

Protective Effect of vitamin C against Aspartame Toxicity to the Testes: A review article

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Abstract

Background: Aspartame is one of the most widely used artificial sweeteners. Aspartame has been shown to induce oxidative stress and lipid peroxidation; most serious effects result from chronic exposure due to these effects. Also it shows organ and species toxicity with relation to the liver, kidney, brain, testis and other organs. **The aim of this study** is to spotlight on aspartame hazards on infertility & possible protective effects of vitamin C against these hazards.

Introduction

As a sweetener aspartame can be found in 6000 products including carbonated soft drinks, chewing gum, candies, desserts, yogurt, table top sweetener and many pharmaceutical products such as sugar-free cough drops and vitamins (**Butchko and Stargel, 2001**). So far, aspartame is the most controversial artificial sweetener due to its potential toxicity problem. In several studies it is found to be toxic and cause different health problems including liver and testicular dysfunction (**Butchko and Stargel, 2001; and Roberts, 2007**) Infertility is one of the major health problems in life, and approximately 30% of this problem is due to male factors (**Hozayen et al, 2014**). In mammals, the testes have a dual function: spermatogenesis and steroidogenesis. However, some conditions can interfere with spermatogenesis and reduce sperm quality and production. Various factors such as medication, chemotherapy, toxins, polluted air, lack of nutrients and vitamins can adversely affect spermatogenesis and sperm production (**Mosher and Pratt,**

1991). Similarly, in a natural or normal spermatogenesis, apoptosis can be taken place. Normal spermatogenesis is set appropriately and the balance between cell proliferation and apoptosis is continuously present (**Allan et al., 1992**).

Vitamin C is a powerful antioxidant. The term antioxidant has been defined as, "any substance that, when present at low concentrations compared to those of an oxidisable substrate, significantly delays or prevents oxidation of that substrate" (**Halliwell, Gutteridge, 1995**). Vit C is also classified as a chain breaking antioxidant; specifically an aqueous phase chain breaking antioxidant (**Young and Woodside, 2001**).

The plasma testosterone level is considered to be a useful indicator of testicular function (**Kaplan, 1986; and Nair & Dajamoban, 2014**). Testosterone is the main secretory product of testis and acts as both an endocrine and local factor within the testis (**Weinberge et al., 2010**).

Objectives:

Based on valid research, this review

aimed to provide concrete information on the effects associated with consumption of aspartame in human health regarding testicular dysfunction, and possible protective effects of vitamin C against this major hazard.

Aspartame toxicity to the Testis:

Aspartame damages the hypothalamus, which produces gonadotropin releasing hormone (GRH) which goes down the pituitary stalk stimulating the pituitary gland to produce gonadotropins, which in turn stimulates the testicles to produce testosterone (USEPA, 1996 and Puica et al., 2009). Also, by another route aspartame is completely metabolized in the gut and absorbed as aspartic acid, phenylalanine, methanol, and diketopiperazine. Above 86 ° F, the methanol in aspartame decays forming formaldehyde and formic acid. When ingested, methanol attacks the eyes, CNS, and the GI tract and can damage the liver, kidneys and testes (Pohannish, 2002).

The testis has shown to be highly vulnerable to increased aspartic acid and methanol, as it crosses blood testes barrier and reduce spermatogenesis. The reduction in the testicular weight of aspartame treated rats may be due to reduced tubule size, spermatogenic arrest and inhibition of steroid biosynthesis in Leydig cells (Nandi et al., 1999). Excessive reactive oxygen species (ROS) production that exceeds critical levels can overcome antioxidant defense system in the spermatozoa and seminal plasma causes oxidative stress (Gil-Guzman et al., 2001). The controlled generation of highly ROS serves as a second messenger system in numerous different cell types. However, its unrestrained production is considered as an important factor in the tissue damage (Young et al., 1999).

Testicular Protection by vitamin C:

Vitamin C is an important physiological antioxidant, recorded at

high concentrations in the seminal fluid (Dawson et al., 1987). It is available at significant levels in fruit and vegetables; particularly citrus fruits, tomatoes/tomato juice and potatoes. Vitamin C supplements have been shown to improve the quality of sperm in heavy smoker men (Dawson et al., 1992).

Vitamin C (ascorbic acid) also contributes to the support of spermatogenesis at least in part through its capacity to reduce α -tocopherol and maintains this antioxidant in an active state. Vitamin C itself is maintained in a reduced state by a GSH-dependent dehydroascorbate reductase, which is abundant in the testes (Paolicchi et al., 1996). Deficiencies of vitamins C or E leads to a state of oxidative stress in the testes that disrupts both spermatogenesis and the production of testosterone (Johnson, 1979). Conversely, ascorbate administration to normal animals stimulates both sperm production and testosterone secretion (Sonmez et al., 2005). This vitamin also counteracts the testicular oxidative stress induced by exposure to pro-oxidants such as arsenic, PCBs (Arochlor 1254), cadmium, endosulfan and alcohol (Senthil et al., 2004 and Sen Gupta et al., 2004).

Summary and Conclusion:

Aspartame has been shown to induce oxidative stress and lipid peroxidation; most serious effects result from chronic exposure due to these effects especially on the testes. Vitamin C the important physiological antioxidant counteracts the testicular oxidative stress induced by aspartame contributes to the support of spermatogenesis at least in part through its capacity to reduce α -tocopherol and maintains this antioxidant in an active state.

Recommendations:

- ❖ As chronic aspartame use is hazardous to the testes, alternative sweeteners and methods should be used in diabetic and obese patients.
- ❖ Vitamin C counteracts or decreases the testicular induced damage caused by chronic aspartame intake due to its strong antioxidant properties.
- ❖ Further studies should be done on the FDA approved dose of aspartame on various organs including the testes.

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