organization (WHO) defines infertility as the inability of a couple to achieve conception or bring a pregnancy to term after one year or more of regular unprotected sexual intercourse.[1]

Although certain cases of male infertility are due to anatomical abnormalities, such as varicocele, ductal obstruction, or ejaculatory disorder, an estimated 40-90% of cases are due to deficient sperm production of unidentifiable origin [2]. Infertility is a major clinical concern, affecting 15% of all reproductive age couples.

Male factors, including decreased semen quality are responsible for 25% of these cases [3,4]. Currently, the etiology of sub optimal semen quality is poorly understood, and many physiological, environmental, and

genetic factors, including oxidative stress, have been implicated [5].

Selenium (Se) is important for reproductive function such as testosterone metabolism and is a constituent of sperm capsule selenoprotein.

The administration of Se to sub-fertile patients induce a statistically significant rise in sperm motility [6]. Se is an essential trace element occurs in organic and inorganic forms. The organic form is found predominantly in grains, fish, meat, poultry, eggs, and dairy products and enters the food chain via plant consumption. Typical dietary intake of Se in the USA is 80-120µg/daily, and the recommended daily allowance is 70µg in men and 50µg in women [7]. Sperm capsular selenoprotein has an important structural role in spermatozoa in the form of glutathione peroxidase GSH-

Px [8]. Increased reactive oxygen species (ROS) decrease fertility because ROS attacks the membrane of the spermatozoa, decreasing their viability.

Increasing Se encourages antioxidant GSH-Px activity, thus decreasing ROS and leading to increased male fertility [9,10].

Vitamin E is one of the most important antioxidative molecules, rising mainly in the cell membranes. It is thought to interrupt reactions with lipid peroxidation and is a free radical scavenger generated during the univalent reduction of molecular oxygen and also normal activity of oxidative enzymes [11]. These radicals will lead to peroxidation of phospholipids in the mitochondria of the sperm and thus to their ultimate immotility [12]. It is possible that vitamin E enhances the production of the scavenger antioxidant enzymes [13].

Material and Method

110 infertile men 10 of them excluded (lose of follow up), only 100 patient submitted to this study.

Ten (10) patients with secondary infertility, 90 patients with primary infertility.

The patient had normal sperm count but with teratospermia, and asthenospermia, followed for 90 days.

These patients with no medical condition could account for infertility.

Age range between 19-50 years old, duration of infertility range between 1-10 years.

All patient with sperm count more than 15 million, failed to concept more than one year, and normal female partner.

Exclusion include: abnormal physical test, bilateral undesended testicl, testicular atrophy,

hypogonadism, varicocel, genital surgery, oligospermia, or azospermia.

Patients were treated with selenium 200 mg/day (L-selenomethionine), in combination with 400 IU vitamin E (α tocoprenol).

All patients send for seminal fluid analyses with abstains of 48-72 hours before giving antioxidant and every month (follow up and to see if any infection). The most important one is the last one after 90 days, those conceders in the study.

Normal WHO values included a sperm concentration of 20 million spermatozoa/ml or greater (now considered more than 15 million/ml), and 50% or greater motility with forward progression, with 14% normal forms were considered normal.

Results

From 110 patient 10 patients missed from the beginning difficult to follow them because it followed in private clinic (table 1).

Only 100 patients included in the study, following treatment with selenium and vitamin E after 90 days at the end some of the patient came and a have, positive pregnancy test and other didn't came after the end of 90 day, so the patients get improvement with treatment is 55 (55%), other patients didn't get benefit from treatment about 35 (35%). (Table 2).

The patients that get improvement with treatment that improved in motility from 10-30%, to 15-45% after treatment with 44%. And those patient with improvement in morphology from 1% before treatment to 6% in seminal analysis in 4% of the patients, and number of the patients that get improvement in motility and morphology about 7% from the total (from 1% -10-30% before treatment to 6% -15-45% after treatment).

Table 1 no. of patients submitted to study:

Total no. of patients	No. of patients submitted to the study
110	100

Table 2 patients response to treatment:

No. of patient improved with treatment	No. of patient with no improvement	No. of patient get pregnancy or missed from follow up
55 (55%)	35 (35%)	10 (10%)

Table 3 patient improvement with treatment:

Patients with improvement with motility	Patients with improvement with morphology	Patient with improvement in motility and morphology
44 (44%)	4 (4%)	7 (7%)

Table 4 before and after treatment:

	change in motility 44%	Change in motility an morphology 7%	Change in morphology 4%
Before treatment	From 10-30 %	1% 10-30%	1%
After treatment	From 15-45%	6% 15-45%	6%

Discussion

Selenium is an essential trace element for humans and animals [14]. Se is essential for sperm function and male fertility. Se deficiency has been linked to reproductive problems in rats, mice, chickens, pigs, sheep, and cattle,[15] Se supplementation has been reported to improve reproductive performance in sheep and mice [16], However, high Se intake has been associated with impaired semen quality [17]. This improvement is supplementation dependant, as all of the parameters returned to baseline values during the post treatment period [18]. Se is incorporated into enzymes that regulate normal body processes. In order to protect human population from excessive consumption of Se, 500µg of Se was generally accepted as the maximum acceptable daily intake. Therefore, it can be predicted that chronic selenosis occurs with daily

intake of 1000-1500µg of element Se [19].

Selenium and glutathione are essential to the formation of phospholipids-hyperoxide GSH-Px, an enzyme present in spermatid that becomes a structural protein comprising over 50% of mitochondrial capsule in the mid-piece of mature spermatozoa. Deficiencies of either substance can lead to instability of mid-piece, resulting in defective motility.[3]

Vitamin E is a well-documented fat-soluble antioxidant and has been shown to inhibit free radical- induced damage to sensitive cell membrane [20]. Oral supplementation with vitamin E significantly decrease malondialdehyde (MDA) concentration and improved sperm motility [13]. The recommended dietary allowance of vitamin E is 15 mg/day, and the tolerable upper intake level of any α -tocopherol form is

1000mg/day. Although in most healthy adult short-term supplementation with up to 1600IU of vitamin E appears to be well tolerated and have minimal side effect, long-term safety is questionable [21]. Vitamin E and C also play critical roles as non enzymatic antioxidants. Vitamin E plays a vital role in protecting cell membranes from oxidative damage trapping and scavenging free radicals within cellular membranes.

Suleiman et al [13] investigated the effects of vitamin E on sperm motility. A total of 11 out of 52 treated patients (21%) impregnated their spouses, and improved motility of sperm was seen in 31 subjects.

Oxidative stress is induced by ROS or free radicals. Although ROS have been shown to be required for sperm capacitation, hyper activation, and sperm-oocyte fusion [19], excessive levels of ROS can negatively impact sperm quality. Increase level of ROS have been correlated with decreased sperm motility [22], increased sperm DNA damage [23], sperm cellular membrane lipid per oxidation [24], and decreased efficacy of oocyt- sperm fusion [25]. these free radicals induce sperm cell injury through several pathways and can significantly impact both sperm quality and function [25,26].

In a systematic review of the effect of oral antioxidants (vitamin C and E, zinc, Se, carnitine) on male infertility by rose et al. [26], 17 randomized trials, including a total of 1665 men, were identified. Of these trials, 14 (82%) showed an improvement in either sperm quality or pregnancy rate after antioxidant therapy.

In one study, 69 infertile Scottish men were given placebo, Se, or Se in combination with vitamin A, C, and E for 3 months. At the end of the trial, both Se-treated groups had significant improvements in sperm motility;

however, sperm density was unaffected. During the course of the study, 11% of the participants in the treatment groups impregnated their partner [26].

Hawkes et al [17] investigated the effect of dietary Se on sperm motility in 11 cases of healthy men interestingly; they found that high Se diet (297µg/day) could impair sperm motility. However, my prescribed dose was 200µg/day.

References

1. Ppwe PJ, Cmhaire 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. Griffin JE, Wilson JD. Disorder of the testes. In :Issilbache rKL, Braunwald E, Wilson JD, MartinJB,FauciAS ,Kasper DL, editors .Harrison's principle of internal medicine. 13th ed . new York: McGraw Hill; 1994:2006-2017.
3. UrsiniF, Heim S Kiess M, et al. dual function of the selenoprotein PHGPx during sperm maturation. Science 1999;285:1393-1396.
4. Sharlip D,JarowJP,Belker AM,et al. Best practice policies for male infertility. Fertile sterile. 2002;77(5):873-882.
5. Vine MF .Smoking and male reproduction: a review. Int J androl,1996;19(6):323-337
6. MacPharsonA,Scott R .Ytes R ,The effect of selenium supplementation in sub fertile males. In :Anke M ,Meissner D ,Mill C F, editors .proceedings of the eighth international symposium on trace elements in man and animals 1993. jena(Germany): verlg media turkistik;1993:566-569.
7. National Academy of Science s ,Recommended Dietary Allowances, 10th ed .Washington (DC); National academy press;1989: 217-224.

8. Surinap P F ,Blesbois E, Grasseaul, et al .Fatty acid composition, glutathione peroxidase and super oxide dismutase activity and total antioxidant activity of avian semen. Comp biochem physiol B Biochem Mol boil. 1998;120(3):527-533.
9. Irvine DS. Glutathione as a treatment for male infertility. Rev reprod.1996;1(1):6-12.
10. Klein EA. Selenium: epidemiology and basic science. J Urol.2004;171(2pt2):s50-s53;discussion s53.
11. Palamanda JR, Kehrer JP, INVOLVEMENT OF VITAMIN E and protein thiols in the inhibition of microsomal lipid peroxidation by glutathione. Lipids. 1993;28(5): 427-431.
12. De Lmirande E, Gagnon C. Reactive oxygen species and human spermatozoa, I . Effect on the motility of intact spermatozoa and on sperm axonemes. J Androl,1992;13(5):368-378.
13. Selenium SA, Ali ME, Zaki, el-Malik,Naser MA. Lipid peroxidation and human sperm motility: protective role of vitamin E . J androl 1996;17(5):530-537.
14. Hawkes WC Turek PJ . Effect of dietary selenium on sperm motility in healthy men. J Andriol. 2001;22(5);764-772.
15. Combs GF Jr, Combs .SB .The role of selenium in nutrition. San Diego (ca):academic press;1986.
16. Tang CC, Chen HN, Rui HF . The effect of selenium on gestation, fertility, and offspring in mice boil trace elem. Res 1991;30(3) 227-231.
17. Hawkes WC ,Alkan Z, Wong K. Selenium supplementation does not affect testicular selenium status or semen quality in north American men. J Androl. 2009;30(5):525-533.
18. Vezina D, Mauffette F, Robert KD, Bleau G. Selenium- vitamin E supplementation in infertile men. Effect on semen parameters and micronutrient level and distribution. Boil trace elemmmmm res .1996;53(1-3):65-83.
19. Atiken RJ, Ryan AL, Baker MA, McLaughlin FA . Redox activity associated with maturation and cap citation of mammalian spermatozoa. Free radic boil med .2004;36(8):994-1010.
20. Aitken RJ ,Clarkson JS ,Hargreave TB ,Irvine DS, Wu FC. Analysis of the relationship between defective sperm function and generation of reactive oxygen species in cases of oligo zoospermia.J Adrol.1989;10(3):214-220
21. Vastassery Gt, Bauer T, Dysken M. High doses of vitamin E in the treatment of disorder of the central nervous system in the aged. Am J Clin Nutr. 1999;70(5): 793-801
22. Eskenazi B, Wyrobek AJ, Slotter, et al. The association of age and semen quality in healthy men. Hum reporod. 2003;18(2):447-454.
23. Armstrong JS ,Rajasekaran M, Chamulitrat W, Gatti P, Hellstrom WJ, Sikka SC. Characterization of reactive oxygen species induced effect on human spermatozoa movement and energy metabolism. Free radic boil med. 1999; 26(7-8) : 869-880.
24. Atiken RJ, Harkiss D , Buckingham DW. Analysis of lipid peroxidation mechanisms in human spermatozoa. Mol reprod dev. 1993;35(3):302-315.
25. Agrawal A, Prabhakaran SA, Sikka SC. Clinical relevance of oxidative stress in patients with male factor infertility: evidence-based analysis AUA Update Ser. 2007;26:1-12.
26. Saleh RA ,Agrwal A. Oxidative stress and male infertility: from research bench to clinical practice .J Androl. 2002;23(6):737-752.