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Diet and Nutritional Factors in Male (in)Fertility – Underestimated Factors

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Abstract

Abnormalities in male fertility constitute about 50% of all infertility causes. According to some data, the quality of human semen has deteriorated by 50-60 % over the last 40 years.

A high-fat diet and obesity, the development of which is encouraged by the western lifestyle, affects the structure of spermatozoa, but also the development of the offspring and their health in later stages of life. In obese individuals, disorders on the hypothalamic-pituitary-gonadal axis are observed, as well as elevated oestrogen levels with simultaneous decrease of testosterone, LH and FSH hormone levels.

Healthy dietary models clearly correlate with better sperm quality and a smaller risk of abnormalities in parameters, such as sperm count, sperm concentration and motility, as well as lower sperm DNA fragmentation. Apart from mineral components such as zinc and selenium, the role of omega-3 fatty acids and antioxidant vitamins should be emphasized, since their action will be based primarily on the minimization of oxidative stress and inflammation process. Additionally, the incorporation of carnitine supplements and coenzyme Q10 in therapeutic intervention seems also promising.

Therefore, it is advisable to have a varied and balanced diet based on vegetables and fruit, fish and seafood, nuts, seeds, whole-grain products, poultry and low-fat dairy products.

Keywords: semen quality, male infertility, nutritional model, diet

1. Introduction

Infertility, i.e. the inability to get pregnant, despite a regular, minimum yearly sexual intercourse without using any contraceptive, affects an increasing proportion of society [1-5].

It is estimated that as much as 15%, i.e. about 70 million couples in the world's reproductive age, experience problems with getting pregnant, with approximately half of the cases related to male infertility [2,4,6]. It is reported that an estimated 35% of infertility cases involve only women, 20% both women and men, 30% involve problems only on the part of the man, and 15% of infertility cases remain unexplained [1].

Among the causes of male infertility, the most common are oligospermia, i.e. low sperm concentration in semen, asthenozoospermia – an absolute lack of motility, or decreased motility of spermatozoa, and teratozoospermia, which is defined as an insufficient number of spermatozoa of normal structure [7]. Leaver states that these disorders constitute over 90% of male infertility causes [1]. According to an

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extensive meta-analysis covering 185 studies, including over 40 000 men from the developed countries, the number of spermatozoa, i.e. the main factor determining the quality of semen, decreased by 50-60% over the period 1973-2011 [8]. According to research carried out in Poland on a group of 169 young, healthy men with unknown fertility status from the Lower Silesia region, the average and median of 7 parameters determining sperm quality were within the limits of the WHO standards in 2010. However, sperm viability was close to the lower range of the norm, whereas the average percentage of abnormal sperm structure was as high as 85%. Nearly 9% of the studied cases had one, two or three parameters outside the limits of the standard [9].

Environmental factors which significantly affect male fertility include smoking cigarettes and cannabis, anabolic steroid use, excessive alcohol consumption, emotional stress, excessive exposure to high temperatures, age, tight clothing, environmental pollution, sedentary lifestyle, exposure to pesticides and toxins, radiofrequency electromagnetic radiation, as well as cytotoxic drugs, cadmium and lead [1,6,10,11].

Furthermore, recent research data point to the fact that also diet is directly related to the quality of semen, and that the overall lifestyle plays a crucial role in maintaining proper reproductive functions [6,7,12,13].

An inappropriate diet may be directly related to the increase of oxidative stress, but also contribute to the development of obesity, intestinal dysbiosis, type 2 diabetes mellitus and insulin resistance, which are associated with the deterioration of fertility, both in terms of generating oxidative stress as well as hormonal or immunological disorders.

Thus, nutritional intervention seems to be an extremely important element in the treatment of male infertility related to abnormal sperm parameters.

2. Poor nutritional model of male fertility

In recent decades, the main nutritional model of the developing and developed countries has become the so-called western diet [15,16]. As it is presented in Figure 1, western diet is characterized by a high intake of animal proteins, saturated and trans fatty acids and simple carbohydrates as well as a low supply of dietary fibre and essential unsaturated fatty acids (EFA). Additionally, it is a hypercaloric diet with low nutritional density and pro-inflammatory character [16].

It is clear that with the spread of the Western diet model, the parameters evaluating semen quality have deteriorated [22,17]. A diet rich in processed and, according to some sources, red meat, fatty dairy, coffee, alcohol, sweet drinks and sweets, potatoes, and simultaneously deficient in whole-grain products, vegetables and fruits, poultry, fish and seafood, nuts, and lean dairy is associated with poorer semen parameters and reduced fertility [6,7,20,22]. Characteristics of a diet negatively affecting fertility and its proposed modifications is presented in Figure 1.

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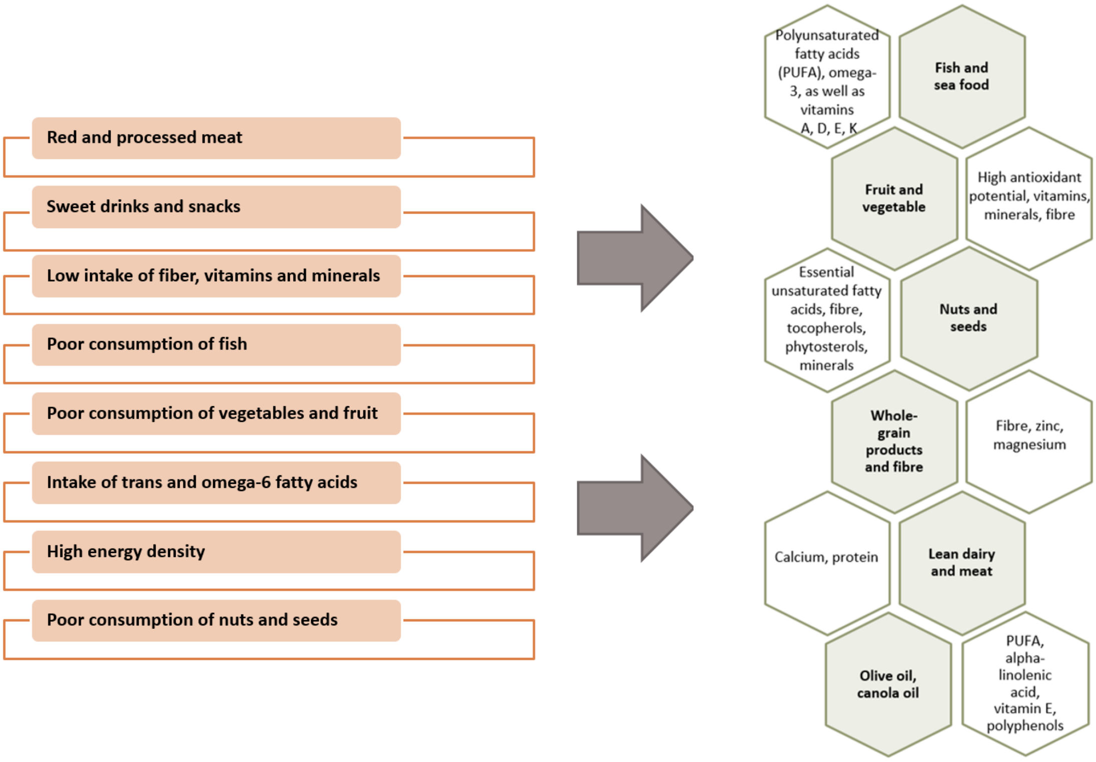

Figure 1. Characteristics of a diet negatively affecting fertility and its proposed modifications [6,7,20].

A high-fat diet and obesity, which the western lifestyle promotes, affect the structure of spermatozoa, but also the development of offspring and their health in later life. In infertile men, improper dietary patterns were observed, such as meal omissions, insufficient intake of antioxidants and high-energy density [7].

It has been observed that trans fatty acids, polyunsaturated fatty acids (PUFA) and, according to some sources, also saturated fats, which are abundant in the Western diet, affect spermatogenesis [6]. In fact, both PUFA, as well as trans-fatty acids, accumulate in the testicles; however, unlike PUFA, the content of trans-fatty acids in the semen and their consumption is associated with poorer sperm quality, as well as with lower sperm concentration in the ejaculate [23,24]. What is more, animal studies suggest that a diet rich in trans fats may be associated with reduced testosterone production and testicular mass, as well as the initiation of pathological changes in the testicles [21,25-27].

A cross-sectional study conducted on a group of 209 healthy men indicates that the intake of trans and omega-6 fatty acids as well as the reduction of omega-3 intake are associated with a deterioration of testicular endocrine function, i.e. lower concentration levels of free testosterone and total testosterone, and with lower testicular volume. [26]. In contrast, according to the cross-sectional study carried out on 701 healthy men, the consumption of saturated fats results in lower sperm concentration in semen and lower semen count [28].

The main sources of harmful fatty acids in the diet are fast-food products, salty and sweet snacks, ready-made confectionery and processed and red meat [29].

According to the available research studies, the consumption of meat, especially processed meat, has a detrimental effect on fertility, which may stem from, such factors as high content of saturated fat and

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trans-fatty acids, the presence of preservatives and hormone residues [30,31]. It has been shown that red processed meat contains more residues of active substances that may affect the endocrine system than unprocessed meat [32]. The trans fatty acids present in meat may also affect the quality of sperm [33]. In the study by Afeiche et al., the consumption of red processed meat inversely correlated with the total number of spermatozoa in the ejaculate as well as with the percentage of progressive sperm motility [34].

Furthermore, it is vital to mention the use of stimulants. Researchers present a consistent view of the adverse effects of smoking on male fertility, both in terms of cigarettes and cannabis [35,36]. Occasional drinking of alcohol does not seem to have a negative effect on the quality of semen; however, daily alcohol consumption results in the deterioration of both semen volume and sperm morphology [37].

It has also been suggested that caffeine intake may impair male reproductive function, probably by means of triggering abnormalities in spermatozoa DNA. Nevertheless, most research studies do not demonstrate a link between moderate coffee consumption and male fertility. In the meta-analysis, covering 57 cross-sectional studies which included 29914 participants, no significant effect of coffee on sperm quality was found [35]. Interestingly, a review of 28 observational studies, which involved 19 967 men, suggested that caffeine from coffee, tea and cocoa beverages did not have a negative impact on the quality of semen, as opposed to sweet drinks containing caffeine, the consumption of which in many studies was associated with a decreased semen volume and count, as well as with lower sperm concentration [38].

There is still no consistent approach to compounds, such as bisphenol A or phthalates, i.e. ingredients in plastic food packaging. Currently, due to the small number of studies and their large limitations, there is not enough evidence to state that exposure to these substances at low or moderate levels has a negative effect on male fertility. Nevertheless, it seems reasonable to consider their adverse effects on reproductive health as possible [6,39,40].

However, the impact of pesticides and pollutants seems worth considering. Danielowicz et al. did not manage to prove that a pro-healthy diet model based on frequent consumption of fruit, vegetables, legumes, soups, properly composed meals, whole-grain products, juices and nuts was associated with better sperm quality. The authors presumed that vegetables and fruits, which were rich in diet, were also a source of pesticides and pollution. In fact, pesticides and insecticides were shown to have a greater impact on the deterioration of semen quality than the beneficial effects of microelements, vitamins and antioxidants contained in vegetables and fruits [17]. This in turn suggests that it is vital to pay particular attention for a daily diet to be based on products from reliable sources.

In recent decades there has been a drastic change in society's lifestyle - with a reduction in energy expenditure, particularly in daily physical activity, the consumption of hypercaloric foods with high glycaemic index and high fat content has increased, with a simultaneous low intake of dietary fibre [41]. This, in turn, has resulted in a significant increase in the proportion of obese individuals worldwide - which has since emerged as a global obesity pandemic [22,41-43]. More than half of Europeans are overweight or obese, and men are much more likely to be overweight than women [44].

It is generally accepted that excessive body weight has a negative impact on the body, contributing to the development of diseases, such as diabetes, hypertension, cardiovascular diseases, cancer, sleep apnoea or osteoarthritis. In fact, the impact of obesity on reproductive functions is also relevant [22,42,43].

Weight loss in obese men seems to be the first, and the most basic step in the treatment of male infertility.

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3. Mechanisms associating improper diet and obesity with infertility

Oxidative stress constitutes the key mechanism which associates improper diet and obesity with both lower semen quality and an increased risk of infertility. Moreover, it is currently considered one of the leading causes of male infertility [12], together with the decrease in antioxidant activity and a dysfunctional activity of mitochondria in spermatozoa. Figure 2 presents the influence of oxidative stress on sperm quality and fertility.

Oxidative stress is reported to represent 30 - 80% of male infertility cases. [14,18]. Additionally, reactive oxygen species (ROS) may impair the motility of spermatozoa and interfere with their ability to connect to the oocyte [18].

As indicated in Figure 2, cell membrane lipids, proteins and sperm DNA are damaged [13] once ROS overcomes the sperm antioxidant barrier. As a consequence, the higher the intensity of oxidative stress, the lower the motility, live sperm count and sperm concentration in the semen, as well as the risk of miscarriage and child development abnormalities [2,18,19]. Moreover, excessive production of ROS is also associated with the deterioration of sperm morphology parameters [46].

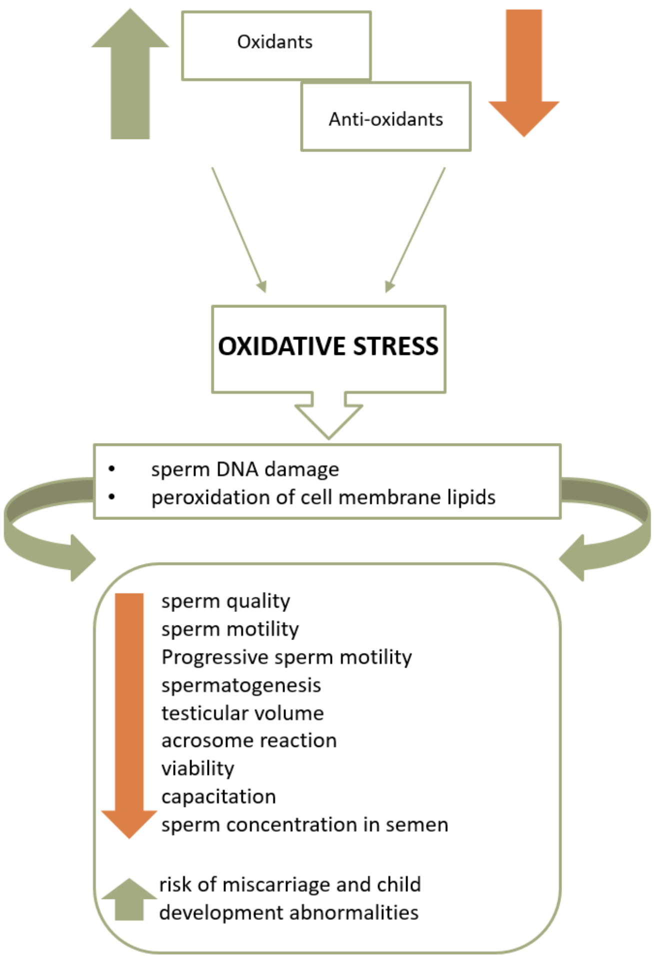

Figure 2. The influence of oxidative stress on sperm quality and fertility [11,47].

Both the consumption of pro-inflammatory products and a low consumption of high antioxidant potential foods, as well as a high glycaemic index and load in the diet constitute factors responsible for the oxidative stress increase. Moreover, glucose metabolism proves to have significant impact on spermatogenesis, whereas hyperglycaemia affects sperm motility and the fertilization process [6].

In addition, in obese individuals, disorders on the hypothalamic-pituitary-gonads (HPG) axis have been observed. Excess fat tissue results in an increased aromatase activity converting testosterone to oestrogen, and consequently to increased oestrogen levels with decreased levels of testosterone, of LH hormone, which stimulates steroidogenesis, as well as of FSH, responsible for spermatogenesis. [22,42,43,45].

Additionally, white adipose tissue (WAT), produces pro-inflammatory cytokines and ROS, the excess of which leads to systemic inflammation and oxidative stress [42].

Elevated serum leptin levels lead to HPG axis disorders, resulting in reduced testosterone secretion from Leydig cells. In fact, Leptin is one of the adipokines produced by the WAT, which stimulates the secretion of gonadotropic hormones [22,42] and regulates satiety.

Apart from leptin, the hypothalamic-pituitary-gonads (HPG) axis and spermatogenesis are also affected by other pro-inflammatory cytokines produced in excess by the WAT, such as tumour necrosis factor (TNFa, tumor necrosis factor-a), interleukin-6, chemerin, resistin or ghrelin [42].

Excessive body weight is also associated with erectile dysfunction, increased temperature in the scrotum, which may have an adverse effect on spermatogenesis. Moreover, it also affects the obstructive sleep apnoea syndrome, potentially leading to dysfunction of the HPG axis and disturbed night-time testosterone secretion due to chronic hypoxia and sleep fragmentation [42,45].

4. Intestinal microbiota disorders and male fertility

The composition of intestinal microbiota is heavily dependent on the diet and may change significantly as a result of dietary modifications. An improper diet, characterized by high intake of fat and monosaccharides, may lead to intestinal dysbiosis, i.e. quantitative and qualitative disturbance of intestinal microbiota composition, resulting in increased permeability of the intestinal barrier [48]. This, in turn, induces chronic inflammation in the body, and is potentially at the root of disorders, such as visceral disease, type 1 diabetes mellitus, inflammatory bowel disease, colorectal cancer and obesity [49,50].

The researchers primarily emphasize that the high-fat diet may increase the amount of Mollicutes and Clostridum, belonging to the Firmicutes type, as well as of Bilophila and Enterobacteriaceae of Proteobacteria, and at the same time may contribute to the reduction of Bifidobacteria, Lactobacillus, Akkermansia muciniphila and Bacteroidetes [51,52].

Bifidobacteria have the ability to modulate the intestinal barrier, reduce the concentration of lipopolysaccharide and alleviate endotoxemia; in turn, Lactobacilus bacteria exhibit anti-inflammatory properties and facilitate transport of short chain fatty acids (SCFA) [50].

It has been suggested that the adverse changes in the composition of microbiota may also result from the lack of soluble fibre fractions in the diet. On the other hand, polyphenols may contribute to the restoration of intestinal barrier integrity [53,54].

Ding et al. investigated the relationship between high-fat diet-induced dysbiosis (45% fat) in mice and spermatogenesis and sperm motility. In mice on a high-fat diet a decrease in Bacteroidetes and Verrucomicrobia was observed, with an increase in Firmicutes and Proteobacteria. After faecal transplantation from mice fed on a high-fat diet to mice on a normal diet, a significant reduction in the number of sperm in the semen and a deterioration in sperm motility were noted, which indicates a

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possible effect of intestinal dysbiosis on fertility. Moreover, the number of Bacteroides and Prevotella increased significantly. It has been suggested that the spermatogenesis deterioration may be caused by elevated blood endotoxin levels, epididitis and disturbances in gene expression in the testes [55].

It was the first research study regarding the influence of intestinal dysbiosis on sperm quality and spermatogenesis; therefore, it is essential to improve the existing knowledge on the relationship between intestinal microbiota and fertility.

5. A dietary model supporting male fertility

Male semen is a mixture of secretions of different glands. It includes acid phosphatase, citric acid, inositol, copper, calcium, zinc and magnesium, fructose, seminogelin, vitamins C and E, prostaglandins, carnitine, glycerophosphato-choline and neutral alpha-glucosidase. Additionally, sperm also consists of protein, carotenoids, electrolytes - sodium and potassium, or glucose, selenium, urea, lactic acid and cholesterol. Depending on the diet, the pH of the sperm ranges from 7.2 to 8.2. Approximately 70% of the semen volume comprises secretions of seminal vesicles. [18,56,57]

Many of these key components, essential for proper spermatogenesis, maturation of spermatozoa and their functioning, have their source in food. Thus, their insufficient supply in the diet may be important with regard to spermatogenesis, sperm quality and male fertility [6,18,58]. According to the available research data, comparing the semen composition of men, in infertile subjects a reduced content of zinc, magnesium, calcium, copper and selenium was observed as compared to men with normal fertility [59,60].

Research studies indicate that healthy dietary models clearly correlate with better sperm quality and lower possibility of abnormalities in such parameters as sperm quantity, concentration and motility, as well as with reduced sperm DNA fragmentation [6,77,78].

The recommended dietary standard is a diet rich in raw vegetables and fruit, whole-grain and fibre-rich products, instead of products based on purified flour, which is indicated in Table 1. Olive oil, oily sea fish from a reliable source, nuts, seeds and stones, avocados are good sources of unsaturated fats, which can make up to 35 % of the calorific value in the diet. Therefore, a good source of protein will be lean poultry and low-fat dairy products, legumes, fish and seafood [6,7,13,14].

What is more, the role of selected minerals, antioxidant vitamins and omega-3 fatty acids should be emphasized, the action of which will be based primarily on the minimization of oxidative stress. Furthermore, it seems promising to include carnitine and coenzyme Q10 supplements in the therapeutic intervention [61].

Dietary component / items	Active substances	Comments / Remarks
Oily sea fish	PUFA, omega-3 Fat-soluble vitamins - A, D, E, K	Fish are often contaminated with mercury and other neurotoxic substances.
Vegetables and fruit	Antioxidants, folic acid, fibre, minerals	It is worth choosing raw vegetables and fruits. Research suggests that pesticide residues may modify the beneficial effect of fruit and

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		vegetable consumption on the quality of semen [17].
Nuts, seeds	EFAs, fibre, tocopherols, phytosterols, polyphenols, minerals	It is important to choose nuts and unroasted and unsalted seeds.
Whole-grain products	Fibre, zinc, magnesium	It is recommended to limit the consumption of refined flour products.
Lean dairy	Calcium, a wholesome protein	It is beneficial to choose low-fat dairy products.
Olive oil, rapeseed oil	PUFA, alpha-linolenic acid, vitamin E, polyphenols	It is advisable to substitute saturated fats with vegetable oils containing unsaturated acid residues.

Table 1. Characteristics of a diet beneficial for fertility [6,7,20].

Zinc constitutes the basic element in the context of male fertility. Both seminal plasma and the prostate gland are characterized by its high content [62,63]. Appropriate level of zinc in semen is essential for the production of spermatozoa, preservation of their correct morphology, sperm count and function, and thus for the proper course of fertilization. Moreover, testicular development and the proper course of steroidogenesis depend on zinc – the deficiency of this element is observed in patients with hypogonadism and underdeveloped secondary sexual traits, as well as in patients with oligospermia, astenozoospermia and azoospermia [59,62,64,65].

Appropriate zinc concentrations in the semen are associated with higher concentration of spermatozoa in the ejaculate, higher motility, viability and increased antioxidant activity due to excessive amount of superoxide anions by inhibiting NADPH oxidase [71]. Zinc in the testes is crucial for spermatogenesis and the physiology of spermatozoa by maintaining the integrity of the genome in spermatozoa and correct structure. Moreover, according to researchers, zinc is effective in protecting sperm from bacterial and chromosome damage [62,64,65].

Another significant microelement is selenium, which is a component of glutathione peroxidase and thus increases the enzymatic antioxidant activity [13]. In several studies lower selenium levels in semen of infertile men were found in comparison to the healthy population. However, both the deficiency and the excess of selenium may result in fertility disorders and abnormal semen parameters [59,67-70]. Moreover, selenium has a protective effect against oxidative stress on sperm DNA, and simultaneously increases motility and sperm viability [71]. In the course of normal spermatogenesis, apart from glutathione peroxidase, selenoprotein P is the key element. In fact, the greatest amount of selenium occurs in the testes in this form.

In addition to selenium, vitamin C and tocopherol also present antioxidant properties by means of free radical neutralization. Therefore, it is important for the diet to be rich in vegetables and fruits, which are the main sources of these elements [66]. Furthermore, apart from its antioxidant properties, tocopherol is likely to have a protective effect against heavy metal damage [7,74]. Vegetables and fruits, especially raw green-leaved vegetables are a source of folic acid, which is important in the course of spermatogenesis, particularly in the supplementation combined with zinc [75]. According to researchers, also coenzyme Q10 may be relevant in terms of semen quality, since in its reduced form, as ubiquinol and ubisemichinone radical, it has an antioxidant effect, and is involved in all energy-dependent processes, including sperm motility. Remarkably, ubiquinone is capable of regenerating other

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antioxidants, such as vitamin C and vitamin E [76]. On the basis of the meta-analysis, patients receiving coenzyme Q10 showed a higher level of this substance in semen, as well as an increased concentration and better sperm motility compared to placebo [66]. However, it is possible that coenzyme Q10 delivered with the diet is not sufficient and does not result in improvement of semen quality parameters – thus, supplementation is recommended [78].

What is more, the supplementation of L-carnitine may also be of importance [79,80,81]. It has been shown to have a positive impact on sperm maturation and motility and spermatogenesis in terms of providing energy supply to sperm by transporting long-chain fatty acids to mitochondria [13,61].

A supplementation combining many antioxidants seems particularly beneficial. All the papers focused on this issue so far have demonstrated beneficial results of multiple antioxidants on sperm parameters [12]. For instance, Gvozdjáková et al. have shown that even a 3-month supplementation with carnitine, ubiquinol and vitamins E and C has a positive effect on sperm density and motility. Additionally, the percentage of abnormal spermatozoa has also decreased [76]. It is worth emphasizing that the consumption of products with high antioxidant potential may also minimize the adverse effects of trans fats on sperm quality [33].

The most frequently used antioxidants, both in monotherapy and combined supplementation, include vitamin E and C, carnitine, coenzyme Q10, zinc, selenium, folic acid and N-acetylcysteine [66].

Omega-3 fatty acids, which are precursors to eicosanoids, are also known to have anti-inflammatory and antioxidant properties. Compared to other body tissues and cells, testes and spermatozoa have a higher concentration of polyunsaturated fatty acids, and effective fertilization depends on the lipid composition of the sperm membrane [7,82]. It has been demonstrated that they positively affect the concentration, number and morphology of sperm and have the ability to modify the composition of the cell membrane by building into it, thus, supporting its functioning [6,9,21,83]. It is also indicated that EPA and/or DHA supplementation with fatty acids significantly increases sperm motility and DHA concentration in semen [84].

A meta-analysis of 16 randomized controlled trials showed a positive relationship between omega-3 supplementation and semen quality parameters in infertile men. Moreover, pro-healthy dietary models containing fish and seafood were also associated with better sperm quality in observational studies [85].

In addition, the consumption of 75g of walnuts per day over a 12 week period was associated with a longer lifespan, motility and sperm morphology. Interestingly, according to another study, the addition of 60g of nut mixture to the Western diet, apart from improving the abovementioned parameters, also resulted in an increase in sperm count [88,89].

It is also recommended to provide an adequate supply of magnesium and calcium. The former constitutes a key element in the course of spermatogenesis and sperm motility, also in the female reproductive tract. Furthermore, calcium affects the motility, hyperactivation and capitulation of sperm and ultimately the acrosome reaction leading to sperm penetration into the oocyte [59]. In addition, copper is also necessary for the proper functioning of sperm, and manganese affects the motility of sperm and the fertilization process [90-93]. Nevertheless, both manganese and copper in excessive amounts have an adverse effect on sperm [94,95]. Knowledge about the impact of selected trace elements and vitamins on male semen is summarized in Figure 3.

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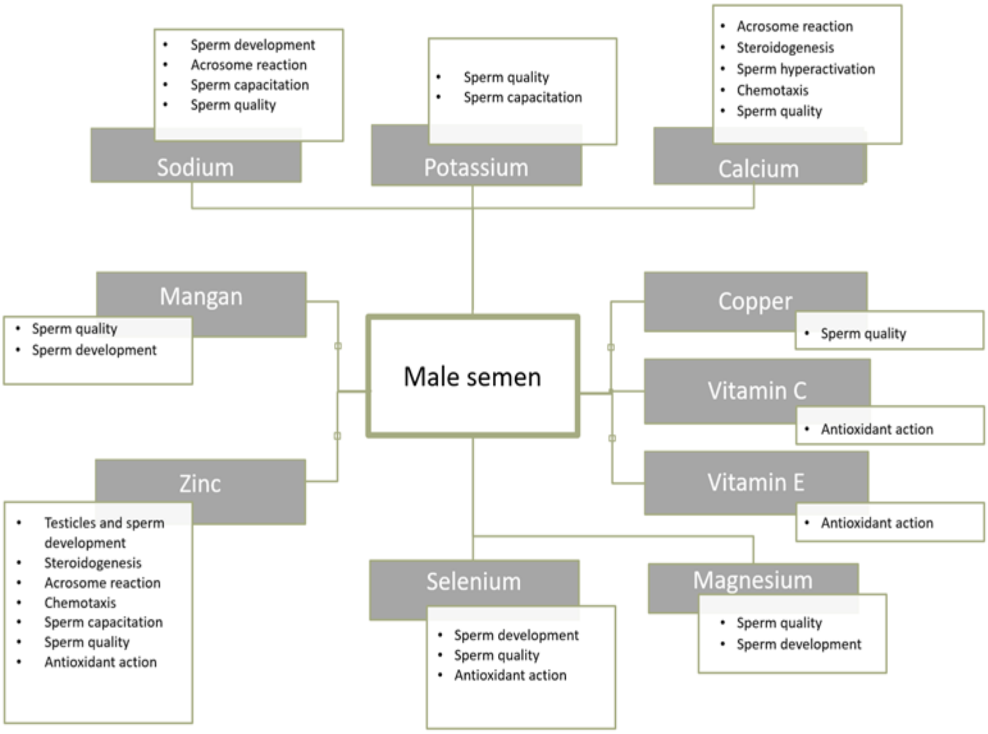

Figure 3. Selected components of male semen and their role [59].

On the basis of the research studies, the role of fibre should also be emphasized. It is an essential element of the diet with regard to fertility due to its potential binding of non-conjugated oestrogens, which is directly associated with lower levels of oestrogen in plasma. In fact, its appropriate levels are necessary to maintain proper reproductive functions [6].

6. Summary

Nutrition can have both negatively and positively affect the quality of semen. The diet should include vegetables and fruit, fish and seafood, nuts, seeds, whole-grain and fibre-rich products, poultry and low-fat dairy products. On the other hand, low consumption of fruit and vegetables, products with an antioxidant potential, a high calorific intake and a diet rich in saturated fatty acids and trans fats, low fish consumption as well as a high proportion of both red and processed meat have a negative impact on the quality of semen which may contribute to reduced male fertility.

Therefore, a modification of lifestyle, especially diet, seems to be the indispensable with regard to male infertility associated with semen quality.

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