Food, Nutrition, and Male Fertility

20

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"The food you eat can be either the safest and most powerful form of medicine or the slowest form of poison"
—Ann Wigmore.

Abstract

In a number of lower organisms and seasonal breeders, availability of food is a key determinant in shaping the time for reproduction and fertility. Therefore, food and nutrition strongly affect fertility, even in nonseasonal breeders. Eating a balanced diet is the key to good overall health. Food habits and their inherent components vary greatly across the globe. Making nutritious food a part of the regular diet can ameliorate health and upkeep fertility. Deficiency of nutrients and antioxidants can decrease fertility as various reports have supported the role of antioxidants in fertility. This chapter provides a comprehensive coverage of dietary elements that provide essential nutrients, cofactors, and antioxidants for the maintenance of good reproductive potential and fertility and improve prophylaxis against infertility.

Keywords

Food and fertility • Vitamins and fertility • Antioxidants and spermatogenesis • Soy food • Coenzyme Q10 • Vitamins A, C, and E

Key Points

- Food and nutrients play vital roles in male reproduction and fertility.
- Food contains antioxidants, N-acetylcysteine, vitamin C, vitamin E, CoQ10, selenium, and zinc that significantly improve sperm health by reducing oxidative stress.

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- Soy foods, fatty acids, and obesogens (endocrine-disrupting chemicals) may compromise spermatogenesis and thus decline male fertility.
- Eating healthy and nutritious diet can reduce chances of male infertility.
- Taking nutritious and balanced diet, avoiding obesity, and including required vitamin supplements can be a good prophylactic measure against male infertility.

20.1 Introduction

Food and reproduction are the basic needs, which mark the very basis of survival and perpetuation of all species. Food and reproduction are closely linked aspects and every species tries to ensure both these essentials for survival. In a number of avian species, food availability is the principal factor that has shaped the timing of breeding season (Davies and Deviche 2014). Lack's theory (1950, 1968) postulated that the breeding timing has a genetic basis and seasonal variations in food supply select genotypes of birds laying eggs such that the nestling stage coincides with the peak in food availability. Similarly, in a number of other species such as wild boar (*Sus scrofa*), the availability of high quality of acorns and olives correlated with higher body weight, more breeding females and a larger litter size than in the years of poor production of these foods (Massei et al. 1996). Further, the age at puberty in beef cows is inversely proportional to the availability of nutrition (Schillo et al. 1992). These evidences clearly indicate an important impact of food and nutrition on fertility.

Humans are not seasonal breeders, but studies on the other animals suggest that food can have a significant impact on fecundity in humans. Worldwide, people eat various kinds of food. Some eat plant products like fruits, vegetable, cereals, pulses, etc., while others eat animal products like red meat, egg, fish, etc. In India, people mostly eat plant-based diet, while in the western countries, people are more dependent on animal-based food products. Some of these products affect male fertility positively while others have negative effects. Vitamins, minerals, and fatty acids are essential parts of the diet and are well known to affect male fertility. The levels of these nutrients vary greatly across the foods described above. Interestingly, similar to the variation in food habits across the globe, semen parameters vary greatly across major populations (Vujkovic et al. 2009). A large fraction of these variations may be explained by differences in food habits. In fact, there is research showing that there are certain fertility foods a man can include to his diet to help increase the odds of conceiving a baby, and other food items can actually impair men's fertility.

Nutritional status and lifestyle factors are considered as crucial determinants of normal healthy reproductive function. Nutrition has a significant impact on sperm health. What men eat reflects in their fertility. Research shows that having a poor diet and regular alcohol consumption, for instance, can compromise the quality and quantity of sperm and make conception more difficult. Food and nutrition are known to affect fertility, and nutrients are accredited to affect molecular mechanisms and balance in physiological functions. The use of nutrients to treat infertility is documented, but there is no specific heed to food and nutritional recommendations for infertility in classical medicine reference books. Therefore, there is a need to write an account of food and nutrition in relation to male fertility. This chapter provides a summary of food and nutrients that improve male fertility.

20.2 Dietary Essentials

20.2.1 Carbohydrate

Very less is known about how carbohydrates influence male reproductive health. An observational study explains that consumption of cereal and fruit was positively associated with semen quality (Braga et al. 2012). Additionally, one case-control study conducted on 30 men suffering from poor semen quality and 31 normal healthy controls reported that the control group had comparatively higher intake of raw or cooked vegetables (lettuce and tomato) and fruits (apricots and peaches), whereas intake of potato was higher and that of fruits and vegetables was lower in the case group (Mendiola et al. 2009). In yet another study, Eslamian et al. (2012) stated that men reporting higher consumption of fruit and vegetables showed lower risk of asthenozoospermia. Subgroup analysis on the basis of fruit and vegetable consumption showed that orange intake was negatively related to the risk of asthenozoospermia. Among vegetables, the intake of dark green vegetables and tomatoes was linked with a lower risk of asthenozoospermia (Eslamian et al. 2012).

20.2.2 Protein

A few studies analyzed the association between different dietary sources of protein with male reproductive health. Swan et al. (2007) described that maternal beef intake as well as anabolic steroids in beef result in an alteration in the male fetus development in utero and have adverse effects on his reproductive capacity. Sperm concentration of son was negatively correlated with mother's weekly beef consumption. In sons of high beef consumers (>7 beef meals per week), sperm concentration decreased by 24.3% in comparison with men whose mothers consumed less beef (Swan et al. 2007). Similarly, an observational study conducted on 250 male patients undergoing intracytoplasmic sperm injection (ICSI) therapy reported that meat consumption was significantly higher in infertile cases as compared to healthy individuals (Braga et al. 2012). A case-control study on 72 asthenozoospermic and 169 normozoospermic patients also reported identical findings. The study showed that the odds of asthenozoospermia were 2.03 times higher in the topmost tertile processed meat consumers. Furthermore, the odds of asthenozoospermia were 0.47 lower for those in the highest tertile of poultry product consumers (Eslamian et al. 2012).

Although soy food is regarded as a vegetable source of protein, some studies indicated that it adversely affects sperm parameters due to its high content of isoflavone. Soybean is a member of family Fabaceae. It is a legume and native of East Asia. It has a significant role in the treatment of some cancers, such as colon, prostate, and breast. Soy and soy-derived products contain isoflavones which mimic the actions of estrogens and may exert adverse effects on male fertility. The intake of 15 soy-based food by 99 males of subfertile couples for a period of 3 months showed that high intake of soy foods and soy isoflavones associated with lower sperm concentration (Chavarro et al. 2008; Modaresi et al. 2011) showed that the 20, 30, and 50% soy diet had a negative effect on male reproductive system in mice with a decline in primary spermatocytes and sperm count (Modaresi et al. 2011). The adverse effects of soy food on male fertility are due to the presence of isoflavones. Isoflavones are the type of naturally occurring isoflavonoids, which act as phytoestrogens and adversely affect sperm health and the male reproductive system.

20.2.3 Fat

More than 33% of the daily caloric intake of the human diet in most parts of the world contains fats and oils together (Bialostosky et al. 2002). Evidence from literature suggests that dietary fatty acids (FAs) may have substantial effects on male fertility. Bongalhardo et al. (2009) showed that birds fed fish and corn showed the highest and lowest n-3 polyunsaturated fatty acids (PUFA), respectively, in sperm. Diet comprising few distinct lipid sources differentially alters the lipid content of sperm head and body membrane, with minor effects on sperm characteristics (Bongalhardo et al. 2009). The fat composition of sperm membrane may affect sperm maturation in epididymis as the epididymal maturation is known to bring significant changes in sperm plasma membrane by extracting certain lipids (Rana et al. 1991).

Three types of natural fatty acids include saturated, monounsaturated, and polyunsaturated. Polyunsaturated fatty acids (PUFAs) are needed for various processes including growth, reproduction, vision, and brain development. Since they cannot be synthesized by the human body, they are regarded as essential fatty acids (Mazza et al. 2007). A clinical study conducted for analyzing the level of PUFA and saturated fatty acids in semen suggested that spermatozoa of asthenozoospermic patients have lower levels of PUFA compared with saturated fatty acids and this may contribute to the poor motility of sperm in these men (Tavilani et al. 2006).

20.3 Dietary Pattern

The dietary pattern has a significant impact on semen quality and hence on male reproductive health. A cross-sectional and observational study was conducted on 188 young men, dependent on two different dietary patterns (Prudent and Western) in the years 2009–2010 at the University of Rochester. Prudent diet included high intake of fish, chicken, fruit, vegetables, legumes, and whole grains, while Western diet included high intake of red and processed meat, refined grains, pizza, snacks, high-energy drinks, and sweets. Semen samples were collected and analyzed for sperm count, motility, and sperm morphology and compared between the two dietary patterns. The consumption of a prudent dietary pattern was found to be significantly associated with higher progressive sperm motility and not associated to sperm concentration and morphology. On the other hand, the consumption of Western diet showed neither positive nor negative association with conventional semen parameters. Therefore, it can be concluded that prudent diet or inclusion of at least a few of prudent components in the diet may help upkeep sperm motility (Gaskins et al. 2012).

20.4 Food Spices

Nigella sativa is a medicinal spice, which is also known as black cumin. It has a potent bioactive compound known as thymoquinone that is used to treat epilepsy and allergies and boost the immune system. Seeds and alcoholic extract of *Nigella sativa* are found to improve spermatogenesis and hence male fertility potential (Mohammad et al. 2009). *Nigella sativa* is used as a food spice in some countries.

Seeds are the major source of the active components of this plant and used in the traditional medicine as a natural therapy for a variety of disorders and manifestations such as headache, dizziness, bronchial asthma, nasal congestion, fever, diarrhea, inflammation, cough, influenza, eczema, toothache, hypertension, diabetes, kidney and liver dysfunctions, lung diseases, rheumatism, parasitic infections, hypercholesterolemia, gastrointestinal disorders, and overall general well-being, for more than twenty centuries (Ahmad et al. 2013).

There are many other plant products like *Asparagus racemosus*, *Chlorophytum borivilianum*, *Crocus sativus*, *Curculigo orchioides*, *Mucuna pruriens*, *Tribulus terrestris*, *Trichopus zeylanicus*, *Withania somnifera*, *Zingiber officinale*, etc. that have potential pro-fertility activities. These plants may not be used as food items, but their human use for overcoming male infertility and sexual debilities has been documented. Some of these products and their specific uses have been described in detail in Chapter 21.

20.5 Nutrients and Vitamins

Humans have evolved with a sophisticated and complex antioxidant protection system to protect cells and organs of the body from reactive oxygen species. It involves a number of components, both endogenous and exogenous in origin, that function interactively and synergistically to neutralize the free radicals (Percival 1998). These components include (1) nutrient-derived antioxidants like vitamin C (ascorbic acid), vitamin E (tocopherols and tocotrienols), carotenoids, and other low molecular weight compounds such as lipoic acid, glutathione, etc.; (2) antioxidant enzymes, like superoxide dismutase (SOD), glutathione peroxidase, and glutathione reductase, which catalyze the quenching reactions of free radicals; and (3) metal-binding proteins, for example, ferritin, lactoferrin, ceruloplasmin, and albumin that confiscate free iron and copper ions that are able to catalyze oxidative reactions. There are many other antioxidant phytonutrients present in an extensive variety of plant foods (Ford

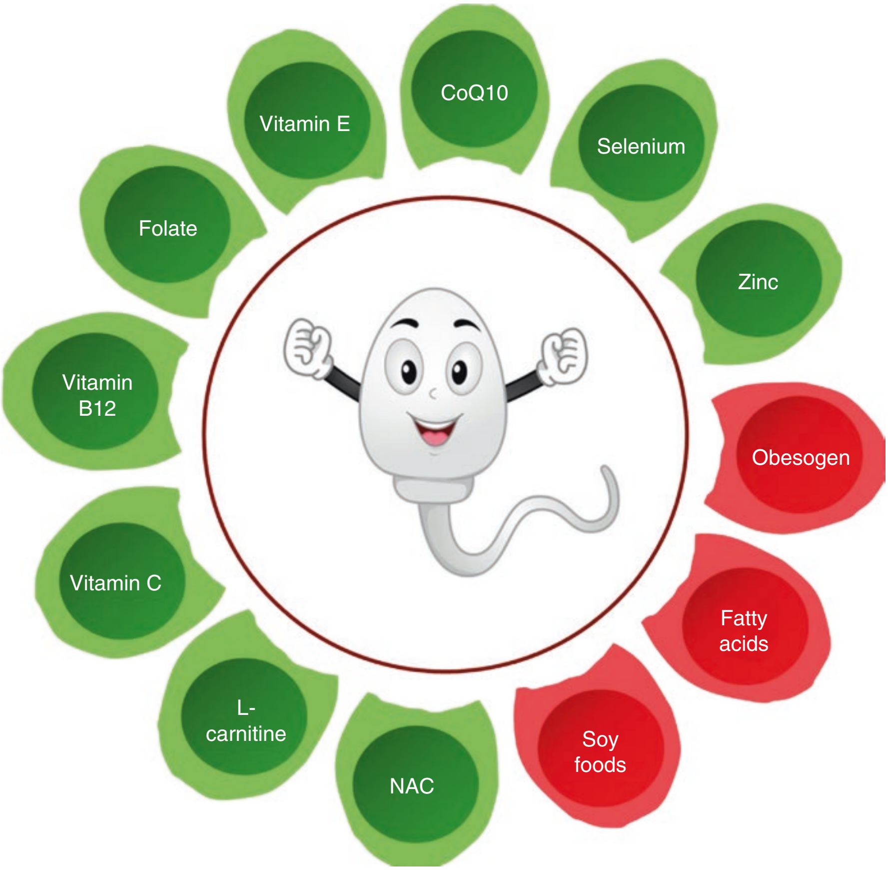

Fig. 20.1 Food/nutrition/vitamins that affect spermatogenesis. The items shown in green have positive effect and those shown in red have negative effect

et al. 1999). The eating habits of various species are set to provide the best reproductive fitness and fecundity. However, due to a number of environmental and stress factors, the regular eating habits may not always remain adequate to maintain the level of various nutrients and extra antioxidants required under these conditions. A detailed description of food and nutrients which improve various parameters of male reproductive health is given below (Fig. 20.1).

20.5.1 Zinc

Zinc is an important trace mineral present in the cells throughout the body. It is required for body's defensive (immune) system to work properly. It plays a crucial role in cell division, cell growth, wound healing, and the breakdown of carbohydrates. It is also required for the sense of smell and taste, during pregnancy and infancy.

Zinc is regarded as one of the most significant trace minerals for male reproductive health; increasing zinc levels in infertile men has been shown to increase sperm count and improve the morphology, form, function, and quality of sperm, thus improving male fertility. Hunt et al. (1992) showed that there is a significant decrease in seminal volume, serum testosterone concentration, and sperm morphology in young men due to zinc depletion in diet (Hunt et al. 1992) According to the World Health Organization (WHO) guidelines (5th edition), the lower reference limit for seminal zinc is ≥2.4 μmol/ejaculate, and level below this range may be a risk for infertility.

Oysters, calf liver, sesame seeds, beef, lamb, pumpkin seeds, yogurt, turkey, peas, venison, and shrimps are the major food sources of zinc. Zinc can be degraded by cooking; therefore, it is important to eat some foods in their raw forms, which are high in zinc.

20.5.2 Selenium

Selenium is an essential trace mineral, which our body requires in small amount. Selenium is necessary for the production of special proteins called antioxidant selenoproteins for protection against oxidative stress caused by the reactive oxygen species (ROS) and reactive nitrogen species (NOS) (Tinggi 2008). It exerts its biological functions through selenoproteins that contain amino acid selenocysteine. There are 25 selenoproteins encoded by the human genome.

Selenium is a requisite element for the production of sperm. A study showed that hyperlipidemia has significant adverse effects on male fertility, which can be ameliorated by diet supplemented with probiotics, inorganic selenium, or selenium-enriched probiotics (Ibrahim et al. 2012). Malondialdehyde (MDA) is a lipid peroxidation marker and the level of MDA is high in semen of infertile men. A vitamin intervention study reported that oral supplementation of vitamin E and selenium caused a significant decrease in MDA concentration in sperm and an improvement in sperm motility (Keskes-Ammar et al. 2003). In another study, a combination therapy with selenium and vitamin E was found to be effective for the treatment of asthenospermia and asthenoteratospermia and the induction of spontaneous pregnancy (Moslemi and Tavanbakhsh 2011). It has also been shown that oral supplementation of selenium and N-acetylcysteine improved all semen parameters, such as sperm count and motility (Safarinejad and Safarinejad 2009). Specific effects of nutrients and vitamins on semen parameters are detailed in Fig. 20.2.

Brazil nuts, mushrooms, cereals, egg, liver, cod, sardines, halibut, tuna, salmon, shrimp, snapper, and turkey are the food products that provide selenium.

20.5.3 CoQ10

Coenzyme Q10 is a naturally occurring quinone, present ubiquitously in the animal body. It is also known as ubiquinone and ubidecarenone. A critical role of CoQ10 is

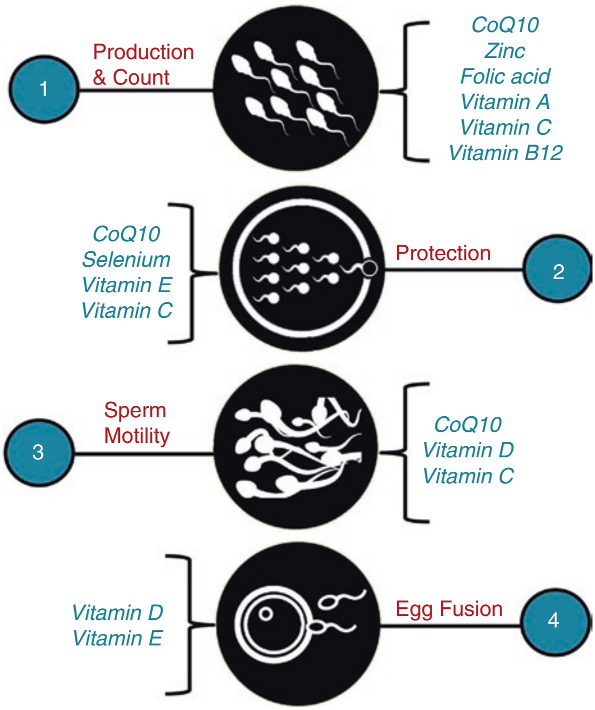

Fig. 20.2 Effect of nutrients/vitamins on specific semen parameters and fertility

as an electron carrier in the mitochondrial respiratory chain complex. It is one of the most important lipophilic antioxidants, protecting the production of free radicals as well as oxidation of proteins, lipids, and DNA. Decreased levels of CoQ10 in humans are observed in many pathological conditions, for example, cardiac disorders, neurodegenerative diseases, AIDS, cancer, infertility, etc. (Bentinger et al. 2007). In these cases, treatment involves pharmaceutical supplementation or increased consumption of CoQ10 with meals as well as treatment with suitable chemical compounds like folic acid or vitamin B group, which significantly increase ubiquinone biosynthesis in the body.

CoQ10 is a vital antioxidant that helps in preventing cellular damage caused by free radicals, thus protecting DNA. CoQ10 is necessary for sperm motility and is, therefore, a crucial nutrient which affects male fertility. In vitro and in vivo studies done by Lewin and Lavon (1997) reported a significant increase in sperm cell motility after treatment with coenzyme Q10 in humans (Lewin and Lavon 1997). Additionally, some other recent studies also have shown that CoQ10 can increase sperm health, particularly sperm motility (Balercia et al. 2004; Balercia et al. 2009; Safarinejad 2009; Mancini and Balercia 2011).

CoQ10 is abundantly present in seafood and organ meats, though it is very difficult to obtain through the diet, especially for vegetarians and vegans. CoQ10 ubiquinol supplementation is the best way to obtain CoQ10.

20.5.4 Vitamin E

Vitamin E is an important antioxidant, which protects body tissues from damage caused by the free radicals. It functions as an essential lipid soluble antioxidant or radical scavenger. It limits the production of free radicals in tissues by reacting with them to form a tocopheryl radical, which will then be reduced by a hydrogen donor (such as vitamin C) and thus return to its reduced state (Traber and Stevens 2011). Vitamin E is also being used as a commercial antioxidant in ultrahigh molecular weight polyethylene used in hip and knee implants to replace defective joints to help resist oxidation (UHMWPE Biomaterials Handbook). Vitamin E also plays a role in neurological functions (Muller 2010) and inhibition of platelet coagulation (Dowd and Zheng 1995). Vitamin E also protects lipids and prevents the oxidation of polyunsaturated fatty acids.

Vitamin E has been shown in various studies to improve sperm health and motility in men. Vitamin E is found to play a significant role in improving the in vitro functions of spermatozoa, which is evaluated by zona-binding test (Kessopoulou et al. 1995). In other studies, vitamin E and selenium supplementation in combination were found to improve sperm parameters like motility (Keskes-Ammar et al. 2003; Moslemi and Tavanbakhsh 2011). It is also known as "tocopherol" that literally means to bear young. It is an important antioxidant that helps to protect DNA damage and maintains the DNA integrity of sperm and egg cells (Kessopoulou et al. 1995).

Vitamin E is abundantly present in spinach, sunflower seeds, olives, papaya, almonds, and dark green leafy vegetables.

20.5.5 Folic Acid/Folate/Vitamin B9

Folate is an important factor required for the production and maintenance of new cells, DNA and RNA synthesis, preventing DNA damage, and thus preventing cancer (Kamen 1997). This is also involved in the biosynthesis of nitrogen bases, nucleic acids, and some amino acids like creatine, methionine, and serine. Folic acid prevents spina bifida and neural tube defects. Its ability to lower the level of homocysteine suggests that it might have a positive influence on cardiovascular diseases. The role of folic acid in maintaining good health may extend beyond these ailments to encompass other birth defects, several kinds of cancer, dementia, Down syndrome, and serious conditions affecting pregnancy outcome (Lucock 2000).

Research suggests that folic acid can potentially improve sperm health. A double-blind, placebo-controlled interventional study showed an increase of about 74% in total normal sperm count in previously subfertile and normal fertile men taking 66 mg/day of zinc with 5000 mcd/day of folic acid (Wong et al. 2002). Folate is required for DNA synthesis pathways and repair. Folate deficiency hinders DNA synthesis, cell division, and reproduction (Forges et al. 2007). Men with low levels of seminal plasma folate have increased risks of low sperm density and count

(Wallock et al. 2001). In an observational study, 70 fertile and 63 subfertile men undergoing in vitro fertilization or intracytoplasmic sperm injection treatment were assessed for semen parameters and tHcy (total homocysteine), folate, cobalamin, and pyridoxine concentrations in seminal plasma and blood. In case of fertile men, seminal plasma folate level was inversely correlated with the DNA fragmentation index (Boxmeer et al. 2009). Fertilization of egg with an abnormal sperm may lead to birth defects such as Down syndrome or an increased chance of miscarriage, making folate pathway crucial for reproductive health.

According to the European Association of Urology, antioxidant treatment (folic acid, vitamin E, zinc, selenium) has a positive effect on semen quality. Lentils, spinach, pinto beans, asparagus, navy beans, black beans, garbanzo beans, kidney beans, and collard greens are the food sources of folic acid.

20.5.6 Vitamin B12

Also known as cobalamin, B12 helps the body convert food (carbohydrate) into fuel (glucose), which is used to produce energy. Vitamin B12 is a critically important vitamin for maintaining healthy nerve cells and helping synthesis and repair of DNA and RNA. Vitamin B12 works closely with folate or folic acid in helping the formation of red blood cells. Folate and vitamin B12 work together to produce S-adenosylmethionine (SAM), a derived amino acid involved in immune function and mood.

It is required for cellular replication and studies suggest that cobalamin deficiency can cause reduced sperm count and motility. In an observational study, 70 fertile and 63 subfertile men undergoing in vitro fertilization or intracytoplasmic sperm injection treatment were assessed for semen parameters and tHcy (total homocysteine), folate, cobalamin, and pyridoxine concentrations in seminal plasma. In the fertile control men, cobalamin was found to positively correlate with sperm count, but inversely correlate with ejaculate volume (Boxmeer et al. 2009). In another study on male albino rats, vitamin B12-deficient diet was given to animals for three different periods, (1) whole period (gestation to mature), (2) gestation period (gestation to weaning), and (3) immature period (3–12 weeks postnatal). This study suggested that dietary vitamin B12 deficiency during pregnancy may induce damage to germ cells of the embryo and affect maturation of spermatozoa (Watanabe et al. 2003).

Food sources rich in vitamin B12 include clams, oysters, muscles, liver, lamb, caviar (fish eggs), lobster, fish, crab beef, cheese, and eggs.

20.5.7 Vitamin C/Ascorbic Acid

Vitamin C is necessary for the development and maintenance of connective tissues and plays a crucial role in wound healing, bone formation, and the maintenance of healthy gums. It also plays an important role in a variety of metabolic functions such as activation of vitamin B and folic acid and conversion of cholesterol to bile acid and tryptophan (amino acid) to serotonin (the neurotransmitter). It is an antioxidant that protects the body from free radical-induced damage.

Infertile men possess considerably more sperm DNA damage than the normal fertile men, and vitamin C is found to improve sperm quality and protect sperm from DNA damage. It also helps in reducing the chance of miscarriage and chromosomal problems. A study conducted on males working in a battery manufacturing industry at Hyderabad (India) showed a significant increase in total sperm count and sperm motility and a significant decrease in abnormal sperm morphology after vitamin C prophylaxis (Vani et al. 2012). Greco et al. (2005) showed that sperm DNA damage can be efficiently treated with oral administration of antioxidants (Greco et al. 2005). Vitamin C also appears to keep sperm from clumping together, making them more motile. In a study that analyzed various semen parameters in oligospermic infertile men, before and after oral supplementation of vitamin C, it was concluded that vitamin C supplementation in infertile men might improve sperm count, motility, and morphology (Akmal et al. 2006).

It is also known as ascorbic acid and is abundantly present in plants and fruits, including red peppers, potatoes, broccoli, cranberries, tomatoes, cabbage, and citrus fruits.

20.5.8 L-Carnitine

This compound is synthesized in the liver, kidney, and brain and is composed of two amino acids, lysine and methionine. It performs a crucial role in the energy supply for tissues during fetal life and in the neonatal stage by regulating the influx of fatty acids into mitochondria. L-Carnitine regulates the level of acylo-CoA and CoA in the mitochondria and provides acetyl moieties for the biosynthesis of acetylcholine (Rospond and Chłopicka 2012). L-Carnitine also plays a vital role in the metabolism of lipids and by transporting long-chain fatty acids into mitochondria for beta-oxidation. L-Carnitine further functions as an antioxidant, favoring fatty acid replacement within previously oxidatively damaged membrane phospholipids. Availability of L-carnitine is compulsory in the developing fetus for various processes underlying fetal maturation.

Carnitine is a vital nutrient for sperm cells to function normally. Sperm requires high concentrations of carnitine for energy metabolism. A study showed a direct correlation between the level of free carnitine in seminal fluid and sperm count and motility (Johansen and Bohmer 1979). In a clinical study, it was found that L-carnitine is a potential factor, which significantly improves sperm motility and increases the rate of pregnancy. It is also a safe therapeutic for the treatment of asthenozoospermia (Wang et al. 2010). Carnitine, acetyl carnitine, L-arginine, and ginseng combined therapy significantly improved progressive sperm motility in men with asthenospermia (Morgante et al. 2010). Balercia et al. (2005) showed that supplementing with L-carnitine helps in improving sperm health and increasing sperm count and motility in the patients with low count and motility. L-Carnitine and L-acetyl carnitine in combination are found to be effective in increasing sperm kinetic properties in idiopathic asthenozoospermia patients and improves the total oxyradical scavenging capacity of seminal fluid (Balercia et al. 2005).

Red meat and dairy products are the major food sources of L-carnitine, but other foods include nuts, seeds, asparagus, brussels sprouts, collard greens, garlic, mustard greens, okra, kale, broccoli, apricots, bananas, bee pollen, artichokes, brewer's yeast, parsley, buckwheat, corn, oatmeal, rice bran, rye, and whole wheat.

20.5.9 *N*-Acetylcysteine (NAC)

N-Acetylcysteine or acetylcysteine (NAC) is a mucolytic agent used to loosen the thick mucus in the disorders such as cystic fibrosis or chronic obstructive pulmonary disease. It is also used for the treatment of numerous disorders, such as doxorubicin cardiotoxicity, ischemia-reperfusion cardiac injury, acute respiratory distress syndrome, bronchitis, chemotherapy-induced toxicity, HIV/AIDS, heavy metal toxicity, and psychiatric disorders. It acts as a crucial antioxidant as it reacts with OH, NO_2,• and CO_3− (Samuni et al. 2013).

NAC is a modified amino acid, which has potent antioxidant properties. It significantly reduces the destructive reactive oxygen species in human semen and improves impaired sperm function (Oeda et al. 1997). Ciftci et al. (2009) concluded from a research that in the NAC-treated group, the total antioxidant capacity of serum was greater and total peroxide and oxidative stress indices were lower as compared to the control group (Ciftci et al. 2009). Few more studies suggested that NAC is an important antioxidant, which can ameliorate sperm health by combating the reactive oxygen species (Safarinejad 2009; Reddy et al. 2011).

Granola, oat flakes, and vegetables like broccoli, red pepper, and onion are major sources of cysteine. Other plant sources include bananas, garlic, linseed, and wheat germ.

Other than derived amino acids, L-carnitine and *N*-acetylcysteine (NAC), a recent study also found some basic amino acids to have a positive effect on male infertility by improving production and quality of sperm. Supplementation with amino acids (lysine/methionine/threonine/tryptophan/valine) in a particular ratio (100:27:73:19:69) in boar diet improved sperm quality and subsequently increased the fertilization capacity and the number of live piglets (Dong et al. 2016).

20.6 Obesogens

Obesogens are the foreign chemicals, which disrupt normal development and balance of lipid metabolism. This may lead to obesity in some cases. There are various potential obesogens found everywhere, and people come in contact with them every day, intentionally or unintentionally, for example, bisphenol-A (BPA), high fructose corn syrup (HFCS), nicotine, arsenic, pesticides, organotins (tributyltin and triphenyltin), and perflurooctanoic acid (PFOA). All endocrine-disrupting chemicals

(EDC) are defined as obesogen and are well known to be associated with early puberty, reproductive dysfunctions, and infertility later in life of humans and animals (Diamanti-Kandarakis et al. 2009; Skakkebaek et al. 2001).

EDCs have transgenerational effects; they affect not only the exposed individual but also the subsequent generations. Ephemeral exposure of a gestating female rat during the gonadal sex determination to the EDCs such as vinclozolin (an antiandrogenic) or methoxychlor (an estrogenic compound) produced an adult phenotype in the F1 generation with decreased spermatogenesis (cell number and viability) and increased incidence of male infertility (Anway et al. 2005). This effect may be transmitted not due to the mutations in the DNA sequence, but through modifications in the factors such as DNA methylation and histone acetylation, which regulate gene expressions. Causes of obesity and its association with male infertility are described in detail in Chapter 11.

20.7 Nutrigenomics

Nutritional genomics or nutrigenomics is the study of how individual genetic differences can affect the way we respond to nutrients and other natural compounds we eat or how nutrients exert health effects by affecting gene expression (The NCMHD Center of Excellence for Nutritional Genomics, University of California, Davis). Nutrigenomics is an approach to understand the relationship between diet and health with integration to individual differences in the genetic makeup. Some of the changes thus introduced may be inherited from generation to generation, resulting in transgenerational effects. Munshi and Duvvuri (2008) explained how nutrients influence gene expression, i.e., mRNA synthesis (transcriptomics), protein synthesis (proteomics), and production of metabolites (metabolomics), by giving the example of genetic polymorphism (SNPs) which may be responsible for variations in individual's response to bioactive food components (Munshi and Duvvuri 2008).

The effect of dietary components on gene expression has not been well explored except a few commonly studied pathways. One such pathway relates folate and homocysteine cycle with the genes participating in one carbon metabolism pathway. MTHFR is the most commonly studied gene from this pathway. A number of studies have suggested a significant impact of MTHFR 677C > T polymorphism with various disorders, including male infertility. At the same time, folate is known to be important for spermatogenesis. Interventional studies have shown that folate supplementation improved sperm concentration in infertile men. A simple explanation for this observation may be adequate functioning of the folate pathway upon supplementation. Interestingly, Aarabi et al. (2015) in a recent study showed that apart from improvement in the blood folate levels, significant changes in the methylation level of differentially methylated regions of several imprinted loci (H19, DLK1/GTL2, MEST, SNRPN, PLAGL1, KCNQ1OT1) in sperm DNA were seen upon supplementation. Interestingly, a recent study has shown significant differences in the MTHFR promoter methylation between infertile individuals and controls (Aarabi et al. 2015). Karaca et al. (2016) showed that the percentage of MTHFR promoter methylation in infertile normozoospermic men was significantly higher in comparison to healthy controls (Karaca et al. 2016).

In another interesting double-blind, placebo-controlled interventional study, Ebisch et al. (2003) analyzed 677 C > T polymorphisms in 13 fertile versus 77 subfertile individuals and studied MTHFR-dependent response to sperm concentration upon folic acid/zinc sulfate supplementation. Daily capsules of folic acid (5 mg) and/or zinc sulfate (66 mg) versus placebo were recommended for 26 weeks. The authors found that the genotype frequencies between the two groups were comparable. Interestingly, sperm concentration increased significantly in wild types, but heterozygous and homozygotes did not show significant improvements. The study concluded that MTHFR genotype had a significant impact on the response to folic acid/zinc supplementation in subfertile individuals (Ebisch et al. 2003). Similar studies in other disorders have supported the role of gene polymorphisms in affecting the response to diet or nutrient supplementation. For example, a study on dietary folate intake showed an inverse association with promoter methylation in colorectal adenomas that was dependent on the MTHFR genotype (van den Donk et al. 2007). Similarly, the influence of a number of dietary or nutritional factors via their effects on promoter methylation and gene expression is likely in addition to their simple availability to act as enzyme cofactors.

20.8 Discussion and Future Directions

Apart from congenital disorders and genetic causes, the major reason for infertility is the hormonal imbalance and/or oxidative stress. Disturbance in the homeostasis of hormone levels and the antioxidant defense may result in increased production of reactive oxygen species, leading to slowing down or arrest of spermatogenesis. Hormonal imbalance may result in compromised spermatogenesis, which can be further decelerated by oxidative stress. Apart from affecting sperm production, oxidative stress can cause DNA damage. DNA of both parents is the future blueprint for the child. Impaired DNA is known to cause miscarriages, birth defects, and developmental problems in the offsprings. Studies have also shown a strong correlation between oxidative stress caused by free radicals and male infertility. If the physiology is otherwise perfect or close to that, food can have a significant impact on sperm production and fertility. Therefore, a general precaution and adequate attention to nutrition can have a sound effect on fertility.

The food products discussed in this book chapter have nutritional value and may not be adequate in regular diet. “Fertilica Choice Antioxidants” contains most of the important antioxidant nutrients in a capsule formulation. This blend is useful for both men and women, but especially for men with low sperm count and poor sperm health. The transgenerational effects of food and nutrition in relation to male fertility cannot be denied. Obesogens (such as endocrine-disrupting chemicals) have transgenerational effects on male fertility and decline the reproductive status of the future male progeny (Schug et al. 2011). Short-term exposure of a gestating female rat during the gonadal sex determination, to the EDCs like vinclozolin or methoxychlor, induces an adult phenotype in the F1 generation of decreased spermatogenic capacity and increased incidence of male infertility. These effects are transferred through the male germ line to the males of F1 to F4 generations. The transgenerational effects may not be transmitted due to mutation in the DNA sequence, but through modifications in the factors like DNA methylation and histone acetylation, which regulate gene expressions.

The capability of an environmental factor (such as endocrine-disrupting chemicals) to reprogram the germ line and promote a transgenerational condition has a remarkable association between evolutionary biology and disease etiology (Anway et al. 2005). It must be noted that fertility, reproductive potential, environment, and evolution are strongly correlated. There is a proof for the role of sperm-derived RNAs in arbitrating paternal transgenerational effects, with several categories of RNA recently discovered in sperm that are amenable to changes in diet, behavior, and stress (Sharma and Rando 2014). The research on the transgenerational impact of environmental factors, endocrine disruptors, and food is still in the infantile phase; further research in this area would bring forth the effects of food and nutrition unseen so far.

Conclusion

People with idiopathic male infertility can treat their disorder by supplementation of zinc, selenium, CoQ10, folic acid, vitamin B12, vitamin E, vitamin C, L-carnitine, and antioxidant-rich diet. Normal fertile individuals can prolong their fertility period by supplementation of a nutritious diet in their regular food habits and by avoiding food items like soy food, fatty acids, and obesogens that are potentially detrimental to spermatogenesis and fertility. We should prefer food therapy over drug therapy to increase the quality and quantity of semen as a measure to avoid or treat male infertility. Nutrigenomics research may open the way to personalized nutrition. Food may be seen as a requirement for regular course of life, but interestingly, food and nutrition play roles well beyond that as they have been shown to affect the DNA that we pass on to our subsequent generations. The impact of environmental toxicants, endocrine disruptors, stress, and other factors that affect fertility can be minimized or reversed by paying a little attention to daily nutritional requirements. Therefore, one must keep an eye on self-nutrition to upkeep fertility and pass the same to the coming generations.

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