2016

The eye is the window to the kidney and brain

Merrill F. Elias
University of Maine - Main, mfelias@maine.edu

Rachael V. Torres
University of Delaware

Adam Davey
University of Delaware

EBioMedicine 5 (2016) 24–25

Contents lists available at ScienceDirect

EBioMedicine

journal homepage: www.ebiomedicine.com

Commentary

The Eye is the Window to the Kidney and Brain

Merrill F. Elias [a,b], Rachael V. Torres [c], Adam Davey [c,*]

[a] Department of Psychology, University of Maine, Orono, ME, United States
[b] Graduate School of Biomedical Sciences and Engineering, University of Maine, Orono, ME, United States
[c] Department of Epidemiology and Biostatistics, College of Public Health, Temple University, Philadelphia, PA, United States

ARTICLE INFO

Article history:
Received 5 February 2016
Accepted 5 February 2016
Available online 6 February 2016

Diabetic retinopathy and age-related macular degeneration are leading causes of blindness among older adults. Both conditions are more prevalent among those with chronic kidney disease (CKD). However, few if any previous examinations of CKD and visual impairment (VI) have been conducted. This gap in knowledge is filled by Wong et al. (2016) in their article published in this issue of *EBioMedicine*.

The prevalence of VI and associations between CKD, VI and other major ocular diseases are reported for Asian adults between 40 and 80 years of age participating in the Singapore Epidemiology of Eye Disease (SEED) Study between 2004 and 2011 (n = 9434). Chronic kidney disease (estimated glomerular filtration rate < 60 mL/min/1.73 m^2) was defined using the Kidney Disease Outcomes Quality Initiative (KDOQI) Work Group definition and diagnosis of VI and other major ocular diseases were based on comprehensive ophthalmological examination. The prevalence of VI and any ocular disease were significantly higher in those with CKD (36.1% and 84.7%) than in those without (12.9% and 54.3%). Moreover, CKD was associated with significantly higher risk of VI, any ocular disease, cataracts, any retinopathy and diabetic retinopathy after adjustment for potential confounders (odds ratios ranging from 1.24 to 1.94).

This paper makes a valuable addition to the literature because adequate vision is fundamental to quality of life and many forms of blindness are treatable and preventable (Wong et al., 2016). One impressive aspect of the study, apart from the very large sample, is that multiple eye disease outcomes are presented in a single study (i.e., those previously mentioned as well as glaucoma). The benefits of comparing different outcomes within the same study, as compared to different studies using different samples and methods, are obvious.

The selection and modeling of covariates to adjust for confounders reflects the authors' understanding that "the high occult burden of ocular disease may be explained in part by risk factors common to both eye and kidney disease" (Wong et al., 2016). The models represent an exhaustive list of theoretically and clinically relevant cardiovascular disease covariates. We were, however, disappointed in the lack of any variable indexing inflammation (e.g., C-reactive protein, but see Table 1 for an extended list), an important mechanism underlying CKD and ocular disease, particularly among those with diabetes mellitus. This is discussed by Wong et al. (2016), although they did not list it as a limitation of their study. Additionally, late stages of CKD were examined in relation to VI and ocular diseases without considering physiological complications of treatment that have been previously identified (Murray, 2008; Chelala et al., 2015).

1. Future Studies

Future studies will benefit from consideration of inflammation as a common precursor of ocular and kidney disease, especially in individuals with diabetes (Semeraro et al., 2015). There is also a broader context for future studies that promises to tie the literature on visual and cognitive outcomes together. It is clear that CKD predicts significantly lower levels of cognitive performance, with the worst performance observed for those with the lowest levels of kidney function (Elias et al.,

Table 1
Inflammatory markers identified in the cardiovascular literature.

Categories of inflammatory markers	Inflammatory markers
Acute-phase reactants	C-reactive protein
	Fibrinogen
	Serum amyloid A
Adhesion molecules	Vascular cell adhesion molecule-1
	P-selectin
	Intracellular adhesion molecule-1
	E-selectin
Cytokines	Interleukin-1β
	Interleukin-6
	Interleukin-8
	Interleukin-10
	Monocyte chemoattractant protein-1
	Tumor necrosis factor-α
Other Mechanisms	A_2 phospholipases
	Erythrocyte sedimentation rate
	Matrix metalloproteinases
	Myeloperoxidase
	Placental growth factor
	White blood cell count

DOI of original article: http://dx.doi.org/10.1016/j.ebiom.2016.01.023.
* Corresponding author.

http://dx.doi.org/10.1016/j.ebiom.2016.02.010

2009, 2013; Davey et al., 2013; Torres et al., 2016). Further, visual impairment has been associated with lower levels of performance on certain cognitive tests in the elderly (Dupuis et al., 2014). This is consistent with our finding that tests of cognition most sensitive to CKD are very often those which require adequate vision to complete (e.g., those indexing visual–spatial organization and memory) (Torres et al., 2016; Elias et al., 2009).

However, visual acuity and other indices of visual function are rarely reported or analyzed as confounders in cognitive studies. Application of the Wong et al. paradigm (Wong et al., 2016) to studies of cognition would help us understand the extent to which cognitive deficits in the elderly are, in part, a reflection of poor vision rather than cognitive impairment.

2. Clinical Importance and Key Message

The Wong et al. study (Wong et al., 2016) is of epidemiological and clinical significance. The prevalence of VI as indexed in those with CKD is 36%, versus 13% among those without CKD. In the former, the odds ratio of VI among individuals without diabetes was 1.11 compared to 1.80 among individuals with diabetes. Moreover, the odds ratio of retinopathy among individuals without diabetes was 1.45 compared with 1.95 among individuals with diabetes. This is unacceptably high risk given that CKD, diabetes and eye diseases are treatable and preventable. Screening for ocular diseases in those with CKD, especially individuals with diabetes, is warranted. More generally, the Wong et al. paper (Wong et al., 2016) tells us that eye is not only the window to the kidney, but also to the brain.

Disclosure

The authors declared no conflicts of interest.

References

Chelala, E., Dirani, A., Fadlallah, A., et al., 2015. Effect of hemodialysis on visual acuity, intraocular pressure, and macular thickness in patient with chronic kidney disease. Clin. Ophthalmol. 9, 109–114.

Davey, A., Elias, M.F., Robbins, M.A., et al., 2013. Decline in renal functioning is associated with longitudinal decline in global cognitive functioning, abstract reasoning, and verbal memory. Nephrol. Dial. Transplant. 28, 1810–1819.

Dupuis, K., Pichora-Fuller, M.K., Chasteen, A.L., et al., 2014. Effects of hearing and vision impairments on the Montreal Cognitive Assessment. Neuropsychol. Dev. Cogn. 22, 413–437.

Elias, M.F., Elias, P.K., Seliger, S.L., et al., 2009. Chronic kidney disease, creatinine and cognitive functioning. Nephrol. Dial. Transplant. 24, 2446–2452.

Elias MF, Dore GA, Davey A. Kidney disease and cognitive functioning. In: Toyoda K, ed. *Brain*, *Stroke and Kidney*. Ronco C (Series Ed.), Contributions to Nephrology (vol. 179). Basal: Karger; 2013: 1–16

Murray, A.M., 2008. Cognitive impairment in the aging dialysis and chronic kidney disease populations: an occult burden. Adv. Chronic Kidney Dis. 15, 123–132.

Semeraro, F., Cancarini, A., dell'Omo, R., et al., 2015. Diabetic retinopathy: vascular and inflammatory diseases. J. Diabetes Res., 58260

Torres, R.V., Elias, M.F., Seliger, S., et al., 2016. Risk for cognitive impairment across 22 measures of cognitive ability in early stage chronic kidney disease. Nephrol. Dial. Transplant. in press.

Wong, C.W., Lamoureaux, E., Cheng, C.Y., et al., 2016. Increased burden of vision impairment and eye diseases in persons with chronic kidney disease — a population-based study. EBioMedicine 5, 193–197.