Monosodium Glutamate-Induced Male Reproductive Dysfunction

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Contributor: Abolanle Kayode, OMOWUMI KAYODE, Damilare Rotimi, Tomilola Olaolu

Reproductive dysfunction is often characterized by malfunction of the reproductive tissues, which may lead to disruption of the synergistic rhythm that should bring about a progression of sexual events and the conception of new life. This may therefore result in the sexual dysfunction and infertility that can be seen in couples having prolonged biological difficulty in reproducing their offspring after having unrestricted sexual intercourse for at least twelve months. Several factors have been implicated in the cause and progression of reproductive dysfunction, including poor nutrition, drug side effects, disease states, and toxicant ingestion. A well-known food additive that has been found to be potent at initiating reproductive anomalies in males is monosodium glutamate (MSG).

Keywords: antioxidant enzymes ; monosodium glutamate ; reactive oxygen species

1. Introduction

The adult male reproductive system consists of two testes, each joined to its own epididymis and connected to the penis via the vas deferens, and functioning majorly in the production and transportation of sperm for the fertilization of an ovum, leading to the development of an offspring [1]. Germ cells develop in the testes and travel through the epididymis (caput to cauda) where they mature and gain motility [2]. During copulation, sperm is released as semen into the female reproductive tract, where the final stages of maturation takes place (capacitation) and leave the sperm ready for fertilization should an ovum be present [3].

Male reproductive dysfunction describes a condition where one or more of the components of the male reproductive system is malfunctioning or performs below its expected capability. This may have a debilitating effect on the individual and may result in other secondary conditions [4]. Some of the implicated factors for male reproductive dysfunction include hormonal disorders, reactive oxygen species, testicular inflammation, endocrinal disturbance, genital infection, heat, smoking and alcohol, illness, injury, chronic health problems, heavy metals, genetic defects, exposure to radiation, lifestyle, and diet [5].

The German chemist Karl Heinrich Ritthausen discovered monosodium glutamate. MSG is a subset of glutamate which is an important but “non-essential” amino acid found in several foods, including beef, milk, tuna, and vegetables, and plays an important role in human metabolism [6]. MSG is formulated from water, glutamate, and sodium, and it is a major food flavor enhancer, which serves to exaggerate the inherent flavor of foods. The induction of myriad undesirable conditions such as weakness, numbness, muscle pain, headaches, dizziness, and flushing have been associated with MSG consumption [7].

Glutamate can be metabolized into free amino acids absorbed into the gut for further breakdown [7]. The metabolized products include α-ketoglutarate via transamination (alanine transferase and aspartate transferase) and deamination using glutamate dehydrogenase, glutamine substrate through glutamine synthetase, and precursors for glutathione and N-acetylglutamine generation. The product, α-ketoglutarate, enters the tricarboxylic acid (TCA) cycle in the mitochondrial matrix for the production of energy and release of CO_2. Therefore, increased glutamate in the diet could increase energy generation by increasing the level of transamination and deamination, conversion of amino acids into glucose (gluconeogenesis), and conversion to other products like glutathione, GABA, N-acetylglutamate, and γ-carboxyglutamine [8].

2. Mechanism of MSG-Induced Testicular Alteration

The action of MSG on the male reproductive morphology and function may be as a result of its diverse influence on cells, thereby initiating spermatogenic alterations, oxidative damage, histological alteration, and gonadotropin imbalance which

may eventually culminate into reproductive abnormalities in the males as shown in **Figure 1**.

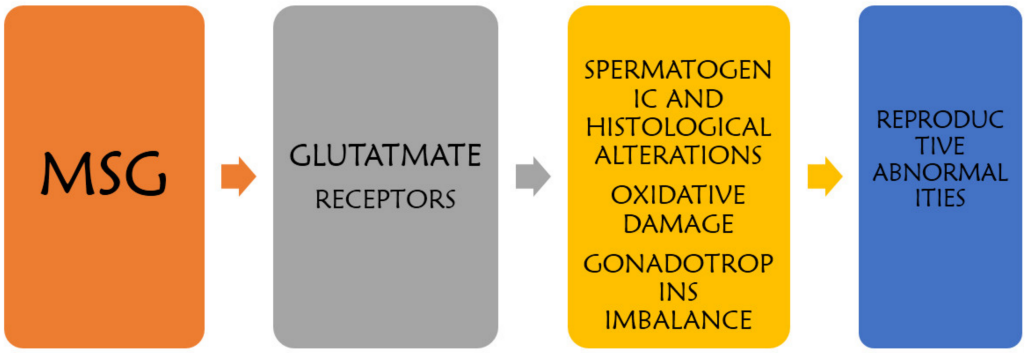

Figure 1. Mechanism of MSG-induced testicular alterations.

There seems to be a scarcity of empirical data on the evaluation of MSG intake on human male reproductive functions; mostly, available animal model studies are extrapolated to humans.

2.1. Oxidative Stress

The organs of the reproductive system are targets of reactive oxygen species (ROS) because of adipose tissue present in these organs [9]. Studies have revealed an increase in the lipid peroxidation (malondialdehyde, MDA) and decreased antioxidant activity (reduced glutathione, GSH) as well as noticeable increase in testicular oxidative stress and a corresponding reduction in antioxidant/antioxidant enzyme activities after MSG administration [7][9][10]. Increased production of free radicals caused by MSG could lead to lipid peroxidation and sperm membrane dysfunction, sperm DNA damage, and impaired sperm movement. The abundance of unsaturated fat (plasma membrane) and low levels of antioxidants (cytoplasm) make the testes and sperm cells susceptible to oxidative stress [11]. Patients with asthenozoospermia were found to have a high ROS generation in seminal plasma as well as sperm membrane damage mediated by MSG [7][10]. The direct implication of this ROS-induced damage on membrane integrity are impaired sperm motility and viability [11]. Therefore, therapeutic agents such as antioxidants may be useful in reversing MSG-induced reproductive toxicity.

2.2. Neurotoxicity

The neurotoxic effect of MSG causes excitotoxicity in the brain through disruption of the hypothalamic–pituitary-axis pathway (HPA) [9]. Glutamate is an excitatory neurotransmitter, and a high influx of neuron intracellular calcium caused by high glutamate may lead to neuronal death. HPA disruption may reduce levels of sex hormones, including testosterone, follicle-stimulating hormone, and luteinizing hormone. This ultimately leads to alterations in sperm quality [12]. Spermatogenesis is totally dependent on the sex hormones and androgen-dependent organs of the reproductive system, which include the prostate gland, epididymis and seminal vesicles. Any androgen hormone (i.e., testosterone, luteinizing hormone, and follicle-stimulating hormone) disorder will therefore have a negative impact on the reproductive tissues [7].

2.3. Histomorphological Alterations

Alterations of the testicular histopathology such as spermatogenic arrest, low sperm production, and edema have previously been reported [7][9][13][14]. Meanwhile, another study observed no overt histopathological changes in the MSG-treated animals [15]. Low spermatogonia levels have been linked with maturation arrest in MSG-exposed animals, and this correlates with a low level of testosterone leading to inhibition of spermatogenesis [7][13][14][15][16][17][18]. Other studies, however, observed improved testicular histopathology after the administration of selenium, vitamin E, and curcumin, respectively [7][19]. Treatments such as graviola extract, vitamin C, vitamin E, camel milk, propolis, quince extract, and curcumin have proven to provide protective effects against MSG-induced histomorphological testicular toxicities [10][11][12][19][20][21].

2.4. Glutamate Receptor Dysfunction

Another mechanism of MSG-induced male reproductive toxicity is via glutamate receptors, as MSG directly affects the glutamate transporter on the epithelium of seminiferous tubules. Glutamate receptors are found in different organs and tissues, including the endocrine glands, hypothalamus, thymus, ovaries, liver, kidney, and testis. The testis has been found to exhibit morphological alterations subsequent to MSG treatment due to mal-expression of glutamate receptor in the testis [7][12][13].

2.5. Brief Clinically Observed Adverse Effect of MSG

Clinical trials conducted in the past have revealed the interplay between MSG and hunger and food intake. In one study, 32 volunteers were screened for the effect of MSG on food intake. It was observed that those who consumed soup containing MSG had increased hunger and food intake when compared to those who took soup without MSG [8][22]. In another study involving 100 French men given an MSG-added diet, an obvious increase in food intake was noticed [8][23]. There have been clinical reports on the direct relationship between MSG intake and obesity in humans [8][24][25][26]. Clinical trials have also shown that the consumption of MSG could result in certain allergic reactions in humans [8].

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