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Nutrition And Cataract

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There are 27 to 35 million blind people in the world¹. Cataract is the leading cause of visual disability and blindness all over the globe. There is a high incidence of cataract blindness in India. More than 50 per cent of the 9-12 million blind people in the country have surgically curable cataract². Most cases of cataract are seen in subjects over 55 years of age. The disease is becoming more frequent as the life span of the population increases. While the majority of cases occur in older age groups, young subjects are not exempt, and, in them, the rate of maturation is faster.

Identification of the risk factor(s), and unravelling the mechanism(s) through which the human eye loses its transparency and turns opaque, would help to develop an effective preventive approach to cataract blindness. During the past few years, the National Institute of Nutrition (NIN) at Hyderabad has been conducting studies to elucidate the possible role of nutritional factors in cataractogenesis.

PATHOGENESIS OF CATARACT

The normal human eye lens is a transparent, pale yellow resilient bi-convex body enclosed in an elastic capsule. It is suspended behind the pupil of the eye by strands which fuse with the capsule. The lens grows throughout life from the epithelium that lines the inner surface of its transparent capsule, the oldest part of the lens being the nucleus whose formation

begins in the fourth week of intrauterine life. The cortex, or outer portion, is the youngest part. The nucleus or the centre is commonly the first structure to become thick and opaque in the aging eye. The high density of lens structural proteins (crystallins) and their spatial arrangement is responsible for lens transparency. Any opacity in the lens, whether it is a small localised one, or one involving the entire lens, is called cataract.

Cataract is caused by a great variety of disturbances of the lens metabolism^{3,4}. The condition is believed to be preceded by conformational changes of the crystallins, possibly due to their age-related chemical post-synthetic modifications. Similarly, light-induced (ultraviolet, UV) photosensitised reactions leading to conformational changes of crystallins affect their structural stability and result in the loss of lens transparency and cataractogenesis.

Oxidative stress: Oxidative stress or damage as a result of increased generation of active species of oxygen and free radicals in the lens has been implicated in the aetiopathogenesis of cataract^{3,5}. Free radicals are a highly reactive species containing one or more unpaired/lone electrons in the outer orbits. They are generated endogenously inside the cells as a result of normal metabolic processes. They can also be produced extracellularly by factors such as natural radiation (sunlight), pollutants, pesticides, smoke from cigarettes and cheap cooking

fuel, etc. Due to their extra electrical charge, free radicals could bind to many normal cellular components including proteins, enzymes, nucleic acids and unsaturated fatty acids in the cell membranes. The product of lipid peroxidation such as malondialdehyde (MDA) can lead to protein cross-linking and consequent aggregation of proteins to high molecular weight (HMW) species with lower solubility. Until intercepted, free radical attack continues in a chain reaction with each target cell perpetuating the reaction in the attempt to re-establish its own molecular stability.

Antioxidant defence system:

To counter the free radical damage, the tissue has an effective antioxidant defence system *in situ*³. Under normal circumstances this defence system is able to cope with free radicals in the tissue by the antioxidant donating an electron to stabilise the free radical. In doing so, it can harmlessly decay itself or regenerate into another antioxidant. Intracellularly, the defence system largely depends on antioxidant enzymes, that is, glutathione peroxidase (GSH-PO), superoxide

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dismutase (SOD) and catalase (CAT) requiring the antioxidant microelements, that is, selenium (Se), copper (Cu), zinc (Zn) and iron (Fe) for effective functioning. Riboflavin functions as an antioxidant as it is needed as a cofactor (flavin adenine dinucleotide, FAD) for glutathione reductase (GSH-R). Other vitamins including ascorbic acid, alfa-tocopherol and beta-carotene (precursor of vitamin A) function as intracellular and extracellular antioxidants.

It is in this context that NIN has carried out a number of studies to examine the role of nutritional factors: vitamins like thiamine, riboflavin, pyridoxine, folic acid, ascorbic acid, vitamins A and E, trace elements such as Cu, Zn, Mg and chromium and the amino acid, tryptophan.

NUTRITIONAL FACTORS

Experimental studies: Use of animal models has been one of the most important tools in research on cataract⁶. These models provide an opportunity to analyse the ocular tissue throughout the course of the ocular disease-process, thereby greatly facilitating elucidation of molecular mechanism(s) involved in human cataractogenesis.

At NIN, lens opacity was induced in rats, raised on diets deficient in riboflavin, low in tryptophan and high in galactose. A common biochemical change observed in lenses from all these experimental models was an increased oxidative stress.

Although experimentally induced riboflavin deficiency in rats has not resulted in production of frank (mature) cataracts in our animals, it was observed that increased oxidative stress, as revealed by higher insolubilisation of proteins otherwise soluble, increased lipid peroxidation as evidenced by increased formation of MDA and altered enzymatic (glutathione redox cycle) and non-enzymatic (glutathione and ascorbic acid) antioxidants, accompanied by osmotic stress as indicated by increased activities of aldose reductase and sorbitol dehydrogenase (polyol pathway), occur, in the lens⁷⁻⁹.

It was observed that a total reversal of the changes occurred after riboflavin supplementation for about two weeks, thus suggesting that the early biochemical changes observed during cataractogenesis could be

normalised by riboflavin administration. By feeding low tryptophan diet, frank cataract was produced in rats and even here an increased insolubilisation of proteins could be demonstrated in the lens¹⁰. In rats with galactose (50 per cent) induced cataract, it was again observed that there were altered oxidant scavenging enzymes, that is, GSH-PO and CAT, accompanied by an altered oxidative stress in lens¹¹. Further, our recent studies involving exposure of rat lens to UV radiation showed significant reduction in the activities of enzymes participating in energy metabolism as well as oxidant scavenging system, indicating adverse effect on the lens metabolism, which might have a bearing on the lens transparency¹². Thus diets low in either riboflavin or tryptophan or high in galactose are identified as possible risk factors that could render the lens tissue vulnerable to increased oxidative stress. In addition, increased exposure to UV light, by itself, could bring about oxidative damage of the lens components involved in the maintenance of transparency.

Observations on humans: However, there are not many studies directly on human subjects implicating nutritional factors in cataract development. Epidemiological data indicate that better nutritional status of certain micronutrients is associated with diminished incidence of certain types of cataract in human subjects¹³. The initial studies carried out on a group of human subjects at NIN revealed that inadequacies of certain micronutrients, such as riboflavin (as measured by enzyme activation coefficient value), zinc and copper, are associated with cataract¹⁴⁻¹⁶. A high incidence of riboflavin deficiency was observed in cataract patients. Nearly 81 per cent of cataract patients had revealed this vitamin deficiency, as compared to 12.5 per cent in age and socioeconomically matched controls. The nutritional status with respect to thiamine, pyridoxine, folic acid¹⁷, vitamins A and E¹⁸, calcium, magnesium, chromium and tryptophan¹⁹ were comparable between groups. In undernourished (as grouped by body mass index) patients, the proportions of insoluble proteins in the lens was found to be significantly higher compared to well-nourished cataract patients, indicating increased insolubilisation of soluble proteins, a common finding in nuclear cataracts²⁰.

In one of our earlier studies¹⁴, we observed galactose intolerance in a significant number of cataract patients thus suggesting that it could also be one of the risk factors of cataract in India. These findings strengthen the possibility of the role of nutrition in general, and riboflavin in particular, in human cataractogenesis. Further, in brown cataracts characterised by the accumulation of pigments formed probably due to increased exposure to incident UV light, significant depletion of the antioxidant water soluble vitamin, ascorbic acid, occurs in the lens²¹.

Bio-chemical studies: To understand the bio-chemical and molecular mechanism(s) underlying lens browning and cataractogenesis, a wide range of bio-chemical parameters were investigated in human cataracts^{5,21-24}. Available evidence suggests that increased exposure to incident UV radiation is associated with occurrence of cataract, especially the brunescient type. An increased aggregation as revealed by HMW proteins and polypeptides, cross-linking as indicated by protein disulfides, conformational change as evidenced by non-enzymatic glycation, crystallin susceptibility to UV-B (290-320 nm) radiation and denaturation and also protein oxidation demonstrated by oxidised proteins were accompanied by reduced glutathione, ascorbic acid and protein sulfhydryl groups, and decrease in enzymatic antioxidant defence as observed by CAT and GSH-PO in the cortical region during lens browning and cataract formation. In contrast, SOD was increased. All these changes suggest that an altered oxidant-antioxidant equilibrium in the lens is the main underlying feature of human and experimental cataracts.

CONCLUDING COMMENTS

Thus our observations on human and experimental cataracts point out the importance of nutritional factors on cataractogenesis. An increased protein modification, possibly due to increased oxidative stress and inadequate antioxidant micronutrients, are indicated during eye lens browning and cataractogenesis. A recent study²⁵ confirmed our observations regarding vitamins of the B group and cataract risk. In addition, these investigators also observed an association between higher concentrations of carotene and vitamin E with reduced risk of cata-

ract. The excessive free radical attack implicated in the development of lens opacities can be protected by antioxidant micronutrients.

The results of our studies thus indicate that since riboflavin deficiency is common in Indian cataract subjects, supplementation of this vitamin could be beneficial, especially in the early stages of cataractogenesis. In addition, it is likely that the requirements of other antioxidant micronutrients could be higher in cataract patients, since there is an increased oxidative stress in the lens observed in our studies.

Therefore, supplementation of antioxidants might have beneficial effects in the development/progression of cataract in Indian subjects, especially since the incident UV light is high in the sub-continent latitude²⁶. However, currently there is no convincing scientific evidence that micronutrient supplementation does influence the development or progression of age-related cataracts. In the absence of clear knowledge with regard to the efficacy of micronutrient supplementation, well designed clinical studies are needed to know whether early supplementation of antioxidant micronutrients would alter development/progression of cataract. Until results from such studies are available, one has to be cautious in claiming the efficacy of these micronutrients in cataract treatment.

Currently, NIN has planned a collaborative study with local eye institutes/hospitals to see whether antioxidant micronutrients' supplementation will alter the clinical course of age-related cataract.

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NUTRITION NEWS

The Platinum Jubilee Celebrations of the National Institute of Nutrition were inaugurated by Dr K. Vijayabhaskar Reddy, Chief Minister of Andhra Pradesh, at a colourful and well-attended function at the Institute on February 27. During the course of the year, several symposia on selected topics in frontier areas of nutrition have been scheduled.

The concluding part of the celebrations will take place on November 25-27, and will coincide with the XXVI Annual Meeting of the Nutrition Society of India. A number of delegates from India and abroad are expected to participate.

Conference on Mother and Child Development: The Central Technical Committee (CTC) of ICDS had convened a conference on this subject at the India International Centre on February 13 and 14. About 60 experts participated. The need for effective coordination of the ongoing programmes such as ICDS, Child Survival and Safe Motherhood and India Population Project was stressed.