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RELATIONSHIP BETWEEN OXIDATIVE STRESS AND OSTEOARTHRITIS - A REVIEW

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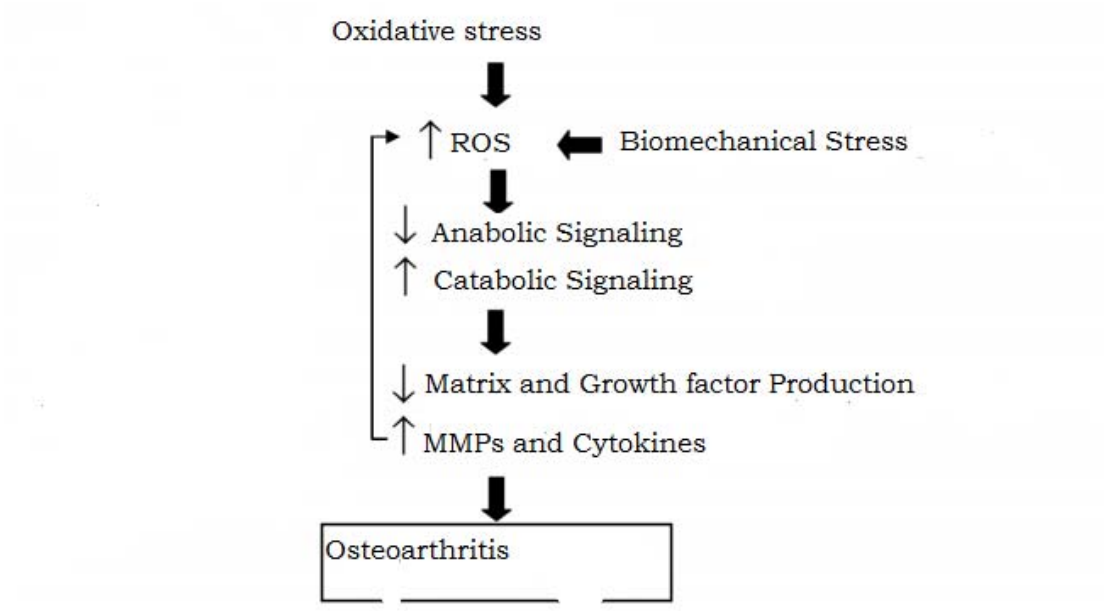
ABSTRACT

Osteoarthritis (OA) is the most common form of arthritis affecting the ageing population and is the leading cause of chronic disability among older people. Osteoarthritis, typically perceived as a degenerative consequence of aging, is a disease with an increasingly well-characterized molecular pathophysiology. The high prevalence of OA with its associated loss of joint function results in expensive and long-term conventional therapies that pose a significant socioeconomic burden. This fact alone makes OA a significant health and economic challenge. There has been progress in defining aetiology and pathogenesis of this disease but exact mechanism still remains obscure. However, lot of studies have shown oxidative stress is related to cartilage degeneration leading to osteoarthritis.

INTRODUCTION

Osteoarthritis is a most common form of arthritis and a major cause of impaired mobility and disability for the ageing populations[1-2]. Osteoarthritis (OA) is a complex disease entity that is difficult to diagnose and define. The Subcommittee on Osteoarthritis of the American College of Rheumatology Diagnostic and Therapeutic Criteria Committee defined osteoarthritis (OA) as A heterogeneous group of conditions that lead to joint symptoms and signs which are associated with defective integrity of articular cartilage, in addition to related changes in the underlying bone at the joint margins[3]. Osteoarthritis (OA) can affect any joint but the most frequently affected sites are the hands, knees, hips, and spine. The prevalence of OA is increasing and this places a globally major burden on individuals; health systems, and social care systems. The term "oxidative stress" represents a condition in which the balance between oxidants and antioxidant defense is upset and excess reactive oxygen species cause oxidative damage to nucleic acids, proteins, and lipids[4]. Oxidation reactions are always taking place in our body, resulting in production of free radicals, which start chain reactions that damage cells. Although oxidation reactions are crucial for life, they can also be damaging; hence plants and animals maintain complex systems of multiple types of antioxidants, such as glutathione, vitamin C and vitamin E as well as enzymes such as catalase, superoxide dismutase and various peroxidases. Low levels of antioxidants or inhibition of the antioxidant enzymes, causes oxidative stress and may damage or kill cells. The majority of free radicals that damage biological systems are oxygen free radicals also known as reactive Oxygen species (ROS). These are the main byproducts formed in the cells of aerobic organisms. These reactive Oxygen species (ROS) are produced both endogenously and exogenously. The endogenous sources of reactive oxygen species (ROS) are Mitochondria, cytochrome P450 metabolism, peroxisomes and inflammatory cell activation[5] nd among exogenous s sources are xenobiotic, chlorinated compounds, environmental agents, metals (redox and non-redox), ions and radiation[6]. These ROS are removed via. enzymatic and non-enzymatic antioxidative mechanism. Mitochondria are the major site of free radical generation; they contain variety of antioxidants which are present on both sides of mitochondrial membrane in order to minimize ROS induced stress. The enzymes mainly involved in balancing ROS are superoxide dismutase (SOD), catalase (Cat), thioredoxin, and glutathione peroxidase, and exogenous antioxidants such as carotenoids, tocopherols, ascorbate, selenium, flavonoids, and other plant polyphenols. Normally, there is an equilibrium between a free radical/reactive oxygen species formation and endogenous

antioxidant defense mechanisms, but if this balance is disturbed, it can produce oxidative stress[7]. Reactive oxygen species (ROS) are both harmful and beneficial in biological systems depending on environment. Beneficial effects of ROS are the physiological roles in cellular responses to noxia such as defense against infectious agents but in contrast, at higher concentrations these are harmful by mediating damage to cell structures, including lipids and membranes, proteins and nucleic acids ; this damage often referred as oxidative stress. This oxidative damage is involved in several chronic exploited human diseases such as diabetes mellitus, cancer, atherosclerosis, arthritis and neurodegenerative diseases and also in the ageing process[8].



Various Clinical and Preclinical studies Suggesting role of Oxidative stress leading Osteoarthritis.

- Studies have shown that oxidative stress caused cartilage senescence and cartilage aging, thereby developing osteoarthritis (OA)[9].
- In another study, it was concluded that higher oxygen free radical production, evidenced by increased MDA and decreased GSH, ascorbic acid, vitamin E support the role of oxidative stress in osteoarthritis (OA).
- Increased oxidative stress with aging may represent an important factor to the development of OA[10] as chondrocytes become more susceptible to oxidant-mediated cell death through the dysregulation of antioxidant systems[11]

- Several studies show an association between mechanical stress and increased production of reactive oxygen species (ROS), as well as decreased antioxidant capacity and exposure to elevated ROS levels is associated with chondrocyte death and matrix degeneration[12]. In joints these ROS generated by cells causes damage to hyaluronan and cartilage matrix component which are important for the mechanical properties of articular cartilage[13]. Therefore, it can be concluded that alteration in oxidant and antioxidant status occurs in rheumatic diseases[14].
- It has been suggested that ROS play a major role in degradation of cartilage which is a main factor in the etiology of osteoarthritis (OA) (15,16). Increased oxidative stress along with ageing has been found to make chondrocytes more vulnerable to oxidant mediated cell death, through the dysregulation of the glutathione system which may reflect the important factor for the development of osteoarthritis in older adults [11].
- In another study it has been found that a single exposure to high levels of pro-oxidant causes the expression genes and antibody epitomes, that are associated with early degenerative changes observed in experimental osteoarthritis[4].
- In another study it was observed that osteoarthritis patients were more susceptible to oxidative damage than healthy controls as evident from increased TBARS and decreased ascorbic acid, GSH, catalse[17].
- A study conducted by Altingdag *et al* on patients of knee OA indicated that oxidant parameters were increased and antioxidant parameters decreased in patients showing that these patients are exposed to potent oxidative stress[18]. Oxidative stress due to ageing and as well as abnormal biomechanical stress results in increased levels of reactive oxygen species (ROS) in chondrocytes and this age ralated oxidative stress may play a central role in cartilage aging through modulation of cell signaling pathways that regulate anabolic and catabolic activity[19].

In addition to above mentioned studies there are few studies showing role of antioxidants in in prevention or at least in prevention of progression of Osteoarthritis at least in progression of osteoarthritis. In one of the study it was found that high intake of antioxidants micronutrients; especially in Vit.C reduces the risk of cartilage loss and disease progression in people with OA[20]. Exogenous antioxidants have been to provide some protection to chondrocytes from the harmful effects of elevated oxidants[12]. There is also evidence that a superoxide dismutase (SOD) simulated combined with methotrexate protects rats with collagen-induced arthritis from the development of OA[21]. Free radical scavengers have been

suggested as potential therapeutic agents for the protection of articular cartilage against progression of OA[16]. Results of various observational studies have also shown to reduce the number of age related disease in study groups[22-23].

SUMMARY

From the above studies it is evident that oxidative stress plays a role in development of OA. From the above studies it can be concluded that approaches and interventions should be intended at to reduce oxidative damage in articular cartilage to prevent development and progression of OA.

REFERENCES

1. Brandt K.D, "Ethiopathogenesis of osteoarthritis", Med Clin N Am. 2008; 93 (1): 1–24.
2. Aziz W.S, Raafat M.B, Hassan N.S, Hanafy A., "Cold Laser as a Complementary Drug in the Treatment of Osteoarthritis", The Journal of American Science 2010; 6(5): 142-152.
3. Roach H.I, Tilley S., "The Pathogenesis of Osteoarthritis", In Bronner F, Farach-Carson MC. Bone and Osteoarthritis. 4th ed. London: Springer-Verlag; 2007: 1.
4. Rahman K., "Garlic and ageing : new insights into an old remedy", Ageing Res Rev. 2003; 39-56.
5. Inoue A, Sato E, Nishikawa M., "Mitochondrial generation of reactive oxygen species and its role in aerobic life", Curr Med Chem. 2003; 2495-505.
6. Valko M, Rhodes C, Moncol J., "Free radicals, Metals and Antioxidants in oxidative stress induced cancer", Chemico-biol inter. 2006;1-40.
7. Tandon R, Verma S, Singh J.B, Mahajan A., "Antioxidants and Cardiovascular Health", JK SCIENCE. 2005; 61-64.
8. Patel V.R, Patel P.R, Kajal S.S., "Antioxidant Activity of Some Selected Medicinal Plants in Western Region of India", Advances in Biological Research 2010; 4(1): 23-26.
9. Yodoh K, Nguyen T, Nakemera H, Hongo-Masute K, Kate T., "Potential involvement of oxidative stress in cartilage senescence and development of OA: Oxidative stress induces chondrocyte telomere instability and down regulation of chondrocyte function", Arthritis Res Ther., 2005; 7(2): 380-391.
10. Dormandy T., "Free-radical pathology and medicine. A review", J R Coll Physicians Lond. 1989; 23(4): 221-227.
11. Carlo M, Loeser R., "Increased oxidative stress with aging reduces chondrocytes Survival: correlation with intracellular glutathione levels", Arthritis Rheum. 2003; 48: 3419–30.

12. Beecher B, Martin J, Pedersen D, Heiner A, Buckwalter J., "Antioxidants Block Cyclic Loading Induced Chondrocyte Death", The Iowa orthropedic Journal. 2005; (27): 1-8.
13. Henrotin Y, Deby-Dupont G, Deby C, Franchimont P.E.I., "Active oxygen species, articular inflammation and cartilage damage", EXS. 1992; 308-322.
14. Ostalowska A, Birkner E, Wiecha M, Kasperczyk A, Kapolka D., "Lipid peroxidation and antioxidant enzymes in synovial fluid of patients with primary and secondary osteoarthritis of the knee joint", Osteoarthritis Cartilage. 2006; (14): 139-145.
15. Basu S, Whiteman M, Maltey D, Halliwell B., "Raised levels of F(2)-Isoprotanes and prostaglandins F (2 alpha) in differnt rheumatic diseases", Ann Rheum Dis. 2001; (60): 67-31.
16. Sowers M, Lachance L., "Vitamins and arthritis, the role of vitamins A,C,D and E", Rheum Clin North Am. 1999; 315-332.
17. Maneesh M, Jayalekshmi H, Suma T, Chatterjee S, Chakrabati A, Singh TA. Evidence for oxidative stress in osteoarthritis. Indian Journal of Clinical Biochemistry. 2005;: p. 129-130.
18. Altingdag O, Erel O, Aksoy N, Selek S, Celik H, Karaoglanoglu M., "Increased oxidative stress and its relation with collagen metabolism in knee osteoarthritis", Rheumatol Int. 2007; 339–344.
19. Loeser R.F., "Aging and Osteoarthritis: The Role of Chondrocyte Senescence and Aging Changes in the Cartilage Matrix", Osteoarthritis Cartilage. 2009; 17(8): 971–979.
20. Pablo Pd, Garce Lo , Mcalindon T.E, "Nutrition and Nutrition supplements and Osteoarthritis. In Coleman LA, editor. Nutritin and health:Nutrition and Rheumatic diseases", Totowa, New Jersey: Humana Press. 2008; 125-158.
21. Cuzzocrea S, Riley D, Caputi A, Salvemini D., "Antioxidant therapy: a new pharmacological approach in shock, inflammation, and ischemia/reperfusion injury", Pharmacol Rev. 2001; (53): 135-159.
22. Mansor J, Stampfer M, Wittelt W., "A prospective study of antioxidant vitamins and incidence of coronary artery diseases in women", Circulation 1991; (84): 2168.
23. Rim E, Stampfer M, Aschemio A, Giovawici E, Colditz G, Willett W., "Vitamin E supplementation anr risk of coronary heart disease aneurysm", N Engl J Med. 1993; 1450-1456.