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Original Research Paper

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OXIDATIVE STRESS AND ANTIOXIDANTS STATUS IN NASAL POLYPS

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ABSTRACT Nasal polyposis is considered to be an inflammatory condition in nasal and paranasal sinus cavities and its aetiology is still unclear.There are very few data on epithelial changes in nasal polyposis and their relationship with free radical damage. Malondialdehyde as a major end-product of lipid peroxidation, and superoxide dismutase and nitric oxide as antioxidants play important roles in oxidative stress. In this study, the concentrations of malondialdehyde,superoxide dismutase and nitric oxide were compared in normal control. The current study demonstrates that there is strong evidence related to oxidative stress in the pathogenesis of nasal polyposis, and antioxidants can have a preventive role in free–radicalmediated tissue damage in nasal polyposis.

KEYWORDS : Free radicals, oxidative stress, antioxidants, nasal polyp, Reactive Oxygen species.

INTRODUCTION:

Nasal polyposis is considered an inflammatory condition in nasal and paranasal sinus cavities and is often encountered in otolaryngology clinics.Despite the prevalence and recognition of this condition for 3000 years, its aetiology has remained unclear. There have been many suggestions about the aetiology of nasal polyposis, including adenoma, fibroma, glandular cyst, mucosal exudates,blockade, glandular hyperplasia, new gland formation, ion transport, periphlebitis,perilymphangitis, cystic dilatation of the excretory duct, vessel obstruction and necrotizing ethmoiditis; however multiple factors may be involved in polyp formation and the precise aetiology of nasal polyposis is still unknown (1-2). Most studies in the literature deal with the inflammatory mechanisms occurring in the lamina propria of nasal polyposis, but few data are available on epithelial changes and their relationship with free radical damage (3).

The reason why polyps develop in some patients and not in others remains unknown. There is a definite relationship in patients with "'Samter triad': asthma, NSAID sensitivity and nasal polyps. However, not all patients with NSAID sensitivity have nasal polyps, and vice-versa. In the general population,the prevalence of nasal polyps is 4% (3). In patients with asthma, a prevalence of 7 to 15% has been noted whereas, in NSAID sensitivity, nasal polyps are found in 36 to 60% of patients (4). It had long been assumed that allergy predisposed to nasal polyps because the symptoms of watery rhinorrhoea and mucosal swelling are present in both diseases, and eosinophils are abundant. However, epidemiological data provide no evidence for this relationship: polyps are found in 0.5 to 1.5% of patients with positive skin prick tests for common allergens (5)

A free radical can be defined as any species containing one or more unpaired electrons.4 A wide range of free radicals can be made in living systems. Because these molecules are highly reactive, they can cause tissue damage, especially in cellular membranes, by reacting with cellular lipids, proteins, nucleotides, and carbohydrates (6) Under normal circumstances, the potential damaging effects of these free radicals are limited by a number of antioxidants in body (7). In addition to the antioxidant enzymes,namely catalase, superoxide dismutase (SOD), glutathione peroxidase (GSHPX), and glucose-6-phosphate dehydrogenase, the blood and some other tissues contain nonenzymatic antioxidants, namely Vitamin A,E and C among others (7–11).

Antioxidants within cells, cell membranes, and extracellular fluids can be up-regulated and mobilized to neutralize excessive and inappropriate free-radical formation.6 Within the strategy to maintain redox balance against oxidant conditions, blood has a central role because it transports and redistributes antioxidants to every part of the body (6-7) It has recently been demonstrated that free–radicalmediated lipid peroxidation (as malondialdehydethiobarbituric acid [MDA] levels) was increased both in blood and in polyp tissue, whereas there were no data regarding antioxidants and the relationship between antioxidants and free–radical-induced lipid peroxidation (12). Our aim is to investigate the possible changes in antioxidant levels and their relationship to oxidant stress produced by nasal polyposis.

MATERIAL AND METHODS:

In the present study, 50 patients were included, with a mean age of 39 (range 15–74) years. Thirteen were female, and 27 were male. The patient group consisted of 31 patients (mean age of 41 years) with nasal polyposis who were selected for polypectomy procedure, and the control group consisted of 19 patients (mean age of 30 years) with septal deviation who were selected for septoplasty and inferior turbinate procedure. Informed consent was obtained from all the patients, and the study was approved by the Institutional ethical committee of SLIMS Medical college and Hospital. None of the patients had allergy, acute infection, systemic disease, or history of drug and supplement intake. None of the patients with polyposis had received systemic or topical steroids for at least 4 weeks before polyp tissue sampling. Tissue samples were obtained freshly during surgeries. The blood and tissue samples were stored at-50°C. Levels of the following antioxidants were measured from the sera of the participants in the study and the control group: Vitamin A, E

and C. Plasma levels of SOD were also measured. As a peroxidation product, the levels of the MDA combination were measured from the plasma.

Statistical analyses were analyzed with use of Mann-Whitney U test. Spearman's rank correlation coefficient analysis was used to investigate the relationship between two quantitative variables. All statistical analyses were performed using SPSS 11.5 for Windows (SPSS Inc., Chicago, IL). Data are presented as mean ± SD.A significance level (P value) of 1% was considered statistically different unless otherwise stated.

RESULTS:

Table. 1: Control and Patient group antioxidants and preroxidation product Serum levels.

Parameters	Control Group	Patient group
Vitamin. A	0.442±0.4	0.312±0.1
Vitamin E	29.12±0.9	16.3±1.74
Vitamin C	69.93±0.8	51.13±3.81
SOD	1693.6±69	1492.8±175.3
MDA	6.36±4.75	14.92±3.83

DISCUSSION:

Free radicals are described as highly reactive molecules with an unpaired electron in the outer orbit.4 These free radicals are produced predominantly as oxygen radicals or reactive oxygen species (oxidant) in aerobic organisms because oxygen is always available in cellular environment,and oxygen is an electrophilic molecule (13). Oxidants are also produced constantly in the human body under normal circumstances. This is an endogenous source of oxidants. Under normal circumstances, the major sources of oxidants and free radicals produced in the body occur by way of the leakage of electrons from mitochondrial and microsomal electron-transport chains,phagocytic cells, and the endogenous enzyme system such as NADPH oxidase, xanthine oxidase, monoamine oxidase, and peroxisomal cytochrome P-450 oxidase. However,they can be generated by exogenous factors such as radiation, air pollutants, cigarette smoking, sun exposure,ozone, nitrogen mustard, bleomycin, acetaminophen, xenobiotics,and chemical warfare agents (14). An excessive production of ROS and/or a deficiency in the antioxidant defence system conduct to an imbalance,which induces injuries to biomolecules, triggering a number of diseases. The tissues of the human body, including ENT organs, are inevitably exposed to OS,causing local injuries.

The reduction–oxidation state of a cell is due to an imbalance between levels of reactive oxygen species and endogenous enzymes such as catalase, superoxide dismutase, glutathione peroxidase and thiol buffers, in particular glutathione and thioredoxin (15). There is a crucial balance between protection against free radicals and their generation. Superoxide dismutase, that catalyses dismutation of the superoxide anion, is the first and the most important line of antioxidant enzyme defence against reactive oxygen species. Dagli et al.(16) showed that blood levels of antioxidants and the oxidant malondialdehyde were significantly different in a group of patients with nasal polyps compared with a control group without nasal polys.

Rhinitis and sinusitis usually coexist and are concurrent in most individuals; thus, the correct terminology is now rhinosinusitis.The diagnosis of rhinosinusitis is made by a wide variety of practitioners, including allergologists, otolaryngologists, pulmonologists,primary care physicians and many others. Therefore,an accurate, efficient, and accessible definition of rhinosinusitis is required. A number of groups have published reports on rhinosinusitis and its definition. In most of these reports definitions are based on symptomatology and duration of disease and a single definition is aimed at all practitioners.

The most damage caused by the free radicals occurs on cellular membrane lipids or proteins. The polyunsaturated fatty acids appear to be particularly susceptible to oxidative damage because of the lowered bond dissociation energy of the allylic hydrogen of the methylene carbons (17) MDA is a by-product that results from the action of free-radical damage to cellular lipids.

MDA levels can contribute evidence of free-radical production in human tissues. Free radicals can result in cellular damage or death and subsequent tissue damage. One study indicated that a disruption of the epithelial lining might be essential for the initiation of polyp formation in the sinus mucosa (18).The present study demonstrates that tissue damage related to free radicals occurs in cases of nasal polyps. We speculate that this tissue damage can occur in the epithelial layer in nasal polyps. However, further studies are needed to define whether this hypothesis is correct.

In a study on mechanisms of oxidant injury of cells, Cochrane (19) demonstrated that oxidants impaired cellular membrane ion pumps; this resulted in an increase of intracellular Na_ and a loss of K_ with movement of Ca2+ from external medium into the cytoplasm. Such a loss in function of ion pumps could result from a direct action of oxidants on the proteins and indirectly from loss of intracellular adenosine triphosphate (ATP). Oxidants also affect cellular energy system, and ATP levels fall in cells exposed to oxidants (19).

In the present study, MDA levels and antioxidants in tissues and blood were measured because there is an interaction between oxidant and antioxidant defense systems in the body. We found that there were statistically significant negative correlations in blood levels of Vitamin A E and C and Antioxidant enzymes SOD in blood levels of MDA in the patient and control groups.

It is clear from the present study that there are abnormalities in lipid peroxidation and antioxidant enzymes in patients with nasal polyposis. Multiple factors may be involved in polyp formation, but the precise aetiology of nasal polyposis is still unknown. A relationship between nasal polyposis and antioxidants has been demonstrated, but the role of antioxidants in nasal polyposis and their effects on nasal polyposis progress are still unclear.

CONCLUSION:

There is strong evidence related to oxidative stress in the pathogenesis of nasal polyposis, and antioxidants may have a preventive role in free radical-mediated tissue damage in nasal polyposis. The present study shows that tissue concentrations of superoxide dismutase, malondialdehyde and in patients with nasal polyposis are significantly different compared with those for individuals in a control group without nasal polyposis. Levels of the oxidant malondialdehyde were significantly higher in the nasal polyposis group compared with the control group, whereas levels of the antioxidants, superoxide dismutase were significantly lower in the nasal polyposis group compared with the control group. This study demonstrates that there is a strong relationship between oxidative stress and pathogenesis of nasal polyposis.

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