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How to prevent premature ageing in early chronic kidney disease?

Chronic kidney disease (CKD) has been associated with premature vascular ageing and death. A study in the current issue of NDT [1] showed that albumin in urine causes Klotho deficiency, thus explaining premature ageing in early CKD stages, even in patients with normal kidney function. What can be learnt?

One in ten adult Europeans suffers from CKD, an impairment of kidney function of a certain degree. While most people fear the need for dialysis or transplantation in the end-stage of the disease, the most concerning consequence is indeed premature ageing and mortality, mainly from cardiovascular causes. Premature ageing was thought to be the result of an accumulation of toxins, usually eliminated in urine. However, this only occurs in advanced CKD stages, especially end stage renal disease. But premature ageing is also common in early CKD stages, when kidney elimination of toxins is still normal. It remained unclear why this was the case - until the discovery of Klotho, the so-called anti-ageing hormone, which is produced by the kidneys. Human CKD is characterized by Klotho deficiency from the very early stages and low Klotho drives the ageing process. But, what drives Klotho deficiency in these early stages of CKD, when renal functions are still near-normal, long before doctors observe a decreased elimination of toxins?

In this new study, the authors explored the hypothesis that the presence of albumin in urine, a hallmark of early stage CKD, may directly and independently decrease Klotho expression. And indeed, they found that albumin directly decreases Klotho expression in tubular cells in culture through epigenetic mechanisms and low Klotho levels were observed in experimental animal models as well as in patients with albuminuria, but who showed normal kidney function. "This early albuminuria-driven decrease in Klotho expression may contribute to the higher risk of premature death and CKD progression in the early stages of human CKD (stage 1 or 2, that is, normal renal function)", explains Professor Alberto Ortiz, senior author of the paper. "In this regard, testing for albuminuria is as important as testing for glomerular filtration to assess CKD".

This observation has short-term and long-term clinical consequences. A key anti-ageing function of Klotho is protection from excess dietary phosphate, and indeed, patients with higher albuminuria had higher serum phosphate levels. "In the short-term, these findings remind us of the need for CKD patients, even at the earlier stages, to avoid the intake of large amounts of phosphate, especially highly bio-available phosphate, as found in food additives. Therefore, CKD patients should favour natural foods over processed foods", explains Professor Ortiz. "With this simple dietetic measure they can maintain healthy vessels. In the long term, the involvement of epigenetic mechanisms may provide additional therapeutic tools to preserve Klotho production when currently available anti-proteinuric therapy fails".

[1] <https://academic.oup.com/ndt/advance-article-abstract/doi/10.1093/ndt/gfx376/4841978?redirectedFrom=fulltext>

About ERA-EDTA

With more than 7,500 members, the ERA-EDTA ("European Renal Association – European Dialysis and Transplant Association") is one of the biggest nephrology associations worldwide and one of the most important and prestigious European Medical Associations. It supports basic and clinical research in the fields of clinical nephrology, dialysis, renal transplantation and related subjects. It also supports a number of studies as well as research groups and has founded a special "Fellowship Programme" for young investigators as well as grant programmes. In order to involve young nephrologists in all its activities ERA-EDTA has created the "Young Nephrologists' Platform" (YNP), a very active committee whose board includes members who are 40 years old or younger. In addition, it has established various working groups to promote the collaboration of nephrologists with other medical disciplines (e.g. cardiology, immunology). Furthermore, a "European Renal Best Practice" (ERBP) advisory board was established by the ERA-EDTA to draw up and publish guidelines and position statements. Another important goal of the ERA-EDTA is education: The series of CME-courses combined with the annual congress offer an attractive scientific programme to cover the need for continuous medical education for doctors working in the fields of nephrology, dialysis and transplantation. The association's journals, NDT (Nephrology, Dialysis, Transplantation) and CKJ (Clinical Kidney Journal), are currently the leading nephrology journals in Europe; furthermore NDT-Educational is the online educational journal of the society, with free access for all users, as well as being a very important and useful feature of NDT-Educational "Literature Review". The ERA-EDTA Registry is a large epidemiologic database comparing countries by assessing nephrology practice throughout Europe. ENP, the European Nephrology Portal, is the latest new initiative of ERA-EDTA: here all those interested in the activities of the Society can find everything that is happening, all in one place! Finally, ERA-EDTA is a member of the European Kidney Health Alliance (EKHA), a consortium of patients, nurses and foundations all related to renal issues that actively interacts with the European Parliament. For more information, please visit www.era-edta.org