

Are women more resistant to cataract ?

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Abstract

Cataract, already a major cause of visual impairment and blindness, is likely to become an increasing problem as the world population ages. It has already been shown that transforming growth factor B (TGF-B) induces changes in rat ocular lenses which are similar to the feature of human anterior subcapsular cataracts.

The protective role of oestrogen in such cases has also been shown. This adds to an increasing importance of hormone replacement therapy in post menopausal women.

Keywords: Cataract; TGF- β ; Oestrogen.

The mammalian lens has a highly organised cellular structure. A monolayer of cuboidal epithelial cells covers the anterior surface of the elongated fibre cells that constitute the bulk of the lens. These cellular elements are enclosed within a thickened basement, the lens capsule. Normally, the lens transmit light and focusses it onto the retina.

Cataract or opacity of the ocular lens is associated with disruption of normal cellular architecture. This is one of the most prevalent eye diseases and is likely to become an even greater public health problem as the world population ages.

Given the magnitude of the problem surprisingly little is known about its cause(s). Epidemiologic studies have identified numerous factors associated with increased risk for cataract such as aging, diabetics, malnutrition, ultra-violet light, sunlight, glaucoma and ocular surgery. The protective role of antioxidant nutrients, vitamins and minerals has been suggested but not proved.¹

The ability of peptide growth factors to induce fibrosis has received particular attention in regard to cataract formation. Platelet-derived growth factor (PDGF) released α -granules of platelets and monocytes, which is a chemo attractant and mitogen for fibroblasts.²

Fibroblast-derived growth factor (FGF) is also a mitogen for fibroblasts and induces an increase in DNA content when introduced porous subcutaneous chambers.³ It plays a key role in normal events in mammalian lens growth and differentiation.⁴

Transforming growth factor β (TGF- β) appears to have a particularly important role in cataractogenesis. This multifunctional growth factor is found in high concentrations in the α -granules of platelets⁵ and is also secreted by activated T-lymphocytes⁶ and macrophages.⁷ Like PDGF it is also chemotactic for both monocytes⁸ and fibroblasts.⁹

Transforming growth factor- β is present in two forms, TGF- β 1 and TGF- β 2. Both are cataractogenic, TGF- β 2 being the more potent isoform.¹⁰ Transforming growth factor β induces abnormal changes in rat lens epithelial explants. These include the formation of spindle shaped cells, capsule wrinkling and an accumulation of extra cellular matrix.¹¹ These changes can be blocked by a pan specific antibody against TGF- β .¹²

Another interesting feature induced by TGF- β is the accumulation of an increased quantity of extracellular matrix (ECM). In anterior subcapsular cataract there is the presence of the Type I collagen and α -smooth muscle actin, which is not found in other forms of cataract. The cytoskeletal protein α -smooth muscle actin has been used as a marker for TGF- β induced cataract.^{13,14}

Transforming growth factor- β and its mRNA have also been detected in the mammalian eye.¹⁵ The ocular media that bathe the lens contain TGF- β , and it has been suggested that under normal conditions TGF- β is present in a latent form.¹⁶ The factors triggering of its activation are not known, but it could be due to irritation, as after lens surgery.

In the quest for prevention of TGF- β induced cataract, the role of the ovarian hormone oestrogen has been investigated.¹⁷ It has been found the oestrogen protects lenses against TGF- β induced cataract. The cataractous changes were found to be sex dependent – male rats being more susceptible than female rats.

These observations support the findings of earlier workers who have studied the epidemiological distribution of cataract in the population.¹⁸ They found an increased prevalence of cataract in the males of equivalent group as compared to females of the pre-menopausal age group. After menopause the prevalence of cataract in male and

female population was the same. This was true whether menopause occurred naturally or as a result of hysterectomy. Further studies have also shown that oestrogen has a protective role, regardless of whether oestrogen is administered in vivo or in vitro.

In summary, the study of whole lenses has identified a molecule capable of inducing lens opacification and early events in cataractogenesis. The opacities induced by Transforming Growth Factor- β are indistinguishable from classic representations of early stages of anterior subcapsular cataract. This finding has paved the way for further constructive research on cataractogenesis.

There is an increasing body of evidence of the importance of replacement of oestrogen in menopausal and post menopausal women. Estrogen finds great use in the prevention of hot flushes, hypertension and osteoporosis. The protective role in cataract could be the foundation for developing new strategies for prevention or treatment of this debilitating disease.

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