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The commonalities of kidney and eye disease

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Abstract

The greater ocular space and the kidney as two distinct organs with vastly different functions and locations in the human body, also share many striking similarities and commonalities. While they differ in location and function, they are alike in terms of internal structure and pathogenic pathways. Further, they have similar risk factors in terms of disease progression. The object of this article is to discuss these similarities and differences.

Commonality

What may be termed chronic kidney disease (CKD) and certain eye diseases such as glaucoma, age related macular degeneration (AMD) and diabetic retinopathy (DR) share many risk factors including age, excessive weight in relation to body type, and smoking [1]. Both of which are risk factors for hypertension. In addition, both have extensive vascular networks and the retina segment and glomerular filtration barrier have closely similar pathways of development. Further, the eye and the kidney share the renin-angiostatin-aldosterone network [2,3]. All these conditions may lead to the development of either or both CKD and some type ocular disease. CKD is a systemic disease that is progressive in nature. Over time it alters the structure and function of the kidney, which may lead to cardiac disease. The disease process may originate with the loss of function of the nephron unit, which leads to renal failure ultimately. This invariably leads to organ failure in other parts of the body, thus the systemic nature of the disease.

Some recent studies have indicated that progressive CKD is linked to the decline of the Klotho. Should Klotho levels decline, renal disease tends to become more pronounced [4,5]. Decline in Klotho has also been linked to AMD, cataract and retinopathy. Animal studies have linked Klotho to calcification of tissue, including vascular tissue, and in the case of the ocular environment lens and retinal differentiation, but this link is somewhat less established in the ocular environment. Klotho appears to negatively influence vitamin D metabolism and phosphate metabolism.

Pathological mechanisms

Table 1 outlines the common underlying pathological mechanisms for both kidney and eye diseases. Both disease conditions have common causes and important similar risk factors.

Table 1. Outlines the common underlying pathological mechanisms for both kidney and eye diseases. Both disease conditions have common causes and important similar risk factors

Pathology	Ocular Disease	Kidney or renal disfunction
Inflammation	X	X
Vascular Disfunction	X	X
Cardiac Disease and associated risk factors	X	X
Genetics	X	X
Arteriosclerosis	X	X
Klotho	X	X
Systemic Disease		X

Glycation end products

Advanced glycation end (AGE) products are structures formed under hyperglycemic conditions or high oxidative stress [6]. They react and act in concert with AGE receptors [7]. These receptors occur on endothelial cells of the kidney and on the human lens of the eye, especially in cataract patients. The AGE effect is one of strong (covalent) cross linking and insolubility of lens proteins. High levels of serum AGE as is the case with CKD patients can induce eye syndromes such as either cataract or in some cases retinopathy [7].

Arteriosclerosis

Chronic kidney disease may increase homocysteine and lipoprotein and increase oxidative stress [8,9]. There is a decrease in transforming growth factor beta. Modeling of AMD suggests that arteriosclerosis can have effects on eye tissues such as Bruch's membrane, and the presence of increased amounts of lipid in either the membrane or the sclera causes choriocapillary pressure, and calcification of the membrane. This is similar to both CKD and AMD.

Association between chronic kidney disease and diabetic retinopathy

Organogenesis specific for ocular and renal functions share several genes including Pax2, BMP7 and WT-1 [3]. Ocular abnormalities due to genetic mutation give rise to issues in both the renal and ocular organ systems. The presence of retinal vascular lesions are somewhat predictive of the on-set of chronic kidney disease. Chronic kidney disease is strongly associated with macular edema, cataract and elevated IOP.

There have been reports suggesting at least a tentative relationship between CKD and DR [10]. There appear to be a common yet not completely understood pathway linking the two. Studies have shown retinopathy associated in individuals with an increased risk for kidney disease. Similar reports exist between individuals with elevated

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intraocular pressure (IOP) and/or glaucoma. Several investigators have seen associations of kidney disease and glaucoma patients.

There seem to be stronger associations between kidney disease and ocular disease of the anterior segment of the eye [11,12]. Calcification of eyelid margins and the cornea have been seen in patients with advanced chronic kidney disease. This is interesting as the cornea is an avascular organ. There is good clinical evidence that central corneal thickness is associated with kidney disease due to endothelial changes in the cornea. It is postulated that increased urea concentrations in the aqueous humor was toxic to the endothelium.

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