An Insight into Antioxidant Therapeutics

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Abstract

Free radicals and oxidants have beneficial and harmful effects on the body. They are generated either during normal cell metabolism or from external agents such as drugs, radiation, nicotine smoke, pollution. Over production of these leads to accumulation in the body resulting oxidative stress. Oxidative stress may result in the development of chronic and degenerative diseases like neoplasm, autoimmune disorders, premature aging, cataract, infertility, metabolic syndrome, cardiovascular diseases and neurodegenerative disorders. The human body has an inbuilt mechanism to deal with oxidative stress to a certain extent. However, we may have to use antioxidants whenever there is imbalance between the productions and counteract mechanisms. This short communication focuses on the use of antioxidants in the treatment of gastric mucosal disorders, male infertility and on statin induced new onset Diabetes mellitus and myopathy.

Introduction

Oxidative stress is defined as disturbance in physiological hemostasis of the biological system due to imbalance between reactive oxygen species and ability of the human body to clear it. Reactive oxygen species are continuously produced in human body due to cellular metabolism, physical and psychological stress, various drugs, environmental toxins, and ultraviolet exposure. Reactive oxygen species plays an important role in cell signaling, regulation of growth factor, immunomodulation, and cellular apoptosis. Oxidative stress is implicated in pathogenesis of various diseases which includes liver injury, neurodegenerative diseases, inflammatory joint diseases, Diabetes mellitus, infertility, aging, cataract, shock related cell injury, myopathy, atherosclerosis, essential hypertension as well as other disorders.

Role of Antioxidants in Male Factor Infertility

Infertility affects 8% to 12% of couples worldwide with regional variations, male factor infertility being an important cause in about 50% of cases. Spermatogenesis, involves increased mitochondrial oxygen consumption by the germinal epithelium of testis. Increased lipid peroxidation in the testis contributes to the suggested vulnerability of this organ to oxidative stress. The attributable causes include exposure to toxins, smoking, alcohol, obesity, radiation, drugs, urogenital abnormalities, and inflammatory conditions affecting the male reproductive tract. To protect this testis has antioxidant defence system characterized by various enzymes like NADPH reductase, glutathione peroxidase, superoxide dismutase, catalase. Apart from these enzymes there are various small molecule factors protecting the testis from oxidative damage including zinc, vitamin C, vitamin E, melatonin. There are many drugs implicated in causing male infertility which includes antineoplastic drugs like cyclophosphamide, busulfan, cisplatin, melphalan, chlorambucil. Other class of drugs known to cause infertility includes corticosteroids, estrogens, neuroleptic agents, spironolactone, cimetidine, and even thyroid supplements. All these factors cause infertility in males by causing oxidative damage to testicular membrane thereby leading alteration in sperm counts, structural and DNA damage to sperms and by causing disorganization of seminiferous tubules of testis. Our research mainly focuses on use of Coenzyme Q 10, L-Glutamine, Atorvastatin, Melatonin as antioxidants in the treatment of reversal of fertility changes caused by anticancer drugs, nicotine exposure and physical stress induced infertility. As per literature evidence there are few studies have been carried out using Coenzyme Q 10, L-glutamine, melatonin, and Atorvastatin as antioxidants. It was proved that exogenous administration of Coenzyme Q 10 helped improving sperm parameters in idiopathic asthenozoopermia. Glutamine, an abundant amino acid in human body, besides its role as a constituent of proteins and...
its importance as metabolic fuel, has nonnutritive effects, including regulation of the cellular redox balance, cell volume, glutathione metabolism, and attenuation of oxidative stress [9]. Several studies have shown that glutamine administration attenuates oxidative stress and protects against chemotherapeutic agent induced organ injury [9]. Hence coenzyme Q 10 and L-glutamine can be potentially used in reversing the fertility changes caused by anticancer drugs and our area of research focuses on use of Coenzyme Q 10 and L-Glutamine in reversing methotrexate induced testicular damage.

Recently it was found out that Nitric oxide has been implicated as the major free radical in nicotine induced oxidative stress injury to testicular tissue leading to irreversible infertility [10]. Melatonin, a natural antioxidant found in human body is also one among well-known hormone inhibiting nitric oxide levels [11]. So, our research also throws light on the use of melatonin in the treatment of nicotine induced testicular damage and on treatment of anticancer drug induced testicular damage. The major idea behind using these antioxidants in reversing the testicular damage caused by anticancer drugs is purely due to its protective role in testis as well as in maintaining the positive nitrogen balance in cancer patients and in preventing injury to other organs due to anticancer drug induced oxidative stress. Use of Atorvastatin in hyperlipidemia induced male infertility is well known but there was one pilot study done which said Atorvastatin has detrimental effects in sperm parameters and cause infertility [12]. But the use of Atorvastatin as antioxidant in atherosclerosis has been proven recently and henceforth the use of Atorvastatin as a potential antioxidant in treatment of stress related male infertility is one such focus of interest in our research [13].

Role of Antioxidants Statin Induced New Onset Diabetes mellitus

In February 2012, Food and Drug Administration released the information that Statins increase hemoglobin (HbA1C) and fasting serum glucose levels. Statin therapy was associated with 9% increased risk of incident diabetes in a recent meta analysis involving randomized controlled trials [14]. Over-production of NO, suppression of insulin secretion by oxidative stress has been found to be the major cause in hyperglycemia associated with statins. Oxidative stress by Atorvastatin has been found to inhibit adipocyte differentiation and hence impair insulin sensitivity [15]. Reported various effects of coenzyme Q10 treatment in streptozotocin-induced diabetic rats [16]. Literature evidence says supplementing a high-fat diet with Glutamine attenuated hyperglycemia in a diabetic rodent model [17]. So further research can be implicated in using Coenzyme Q 10 as well L-glutamine in the treatment and prevention of Statin induced glycemic changes and hence it has been the focus of interest of our research agenda. Although statins are well tolerated by most people, the association of their use with a low incidence of myopathy is well established, however, the risk of rhabdomyolysis with the currently marketed statins is very low [18,19]. Statin-induced myopathy is a heterogeneous condition with multiple pathophysiologic causes. It may be due to the mechanism of action of the drug per se, interactions with other drugs, or genetic, metabolic, immunological vulnerabilities. Muscle metabolism is adversely impacted by statin therapy through various mechanisms. The lack of CoQ10 has been postulated to be an etiologic factor for statin-associated myopathy [20]. Also, literature says possible role for Glutamine in stimulating anabolic processes, including muscle glycogen and protein synthesis [21]. Hence future research could be done using L-Glutamine and Coenzyme Q 10 in reversing as well preventing statin induced myopathy. So, our area of research mainly focuses on using these antioxidants in targeting both myopathy as well as glycemic changes induced by statins by supplementing these drugs along with the statins during treatment and to find out whether physical exercise as a part of treatment regimen during statins ameliorates or attenuates myopathy when implemented along with antioxidant treatment.

Role of Antioxidants in the Peptic Ulcer Disease

_Helicobacter pylori_, non-steroidal anti-inflammatory drugs (NSAIDS), emotional stress, alcohol abuse, and smoking are the principal etiological factors associated with peptic ulcer [22]. The exact mechanisms have been studied upon since years, some of them being impairment in the gastric mucosal anti-oxidant mechanism, production of free radicals and local irritation of the mucosa [22]. Gastrooduodenal ulcers, GI malignancies, and inflammatory bowel disease (IBD) arise in part from oxidative stress. There are various studies suggesting that oxidative stress is one of the major factors in the pathogenesis of peptic ulcer disease. There are few studies which proved the effectiveness of coenzyme Q 10 in preventing analgesic induced peptic ulcer [23]. Recent evidence has implicated stress induced gastric ulcers are mainly due to free radical damage to the gastric epithelium. So, our research focuses mainly on using Coenzyme Q 10 and L-glutamine in the treatment of peptic ulcer disease due to stress and ethanol as both share the common pathway of free radical induced gastric damage. Also, various plant products have been identified which have anti-inflammatory as well as antioxidant property. The sesame oil lignan sesamol (3,4-methylenedioxyphenol) is said to have potent antioxidative properties [24]. Bisphosphonates are known to cause gastric irritation and peptic ulcers. The mechanism of bisphosphonate induced gastric injury is mainly via generation of free radicals [25]. So, the aim of our research is to study the effect of sesame seed extract on bisphosphonate induced gastric ulcers and to find out the role of sesame seeds as effective drugs in management of peptic ulcer disease via their antioxidant mechanism.

Conclusion

The role of antioxidants in treatment of various diseases like peptic ulcer, male infertility, statin induced new onset _Diabetes mellitus_ and myopathy is an emerging trend in the medical field. So, future research must be done using these novel antioxidant molecules like coenzyme Q 10, L-glutamine, Melatonin to find appropriate dosages and also to find out correct treatment protocols to use these agents. From pharmaceutical point of view different formulations of these agents can be tried for treatment of various diseases. Further clinical trials can be undertaken to add to the current evidence database for practicing safe medicine with these agents.

References


