

The Relationship of Vitamin E to the Fertility in Men

Aseel N.S.Ali

Biology department ,College of Education,University of Al-Qadisiyah

Corresponding author E.mail: Aseel.Najah@qu.edu.iq

Abstract

Vitamin E has a multiple physiological actions, There is a close association between vitamin E levels and male fertility, As it has a direct positive relationship with testosterone hormone and luteinizing hormone. Most of the vital activities of this compound are due to its activity as an antioxidant factor, as it plays an important role in preventing the oxidation of lipids in biomembranes by reducing free radicals and other oxidizing factors. and preventing the formation of lipids peroxides.

Keywords: Vitamin E, antioxidants, male fertility, seminal fluid

1-Introduction

Vitamin E was discovered in 1922 by the two scientists Herbert Evans and Khathrine Bishop while conducting experiments on animals, where an important substance was observed in leafy vegetables and oilseeds, as its presence in these foods was associated with increased fertility in these animals. In 1936, Emmerson and Evans was able to isolate it from wheat precursors and determine its chemical composition, and P.Karrer 1938 succeeded in its composition and called it the scientific name tocopherol, which is derived from the Greek name tocos, which means offspring and pherein which means bringer of offspring. It is a fat-soluble vitamin present in all biological membranes and is stored mainly in fatty tissues and in the liver and muscles. Vitamin E is an essential antioxidant in the body. It protects the polyunsaturated fatty acids in cell membranes from oxidation (1).

Vitamin E is one of the antioxidants in the seminal fluid and its concentration in the seminal plasma is about 0.32-0.52 micromol / liter (2). This vitamin has a great role in maintaining normal sperm movement due to the fact that vitamin E works to stabilize the plasma membranes chains of sperm cells as it works directly on the neutralization of negative superoxide roots (O_2^-), hydrogen peroxide (H_2O_2), and hydroxyl ($OH\cdot$) (3,4). Thus, it works to inhibit the effectiveness of fat oxidation and maintain normal sperm movement (5).

2-Role of antioxidants in treatment of male infertility

There are a number of studies conducted in vivo or in vitro explaining the protective role of antioxidants in protecting sperm and maintaining or improving semen quality, as these studies indicated that the preservation and freezing of human sperms lead to an increase in stress. Oxidative stress, which causes a decrease in the percentage of motile sperm (6,7). While another study reported that preserving sperms in the presence of vitamin E at a concentration of 10 mmol / liter preserved the percentage of sperm motility compared to samples that were preserved without adding the vitamin (8).

It was also observed when people with Oligoasthenoteratospermia Syndrome (OAT) were given a dose of 400 mg / day of vitamin E and selenium at a dose of 100 mg / day by mouth for one month, it caused an increase in the concentration of vitamin E and selenium in the seminal plasma in addition to a significant improvement in Sperm parameters that included the percentage of motile and normal form of sperm (9).

It was also found that the process of preserving the sperm in the Ranker solution causes a significant increase in the level of malondydehyde and reduces the movement of sperm, while when adding vitamin E to the solution, the level of MDA and sperm movement and vitality was maintained (10).

In another study to note the role of vitamin E and vitamin C in maintaining the movement of sperm during the Freeze-Thaw process, after a two-hour incubation period, it was found that vitamin E reduces sperm motility while vitamin C did not show any difference in results compared with control samples, (8). Whereas, when smokers were given vitamin C at doses of 100 and 200 mg / day orally, it was

observed that there was a significant improvement in sperm parameters, which were concentration, normal shape, and viability (11).

Low levels of vitamin E in all patients with infertility represent a possible consequence of the infertility status because the importance of vitamin E - mainly as an antioxidant - in male fertility (4,12). E agrees with previous studies that demonstrated the importance of this vitamin in improving sperm motility in vivo and ex vivo by preventing or reducing the negative effects of free radicals and Reactive oxygen species (ROS) (13), which causes damage to the DNA of the sperm, and reduces high-energy compounds such as adenosine triphosphate (ATP), which is a prerequisite in the movement of the sperm, and it causes lipid peroxidation in the cellular membranes of the sperm, all these effects reduce the movement of sperm and cause asthenic state (14,15,16).

In patients with oligospermia, vitamin E deficiency is an important cause of oligospermia, and studies have confirmed the role of vitamin E in addition to other antioxidants such as vitamin C in improving sperm concentration in many infertile patients (17), and these Results have been observed in the experimental animals treated with sodium fluoride - a highly toxic substance - which caused a significant decrease in the total number of sperm in the epididymis, except that dosing these animals with vitamin E caused a significant increase in the concentration of sperm in the epididymis (18), as indicated by one of the studies that the types of active oxygen are produced mainly either from leukocytes or by the sperm themselves in men with oligozoospermic men (19), and these observations were evident in the results of one of the studies that indicated a high percentage of the active oxygen types in the semen of infertile men, especially those with oligospermia (20), and the production of these types increases in cases of varicose veins, thus increasing the oxidative stress, It causes damage to the sperm and consequently failure of the sperm dysfunction and this may occur in the semen during the liquefaction period, or in the epididymis (during the period of storage) or in the testis (21).

3-The relationship of Testosterone hormone with vitamin E

In a study to (22) indicated the results of the study showed that the relationship between testosterone hormone and vitamin E in the control group is an inverse significant relationship, meaning that an increase in the levels of one of them is

accompanied by a decrease in the levels of the other, and this relationship is consistent with studies results that indicated that an increase in the testosterone hormone weakens the effectiveness of antioxidant (23). Other studies also indicated that dosing rats with testosterone hormone caused a significant decrease in the levels of nitric oxide (No) which has an important role in the process of spermatogenesis (24,25). On the other hand, vitamin E prevents changes resulting from a decrease in nitric oxide and an increase in the types of active oxygen, and nitric oxide increases some of the stimulating actions of vitamin E (26,27).

As for patients with latency, the relationship was a significant linear one, and since low levels of vitamin E are accompanied by damage to fats and proteins in cellular membranes, so it is possible for such effects to occur in the cells of leydic , and a decrease or a stop in the production of testicular fat hormone, one indicated Studies on mice indicate the contribution of active oxygen species to inhibiting the manufacturing process of steroids in Leydic cells, as Leydic cells are in direct contact with these types, which have been observed to affect a certain stage of steroid hormone synthesis, and it has been indicated that these types close the block phase of transfusion. Cholesterol, thus hindering the production of steroid hormones (28).

4-The relationship of Follicle Stimulating Hormone FSH with vitamin E

No relationship was observed between FSH and Vitamin E in fertile subjects(22), although one of the studies that was conducted in vitro indicated that there was a relationship between levels of vitamin E and the hypothalamus in rats and their stimulation to produce Gonadotropins releasing hormones with the contribution of various factors such as nitric oxide as well as (NMDA) N-methyl-D-aspartic acid (29). This may be due to the fact that the action of vitamin E at the level of the pituitary gland differs from its action at the level of the hypothalamus, that is, vitamin E may not have a stimulating effect to increase the production of a Follicles stimulating hormone, or its effect may be slight and insignificant, and there may be a difference in in vitro studies from those occurring in vivo as a result of the difference in the physiological concentrations of many enzymes, oxidizing factors, hormones and others depending on the physiological state.

As for the group of oligospermia patients, the relationship was linear and significant compared to the control group, and this due to the side effects of the disease condition, but at the same time this result came in agreement with some studies that indicated the role of vitamin E in Gonadotropinsrelesing hormones production. It is possible that this result may be attributed to an increase in oxidative stress due to low levels of vitamin E, and thus this may affect the pituitary gland's production of FSH in these patients.(22)

5-The relationship of luteinizing hormone LH with vitamin E

There is a significant linear relationship between the LH and Vitamin E as previous studies indicated the positive relationship between Vitamin E and LH production in Group of healthy controls (22). These studies showed that this linear relationship is contributed by some factors such as nitric oxide. Which is believed to increase the effect of vitamin E in stimulating the production of the luteinizing hormone (30). Also, the results of another study confirm that the LH increases with an increase in the concentration of vitamin E when incubation of the medial basal hypothalami (MBH) for rats with different concentrations of vitamin E (22, 88, 176 micromol) for different periods of time (1 minute, half a minute), it was observed that the highest concentration of vitamin E (176 micromol) was the reason for the highest stimulation of the production of LHRH (Luteinizing hormone releasing hormone). And with a time interval of one minute (29).

In patients with azoospermia, the relationship was the opposite, not significant, and this relationship may return - as in the case of follicle stimulating hormone – to the effect of the pathological condition that may interfere with the neuroendocrine function, and just as there are factors that increase the stimulation of vitamin E to produce LH, it is possible there are factors that negatively affect the relationship between LH and Vitamin E, and these factors may increase under certain physiological and pathological conditions, thus creating an inverse relationship between LH and Vitamin E, or at least causing a lack of relationship between the two, as in symptomatic patients.(22)

6- The relationship of Prolactin hormone with vitamin E

The results showed an inverse relationship between the prolactin and vitamin E in all study groups, except for a group of patients with asthenia, in which no relationship was clarified, and this inverse relationship can be explained on the basis of the relationship of antioxidants - in general - with dopamine, which is the main inhibitory factor for the milk hormone (22). Several previous studies have shown the role of some antioxidants, such as Selenium and Melatonin, in preventing the decrease and depletion of dopamine levels in mice treated with methamphetamine, which was observed that an injection in mice caused depletion of dopamine through its effect on the nerve endings responsible for the secretion of dopamine, along with some other effects (31,32,33), from these results notes the linear relationship between antioxidants and dopamine, and this explains the inverse relationship with the milk hormone in all study groups except for patients with asthenia, as it is found in this group that The changes that may be caused by low or high levels of vitamin E are completely separate from the possible changes that may occur in the levels of the milk hormone(22).

References

- 1-Bagchi, K. & Puri, S. (1998). Free radicals and antioxidants in health and disease. *La Revue desant de to mediterranee*, 4 (2): 350-360: (Review).
- 2-Buettner, G.R. (1993). The pecking order of free radicals and antioxidants lipid peroxidation, alpha-tocopherol and ascorbate. *Arch. Biochem. Biophys.*, 300:535-543.
- 3-Bolle, P.; Evandri, M.G. & Saso, L. (2002). The controversial efficacy of vitamin E for human male infertility. *Contraception*, 65: 313-315.
- 4-Agarwal, A. (2004). Increased seminal reactive oxygen species levels in patients with varicoceles correlate with varicocele grade but not with testis size, *82*: 1684-1686.
- 5-Aitken, R.J. & Clarkson, J.S. (1988). Significance of reactive oxygen species and antioxidants in defining the efficacy of sperm preparation techniques. *J. Androl.*, 9 (6): 367-376.

- 6-Crister, J.K.; Huse-Benda, A.R.; Aaker, D.V. *et al.* (1988). Cryopreservation of human spermatozoa. The effect of cryoprotectants on motility. *Fertile. Steril.*, 50: 314-320.
- 7-Mazzilli, F.; Rossi, T.; Sabatini, L. *et al.* (1995). Human sperm cryopreservation and reactive oxygen species production. *Acta. Europea. Fertilitatis*, 26: 145-148.
- 8-Askari, H.A.; Check, J.H.; Peymer, N. (1994). Effect of natural antioxidants tocopherol and ascorbic acids in maintenance of sperm activity during freeze-thaw process. *Arch. Androl.*, 33: 11-15.
- 9-Kodama, H.; Yamaguchi, R.; Fukuda, J. *et al.* (1997). Increased oxidative deoxyribonucleic acid damage in the spermatozoa of infertile male patients. *Fertile. Steril.*, 68: 519-524.
- 10-Verma, A. & Kanwar, K.C. (1999). Effect of vitamin E on human sperm and lipid peroxidation in vitro. *Asian. J. Androl.*, 1: 151-154.
- 11-Dawson, E.B.; Harris, W.A.; Teter, M.C.; *et al.* (1992). Effect of ascorbic acid supplementation on the sperm quality of smokers. *Fertile. Steril.*, 58: 1034-1039.
- 12-Greco,E; Scarselli,F.; Iacobelli,M.; Ubaldi,F.; Ferrero,S.; Franco, G.; Anniballo,N.; Mendoza,C. and Tesarik,J.(2005) Efficient treatment of infertility due to sperm DNA damage by ICSI with testicular spermatozoa.*Hum.Reprod.*20(1); 226-230.
- 13-Lee, W.M.; Wong, A.S.; Tu, A.W.; Chung, C.H.; Li, J.C. and Hammond ,G. L. (1997) Rabbit sex hormone binding globulin :primary structure /function analysis by expression Escherichia coli .*J. Endocrinol.***153**(3):373-384.
- 14-Hughes, C.M.; Lewis, S.E.M.; Mckelvey –Martin, V.J. and Thompson, W. (1998) The effects of antioxidant supplementation during percoll perperation on human sperm DNA integrity. *Hum.Reprod.*13 (5) 1240-1247.
- 15-Mahmoud, A .M.A; Comhair, F.H.and Christophe, A.B. (1999) Oral Antioxidant and male infertility .*Hum. Reprod.* **14** (12): 3149-3151.

- 16-Olson, S.E. and Seidel, G.E. (2000) Culture of in vitro – produced bovin embryos with vitamin E improves development in vitro and after transfer to recipients. *Biol.Reprod.***62**: 284-252.
- 17-Rolf, C.; Cooper, T.G.; Yeung, C.H. and Nieschlag, E. (1999) Antioxidant treatment of patients with asthen- ozoospermia or moderate oligoashenozoospermia with high –dose vitamin C and vitamine E: a randomized, placebo–controlled, double–blind study .*Hum. Reprod.***14** (4):1028-1033.
- 18-Chinoy, N.J. and Sharma, A. (1998) Amelioration of fluoride toxicity by vitamins E and D in reproductive functions of male mice .*Fluoride* **31**(4):203-216.
- 19-Martin –Du pan, R.C. AND Sakkas, D. (1998) Is antioxidants therapy a promising strategy to improve human reproductive? Are anti – oxidants useful in the treatment of male infertility? .*Hum.Reprod.***13**. (11): 2984-2985.
- 20-Ochsendorf, F.R. (1999) Infection in the male genital tract and reactive oxygen species.*Hum.Reprod.Upd.***5** (5):399-420.
- 21-Allamaneni, S.S.R.; Naughton, C.K.; Sharma, R.K.; Jr, .J.T. and Agarwal, A. (2004). Increased seminal reactive oxygen species levels in patients with varicoceles correlate with varicocele grade but not with testis size .*Fertil.Steril.***82**(6):1684-1686.
- 22- AL- Zubaidy,F.M.(2006) Study of some hormones levels and their correlation with vitamin E levels in the serum of infertile men
- 23-Ninni, P.; de Lope, F.; Saino, N.; Haussy, C. and Moller, A.P. (2004) Antioxidant and condition – dependence of arrival date in a migratory passerine .*Oikos* **105**(1):55-64.

- 24-Reynoso, R.; Mohn, C.; Retory, V.; Szwarefarb, B.; Carbone, S.; Rondina, D. and Moguilevsky, J.A. (2002) Changes in the effect of testosterone on hypothalamic nitric oxidesynthetase during sexual maturation .It's relationship with GnRH release. *Neuroendocrinol. Let.* 23: 101 – 104.
- 25-Lue, Y.; Hikim,A.P.S.; Wang,C.; Leung,A. and Swerdloff , R.S.(2003) Functional role of inducible nitric oxide synthase in the induction of male germ cell apoptosis,regulation of sperm number, and determination of testis size: evidence from null mutant mice . *Endocrinol.*144 (7):3092-3100.
- 26-Ganz, M.B. and Seftel, A. (2000) Glucose induced changes in protein Kinase C and nitric oxide are prevented by vitamin E.*Am.J. Physiol.Endocrinol.Metab.*278:E146-E152.
- 27-Lee, N.P.Y. and Cheng, C.Y. (2004) Nitric oxide synthase, spermatogenesis and tight junction dynamics.*Biol. Reprod.* 70:267-276.
- 28-Diemer, T.; Allen, J.A.; Hales, K.H. and Hales, D.B. (2003) Reactive oxygen disrupts mitochondria in MA-10 tumor leydig cells and inhibits steroidogenic acute regulatory (StAR) protein and steroidogenesis. *Endocrinal.*144 (7): 2882-2891.
- 29-Karant, S.; Yu, W.H.; Mastronardi, C.A.and McCann, S.M. (2003) Vitamin E stimulates Luteinizing hormone –relazing hormone and ascorbic acid release from medial basal hypothalamia of adult male rat.*EXP.Biol.Med.* 228:779-785.
- 30-Bhat, G.K.; Mahesh, V.B.; Ping, L.; Chorich, L.; Wiedmeier, V.T. and Brann,D.W.(1998). Opioid– glutamate – nitric oxide connection in the regulation of luteinizing hormone secretion in the rat. *Endocrinol.*139 (3):955-960.
- 31-Imam,S.Z.; El-Yazal,J.; Newport,G.D.; Itzhak,Y.; Cadet,J.L.; Slinkker,W. and Ali,S.F. (2001) Methamphetamine- induced dopamine- rgic neuroprotective: role of peroxynitrite , neuroprotective role of antioxidants and peroxynitrite decomposition catalyts. *Ann. New. Acad. Sci.* 939:366-380. (Abstract)

32-Imam, S.Z.; Jankovic, G.; Ali, S.F.; Skinner, J.T.; Xie, W.; Connely, O.M. and Le, W. (2005) Nitric oxide mediates increased susceptibility to dopaminergic damage in Nurr1 hetero-zygous mice. *FASEB. J.* **19**:1441-1450. (Abstract)

33-Mark, K.A; Sghomonian, J. and Yamamoto, B.K. (2004) High -dose methamphetamine acutely activates the striato-nigral pathway on increase striatal glutamate and mediate long - term dopamine toxicity .*J.Neurosci.* **24**(50):11449-11456. (Abstract)