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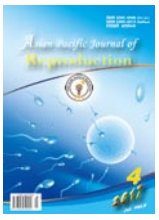

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Effects of dietary vitamin E on male reproductive system

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ABSTRACT

Vitamin E is known as important antioxidant to protect the reproductive system. The free radicals are continuously produced in last few years due to metabolic and nutritional deficiencies. These free radicals are responsible for the production of oxidative stress in animal bodies. This production of extensive amount of oxidative stress caused the detrimental effects on the sperm and various other male parameters. This imbalance between the antioxidants and oxidative stress, leads to the condition of infertility in male. Antioxidants play an important role for eliminating of these free radicals. Vitamin E is one of the best antioxidants for the removal of oxidative stress in male reproductive system. Its use increases the reproductive functions and efficiency of male reproductive system. The deficiency of this vitamin leads to degeneration of germinal epithelium and Leydig cells in seminiferous tubules. The use of selenium and vitamin E has the synergistic effects on the male reproductive system. The objective of this review was to collect the beneficial roles of this vitamin along selenium on reproductive system of birds and different animals. This review will also collect the different doses along the beneficial roles on different parameters of male reproductive system.

1. Introduction

Vitamin E (α -tocopherol) is fat soluble organic compound and commonly present in the cell membranes. This vitamin has the strong antioxidant properties and inhibits the lipid peroxidation created by the free hydroxyl and superoxide radicals. This vitamin protects the cell membrane of sperm cell from damages of ROS. *In vitro* studies have proved that the use of vitamin E improves the motility and fertilizing ability of sperm in the egg penetration of hamster[1]. Similarly, *in vivo* studies, supplementation of vitamin E was found to be effective in reduced number and motility of sperms caused by reactive oxygen species (ROS)[2]. The supplementation of this vitamin through oral route has significant beneficial effects on motility of sperms through the reduction of malondealdehyde (MDA), which is known as the end product of lipid peroxidation[3]. The shortage of vitamin E may damage the reproductive organs like damages in the spermatogenesis, testicular dysfunction and shrinkage of semeneferous tubules. The use of this vitamin enhances the functions of testes in the form of increased in weight of testes and epididymis. Besides the antioxidants properties of this vitamin, antioxidant enzymes like superoxide dismutase (SOD) and glutathione peroxidase are enhanced due to use of this vitamin[4]. The deficiency of this vitamin leads to testicular degeneration in poultry, rats and hamster[5] as well as the lower production of germ cells[6]. The seminiferous tubules making the framework of testes are degenerated due to deficiency of vitamin E[7]. Selenium is known as essential for the testicular function and sperm motility[8]. Lack of selenium causes the testicular malfunctioning like atrophy of semineferous tubules, abnormal spermatogenesis, immature sperms and reduction in volume of testes[9]. Vitamin E possesses the enhanced effects on the sperm motility when given with selenium[10].

There is lot of information about the use of vitamin E in various doses during the cryopreservation of semen. However, there is limited information about the use of vitamin E in diet as well as through oral routes in the bodies of various species. Keeping in view the male infertility due to deficiency of this antioxidant as well their beneficial use in this review was focused.

2. Metabolism and excretion of vitamin E

The absorption of vitamin E is connected to the digestion of fats in body and the absorption of this vitamin is facilitated by the concentration of bile and as well as pancreatic lipase[11]. The media

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part of small intestine is considered as the site for absorption of this vitamin. It may be present in alcohol or esters form, but most of the vitamin E is absorbed in alcohol form. Esters are hydrolyzed in the small intestine, whereas the alcohol goes into the lymph through the general circulation. The Medium-chain triglycerides play an important role in the absorption but polyunsaturated fatty acids inhibit this process. Many studies reported that feces may contain 65%-85% of this vitamin in human, rabbit and hen.

3. Production of ROS and male infertility

More than 25% males fail to produce the functional sperms for successful fertilization[12]. The excess production of ROS is the major cause of infertility by damaging the DNA, genetic components and activities of enzymes[13]. ROS can be useful or harmful depending on the site as well as their level of production[14]. The sperm have the ability to move after the transit stay in epididymus. They require the certain physiological processes like capacitation takes place within the female reproductive tract to fertilize the egg. Under these physiological conditions the adequate amount of ROS is produced[15]. In the ROS, superoxide is considered as the most harmful agent[16]. The male germ cells are vulnerable to ROS due to higher amount of polyunsaturated fatty acids within the cell membrane and cytoplasm[17] (Figure 1).

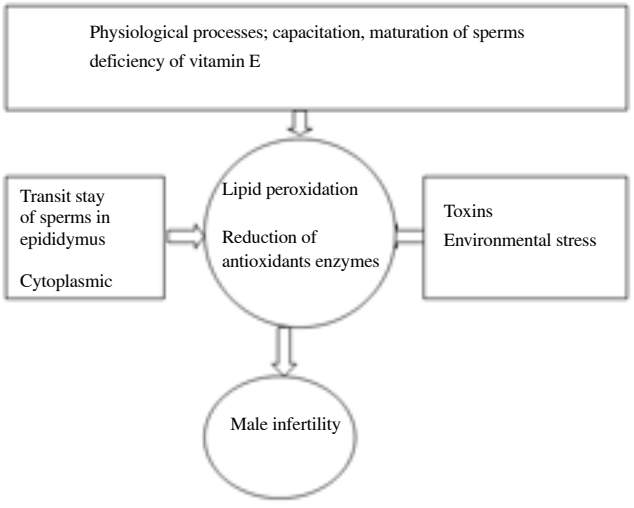

Figure 1. Mechanism of ROS production and infertility.

The production of ROS due to blood leukocytes as well as the damaged sperm could also contribute to infertility[18]. Another major element of ROS is the hydrogen peroxide. The moderate level of hydrogen peroxide had no effect on the viability of sperms but inhibit the movement of sperms by reducing the amount of ATP and phosphorylation of protein in exoneme[19]. These physiological disturbances will lead to lipid peroxidation and death of cells. Almost every ejaculate of semen has the source of ROS in the form of leukocytes and damaged sperms which can cause the oxidative harms to sperms. Therefore, it is considered that damage depends on the concentration of ROS rather than the presence or absence[16]. Poor quality of semen is connected to higher amount of RS due to the presence of more amount of residual cytoplasm. This extra cytoplasm accumulates during the maturation stages of spermatozoa at mid piece[20]. If this cytoplasm occupies more than third of head, it is called as cytoplasmic droplet. The sperms of such a kind are considered as immature with defective functions. They have the capacity of producing the large amount of ROS[21]. Each spermatozoa utilizes the nicotinamide adenine dinucleotide phosphate oxidase and nicotinamide adenine dinucleotide at the level of plasma membrane for the production of ROS[22]. Spermetozoa are equipped with higher amount of mitochondria to produce the energy for the movement of spermatozoa. The production of ROS is increased in uncontrolled amount in the nonfunctional mitochondria which affect the function of mitochondria[23]. This increased amount of ROS will caused the oxidative stress. Oxidative stress can also cause the DNA degradation and breakage of cross liankage of proteins[24]. Spermatozoa having the DNA with damaged integrity cold not fertilize the the oocyte. There was negative correlation was reported between the sperms with damaged DNA and fertilization rate[25]. Apoptosis is the programmed death of cell with the alteration in all the structural and physiological functions. The process of apoptosis is controlled by internal and external factors. Factors affaecting as external stimulators are radiations, high environmental temperature and toxins. Higher concentration of ROS disrupts the inner and outer cell membranes of mitochondria and subsequently apoptosis of sperm cell takes place[26].

4. Mechanism of vitamin E in poultry species

Vitamins had the significant roles in the maintenance as well as regulating functions in male reproductive system. After the first use of this vitamin on male reproductive system of rats, many investigators reported the effects of this antioxidant on the health and reproductive functions of different species. The key evaluation parameters of male reproductive system are volume, sperm motility, sperm concentration and fertilizing ability. These quality parameters can be severely altered by certain stresses and endocrine disrupters, which can contact the body through different sources like diet and body contacts[27]. These adverse effects can be controlled by the use of supporting compounds, including multivitamins, mineral and antioxidants. The spermatozoa in avian species are rich with polyunsaturated fatty acids[28,29]. These compounds play useful roles in the motility and fusion between sperm with egg[30]. The sperms with the higher quantity of polyunsaturated fatty acids are susceptible to reactive oxygen species, subsequently leading to infertility[31]. Therefore, the use of antioxidants for spermatozoa seems to be prerequisite for the regulating the successful fertility in the male reproductive system. Many studies proved that the use of vitamin E has useful effects on the functions of fertility in chickens[32]. The dietary supplementation of this vitamin protects the spermatozoa by maintaining the stability of polyunsaturated fatty acids in the cell membranes. The recommended dose of vitamin E in poultry birds is 10 mg/kg of diet[33]. The findings due to use of this vitamin on the reproductive performance of bird is presented in Table 1.

Table 1

Effects on dietary vitamin E on male reproductive system of avian species.

Species	Dose of vitamin E	Findings	Reference
Male Rhode Island red chickens	α -tocopheryl acetate with dose of 0, 20, 200, or 1 000 mg/kg for 56 d.	The concentration of lipid peroxidation was reduced in group of 200 mg/kg of vitamin. The level of this vitamin E in semen and sperms increased two fold during the last 14 d of experiment.	[28]
Roosters with 30-week-old	Fish/soybean oil containing vitamin E with dose of (30, 200, 400 mg/kg).	This feeding regimen appeared in the form of rise in semen volume, motility of sperm and patency of sperms.	[34]
Male turkeys	α -tocopheryl acetate was fed for 26-39 wk of age in basal feed.	The level of α -tocopheryl was increased two times more in the semen.	[31]
Indian Kadaknath male chicks	*dl*- α -tocopheryl acetate with dose of 10 100, or 200 mg/kg at day first to age of 30 wk.	The evaluation of semen quality during the last three weeks of experiment was found that sperm with abnormal morphology was decreased. However, the fertilizing capacity of sperms was increased significantly.	[32]
Japanese quail	Vitamin in the form of *dl*- α -tocopheryl acetate with dose of 15 IU, 150 IU, or 300 IU/kg feed for 25 wk of age.	During this study, the plasma concentration, weight of testes and volume were not affected but the level of abnormal sperm morphology and dead percentage were decreased.	[35]
White Koluda male geese with age of three year old	Diet containing selenium with dose of 0.3 mg/kg as well as vitamin E with 100 mg/kg feed.	The beneficial effects were manifested in the form of rise of semen volume and sperm concentrations. The concentration of lipid peroxidation in male was also lower.	[8]
Day old male chicks	Vitamin in the form of *dl*- α -tocopheryl acetate with dose of 80 mg/kg feed in maize/soybean for the age of 52 wk.	Findings were present like increased sperm viability, motility and count of sperms.	[9]
ROSS male broiler breeders (60 weeks of age)	Vitamin E selenium with dose of 0.3 mLwas injected.	The hatchability and fertility of eggs improved in treated birds. The activities of hepatic enzymes were not changed. However, the concentration of serum testosterone was increased.	[36]
Geese	Vitamin E with dose of 100 mg/kg	The supplementation of this vitamin improved (P<0.05) the frequency and reduced duration of ejaculation. The semen volume, sperm count, viable sperms and reduced immature sperms significantly higher in treated birds. The concentration of Lipids peroxidation [malondialdehyde in treated and control birds was (0.172 nmol/50×10^6) and (0.320 nmol/50×10^6), respectively].	[37]
Cockerel	Vitamin E, 0, 20 and 200 mg/kg	There was significant increase in quantity of α -tocopherol in semen, testes and liver. This vitamin also increased GSH-Px concentration as well as reduced concentration lipid of peroxidation within spermatozoa.	[38]

5. Effects of vitamin E on male reproductive functions of other animals

Vitamin E is considered as the basic part of antioxidants in sperm[38] and acts as the important protection to reduce the production of reactive oxygen species[30]. The feeding of this vitamin has useful effects on the reproductive performance of boar, rabbit and rams[39]. Similarly the supplementation of this vitamin has the constructive effects on reproductive system of cockerel, rats, dog and fish[40–42]. Spermatozoa require the ROS for normal functions like acrosome functions, capacitation and fusion of spermatozoa during the processes of fertilizations[43]. But the production of excess amount of ROS induces the lipid peroxidation in membrane of sperm[43,44]. Vitamin E is known as lipid soluble and prevents the production of ROS in the sperm membrane during the various motility processes[43]. In addition to scavenging of ROS, this vitamin has the ability to protect the primiary reproductive organs and accessory reproductive organs in male. This vitamin functions as anti-sterility function and its shortage results in the degeneration of germinal epithelium occurs. The continuous and small doses of this vitamin lead to improve the semen characteristics in domestic animals[39,45,46]. Youself also found that this vitamin has ameliorative effects on oxidative stress with dose of 2 IU/kg in pyrethroid induced toxicity (Figure 2).

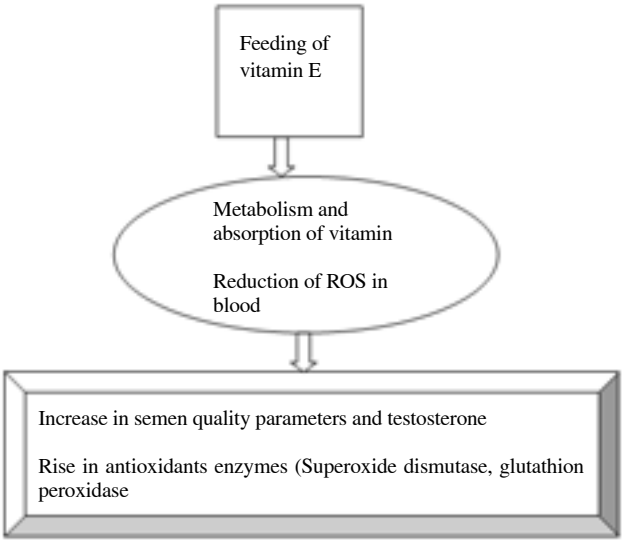

Figure 2. Mechanism of vitamin E as antioxidant in male.

Supplementation of vitamin E with dose of 70 IU/kg caused the significant effects on acrosome reactions and normal morphology in boar[47]. This vitamin also acts on precursor of thrombxanes, prostaglandins and immunoglobulins which promotes the spermatogenesis[48]. SOD is known as the important part of seminal plasma and function to balance the production of free radicals through the process of scavenging activity[49]. This enzyme has the ability to convert the superoxide anion into hydrogen peroxide on both side of cell as well as the conversion of this hydrogen peroxide into water. Reduced quantity of SOD results into poor quality of semen as well as reproductive functions[50]. Glutathion peroxidase (GPx) is considered as the important antioxidant and reduces the amount of lipid peroxidation. This enzyme functions with vitamin E as a reducing agent of hydrogen peroxide[49]. The histological organization of testes is known as the important aspect of spermatogenesis. The supplementation of vitamin E@ 80 IU kid/ day in Boer goats caused the improvement through the number of epithelium, width of semineferous tubules as well as more number of Sertoli and Leydig cells[51]. The sertoli cells also play an important role in the maintenance as well as the transport of androgens in the testes[52]. The feeding of vitamin E to dogs with poor quality of semen had improved the quality of semen as well as antioxidant status[53]. This improvement may be due to increase in testosterone level as in Table 2. The effects of vitamin E with different doses in the various animals species is presented in Table 2.

Table 2
Effects on dietary vitamin E on male reproductive of other animals

Species	Dose and duration	Findings	Reference
Male rabbits	Vitamin E for 12 wk	The treatment has significantly decreased AST (31.8/1.88 IU/L) in seminal plasma of male rabbits.	[38]
Rabbit buck	Vitamin E (ocopheryl acetate) with dose of 200 mg•kg/ of diet	Addition of vitamin E showed significant antioxidant protection with this dose.	[54]
White boars	Vitamin E (*dl*- α tocopheryl acetate) 40 or 70 IU of /kg of diet	The supplementation of *dl*- α tocopheryl acetate 70 IU increased in libido, combats, head-kicks and sniffing as compared to 40 and 0 IU vitamin E. Similarly, volume, sperm motility, acrosomal integrity, viability, sperm count per mL semen volume and total number of sperm per ejaculate were also improved.	[48]
Boer kids	Vitamin @880 IU/animal/day for 5 mo	There was no significant effect on the antioxidant status of testis.	[55]
Black Sea Trout (Salmo labrax)	Viatmin E @ of 250, 500, 1 000 mg/kg	Milt volume and sperm count were significantly improved with supplementation vitamin E with dose of 250 and 500 mg/kg.	
Rabbits.	Vitamin E 2 IU/kg BW	Sperm count, motility and reduced percentage of dead sperm were significantly increased as compared to control.	[45]
Aohan fine-wool sheep	200 IU	The beneficial effects were present in the increased SOD (77.98/6.24 U/mg protein) and GPx (62.03/4.86 unit activity) concentration in mitochonderia of testes. This indicates that the supplementation of this vitamin improved the defense system of testes.	[56]
Male Goat	Vitamin E with dose of 200, 400 and 800 IU animal/day for 2 mo	The animals with dose of 400 IU showed significantly increased (P<0.05) semen volume and motility activity along lower number of dead sperm. Similarly, the activity of superoxide dismutase and GPx along with concentration of Zn, Cu and Mn were increased in this group. The activity of AST reduced in without any change on the concentration of ALT. However, there was no effect on the semen quality with dose of 800 IU. The increased dose from 0 to 400 IU has the improving effects on semen.	[57]
Rabbits	Vitamin E @ dose 150 IU/kg	There was no significant effect on the level of seminal plasma of AST and ALT.	[46]
Rats	100 mg/kg/day of vitamin E	Improvements in morphometrical measurements were present in the form of increased the mean diameter of seminiferous tubules. Likewise, height of seminiferous tubule's wall and reduced the mean diameter of seminiferous tubule's lumen were observed in treated animals.	[58]
Stallion	1 500 mg of α -tocopherol acetate for 60 d	This dietary supplementation improved antioxidants status. The improvements in treatment vs control group increase in average path velocity [(121.9 ± 3.1) μm/sec in TG and (118.9 ± 4.3) μm/sec in CG), straightness (86.2% ± 2.4%) and (82.6% ± 3.9%) in TG and CG, respectively]. Similarly, viability percentage, total amount seminal plasma antioxidants levels were also improved. The other semen parameters like progressive motility and abnormal morphology of sperm were significantly increased in treated in the semen of stallions after 2 mo of experiment.	[59]
Dog	Tablet of vitamin E with dose of 50 mg α -tocopheryl acetate per anim/day for 28 d.	The mean quality of semen parameters were temporarily increased due to vitamin E. The improvement in these parameters were more significantly improved (P<0.05) after 4 and 5 wk of treatment. The mean values of blood plasma testosterone and seminal plasma SOD activity values slightly increased in the 4 animals after this treatment.	[53]
Turbot (*Scophthalmus maximus*)	D - α -tocopherol acetate was given with dose of 65.14 (control), 244.60 (lower) and 721.60 mg/kg (higher) for 3 mo.	The sperm concentration was significantly increased in lower and higher vitamin E groups as compared to control. However, relative sperm volume and testis-somatic index were significantly increased in group with higher vitamin only. The duration of sperm motility was significantly longer in higher group than in the control, but the non significant difference was present in percent motility among groups. The size of sperm and plasma membrane integrity was higher in lower and control group as compared to control.	[42]
Male rats	Vitamin 100 mg/kg orally for 40 d	Improvement of semen quality parameters (sperm count, motility and normal morphology) and testosterone.	[60]

6. Conclusion

This article reviewed the dietary effects of vitamin E on the male reproductive system of birds and many other animal species. This review indicates that feeding of vitamin E has beneficial effects on the male reproductive system. The beneficial effects were evident in the form of increase of testes weight, semen quality parameters, antioxidants status and testosterone in mammals as well as birds. In birds, in addition to these parameters the hatchability was also improved. It came to know that this vitamin is based on the property of reducing the oxidative stress, which results from the higher amount of polyunsaturated as well as during the physiological processes in sperm. Furthermore the deficiency of this vitamin leads to the infertility in male. On the basis of these findings in this review article, following suggestions can be incorporated in the future to improve the efficiency of male reproductive system;

1. This vitamin needs to be used in the extreme cold and summer season to elucidate the stress of season.

2. Spermatogenesis is under the control of various hormones in male, so the level of various hormones like follicle stimulating and leutinizing hormones may be find out.

3. Association of genes with vitamin E in the form of beneficial or deficient conditions needs to be elucidated.

Conflict of interest statement

The author declares that he has no conflict of interest.

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