



Commentary Article

Nutraceutical management of male infertility-towards new generation therapeutics

Olabode Ekerin^{1*}, Calistus Okechukwu Kenechukwu²**Abstract**

Infertility is one of the most significant public health-related concerns globally. Both male and female factors can cause it. Male factors include poor sperm quality, idiopathic oligospermia, asthenozoospermia, and isolated asthenozoospermia. Many substances, collectively known as nutraceuticals, have been studied for their capacity to enhance hormonal state and sperm parameters through different mechanisms. Nutraceuticals are components in dietary supplements prescribed to prevent or treat a wide range of diseases. This article aims to highlight certain nutrients that can help improve male fertility based on recent advancements in the management of male infertility.

Keywords: Nutraceutical, Infertility, Male, Asthenozoospermia, Dietary Supplements, Nigeria

Background

Infertility is defined as the inability to conceive after 12 months or more of regular unprotected intercourse. It is a significant public health challenge affecting 60–80 million couples worldwide [1]. Studies have also reported that male factor infertility accounts for more than 40% of infertility cases worldwide [2]. Male factors, such as poor sperm quality, are responsible for 25% of infertility cases [3]. Other causes include Idiopathic oligospermia (low sperm counts) [4,5], asthenozoospermia (absence of sperm motility) which is indicated in 19 percent of infertile cases[6], and isolated asthenozoospermia, which can be caused by sperm dysfunction, varicocele, infection, or genetic factors [7].

Nutraceuticals

In 1989, the word Nutraceutical was coined by Dr. Stephen DeFelice from “nutritional” and pharmaceutical. He defined it as food or part of food that aid the prevention and/or treatment of diseases and/or disorder[8]. This concept has gotten a lot of attention in recent years, especially in developed countries, as new therapeutic options that can improve patient health are being developed due to the current knowledge of unbalanced diets[9]. Different studies have also revealed that poor and homogenous diets caused by environmental variables such as air pollution, stress, toxins, and other hazardous compounds in

food may be the reason for the decrease in male sperm quality in the last 50 years [10-12]. This article aims to highlight certain nutrients that can help improve male fertility based on recent advancements in the management of male infertility.

Myo-inositol

Myo-inositol (MYO), a member of the vitamin B complex family, is the most common form in nature produced by the human body [13]. MYO is made from glucose-6-phosphate and excreted through the kidneys and is involved in different systemic activities and signaling pathways in the plasma membrane as a precursor of second messengers [14]. Sertoli cells that respond to follicle-stimulating hormone (FSH) are the major producers in the male reproductive system[9]. The Myo-inositol content of the seminiferous tubule fluid is higher than that of the seminal plasma. A High concentration of Myo-inositol is found in the epididymis, and its depletion has been related to decreased fertility [15]. Several human investigations [16-18] carried out have found a link between altered mitochondrial function (oxidative damage) and decreased motility and fertilization capacity of spermatozoa. Myo-inositol increases mitochondrial membrane potential and restores mitochondrial cristae morphology. It also has a role in various activities, including capacitation, acrosome response, and sperm motility control [19].

L-arginine

It is a basic natural amino acid with a high concentration in the nuclei of haploid cells and a 50% concentration in the nuclei of spermatozoa. Exogenous L-arginine has been demonstrated in

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several studies[20] to have various positive pharmacological effects. It promotes the synthesis of nitric oxide, ensuring a sufficient oxygen supply to muscles that induce penile erections when stimulated at the level of the cavernous bodies of the penis or the anococcygeal muscles. Clinical findings reveal that oral administration of L-arginine to infertile men improves the total proportion of healthy spermatozoa and motility, resulting in successful pregnancies [21].

L-carnitine

In the epididymis and seminal fluid, L-carnitine is found in high concentrations. It is involved in the Beta-oxidation of long-chain free fatty acids in mitochondria [22]. Low L carnitine levels in the mitochondria limit fatty acid synthesis, lowering energy generation and sperm motility [23,24]. L-carnitine supplementation improves seminal parameters, improving sperm quality and motility [25]. According to Italian research, a 6-month therapy with a mixture of L-carnitine and L-acetylcarnitine increased sperm motility, notably in males with asthenozoospermia [26]. A similar study [27] done one year later confirmed the same findings. It also revealed an improvement in the total oxyradical scavenging capacity of seminal fluid in males with idiopathic asthenozoospermia.

Vitamin E

It is an antioxidant that is found inside the cell membrane and thereby prevents free radical-induced damage. Vitamin E functions as a biological lipid peroxidation inhibitor. Malondialdehyde levels in spermatozoa are considerably reduced, and sperm motility is improved when vitamin E is taken orally[28]. Another study [29] indicated that vitamin E and selenium act together to improve sperm motility and sperm count.

Selenium

It is a trace element mainly found in cereals, fish, meat, poultry, and eggs. It is a component of selenoproteins, which are structural components of mature spermatozoa and are involved in testosterone metabolism. Sperm capsular selenoprotein, in the form of glutathione peroxidase, protects spermatozoa against peroxidation [30]. Selenium and/or glutathione deficiencies can result in mid-piece instability of the spermatozoa, leading to poor motility. In males with asthenoteratospermia or asthenospermia, a combination of selenium and vitamin E has been found to enhance sperm quality [31]. Selenium supplementation has been seen to enhance total sperm count, concentration, percentage of normal morphology, and motility in subfertile men [32].

Folic acid

Folic acid, also known as vitamin B9, is a small molecule. It aids cell growth and is required for the production of DNA, transfers RNA and proteins. Male infertility has been linked to a change in folic acid metabolism. A mouse model discovered that a paternal folate deficiency changes the mouse sperm epigenome, which has a detrimental influence on pregnancy outcomes [33]. Folic acid is important for treating low reproductive function and improving sperm quality. Folic acid and zinc were found to increase the concentration of

spermatozoa and improve the morphology of the same in placebo-controlled research [34].

Zinc

Zinc is an important mineral with several biological roles. It plays an essential role in the organization of DNA, RNA, and proteins and the stability of cell membranes and cell division [35]. Zinc is a key component in the functioning of the male reproductive system. Zinc deficiency has been linked to male sterility and infertility, as it is required for spermatogenesis and testicular development [36]. Stress, cigarette smoke, pollution, and alcohol can reduce zinc levels, and zinc deficiency has also been related to low sperm counts and testosterone levels [37]. According to a recent meta-analysis [38], Infertile males had considerably lower seminal plasma zinc concentrations than normal controls. Following zinc treatment in infertile men, sperm volume, motility, and morphology all improved significantly.

Conclusion

This article supports previous findings that the impact of food in male factor infertility needs more investigation. It also implies that eating a healthy diet is a safe approach to increase at least one metric of sperm quality. Future studies should focus on improving our understanding of the impact of food and dietary chemicals on testicular metabolism and sperm production. Further research on the effect of food and/or dietary chemicals in sperm production and testicular cell metabolism might benefit from animal experiments. Furthermore, further clinical research is needed to determine the best dosage and treatment duration.

Abbreviation

MYO - Myo-inositol

Declaration

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Availability of data and materials

Data will be available by emailing bodeekerin@gmail.com

Authors' contributions

Olabode Ekerin (OE) is the principal investigator of this manuscript (Viewpoint). OE is the responsible author for the study concept, design, writing, reviewing, editing, and approving the manuscript in its final form. Calistus Okechukwu Kenchukwu (COK) is involved in writing, reviewing, and editing this manuscript.

Ethics approval and consent to participate

We conducted the research following the Declaration of Helsinki. However, "Commentary Article" need no ethics committee approval.

Consent for publication

Not applicable

Competing interest

The authors declare that they have no competing interest.

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