Copenhagen, May 25, 2018

Can cardiovascular risk be reduced by lowering urate levels?

At this week’s ERA-EDTA Congress in Copenhagen, a study [1] will be presented in which an unusual strategy for reducing cardiovascular risk in patients with chronic kidney disease was investigated. Administration of allopurinol, a drug normally used to lower elevated levels of serum urate (‘gout’), showed positive effects on damaged and thickened cardiac muscle. Dr Elaine Rutherford, lead investigator from the University of Glasgow: ‘In allopurinol we have a well-known, generally well tolerated and inexpensive medication which may also be able, beyond its usual indications, to reduce the risk of cardiac arrest not only in many cardiac patients but also, or especially, in renal patients.’

Chronic kidney disease (CKD) affects 10–15% of the global population [2, 3]. CKD is associated with a poor prognosis, because patients have a high risk of cardiovascular events (cardiac arrest, heart attacks, strokes). The risk increases with deteriorating kidney function and is particularly high in cases of end-stage renal diseases and among dialysis patients. One study conducted as long as 20 years ago showed that the mortality risk of a 30-year-old dialysis patient was approximately the same as that of an 80-year-old person with healthy kidneys [4]. Cardiac arrest is one of the most frequent causes of death, as the 4D study (Die Deutsche Diabetes Dialyse-Studie) [5] showed more than ten years ago. Sudden cardiac death, also known as premature cardiovascular death, involves the interaction of various mechanisms. One crucial risk factor is thickening of the left ventricular wall (left ventricular hypertrophy – LVH), because this can easily lead to oxygen deficiency in tissue and also because cardiac arrhythmias can also develop more quickly [6]. Reducing LVH can therefore lower the risk of cardiovascular events.

Allopurinol, a medication used to lower elevated levels of serum urate (‘gout’), was found to reduce left ventricular mass (LVM) in previous studies with cardiac and diabetic patients [7]. Allopurinol is generally well tolerated, so it may also be an option for treating LVH in patients with no increase in urate. This has been investigated in a clinical study funded by the British Heart Foundation in the UK [1] that will be presented this week at the ERA-EDTA Congress in Copenhagen. In a randomized, double-blind, placebo-controlled trial, 80 hemodialysis patients received either 300 mg of allopurinol or placebo after each dialysis session, over a period of one year. The two groups were similar in their initial characteristics, with normal
levels of urate (average 365 µmol/l; normal range 130-464 µmol/l). LVM was measured in MRI scans at the beginning of the study and after one year. 53 patients were evaluated at the end of the study.

A significant lowering of serum urate by -44±84 µmol/l was found in the allopurinol group; in the placebo group, urate levels increased by +21±100 µmol/l. General analysis initially showed that allopurinol did not have a significant effect on LVM. However, a sub-group analysis revealed that, among those patients whose urate levels fell by at least 20%, there was also a significant decrease in LVM (-2.9±7 g/m², compared to +3.6±10.4 g/m² under placebo).

Dr Elaine Rutherford explains: ‘All the patients had initial urate levels in the upper normal range. Allopurinol did not have the general effect of reducing LVM, but only among those patients whose urate levels fell by at least 20%. So there seems to be a link between reduced LVH and the efficacy of urate reduction, and thus a potential dependence on the allopurinol dose required by each individual. This now needs to be investigated in a study on cardiovascular outcomes among hemodialysis patients – specifically among those who respond to allopurinol with sufficient lowering of urate level, which needs to be discovered in a run-in phase.’

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 the NDT-Educational "Literature Review". The ERA-EDTA Registry is a large epidemiologic database comparing countries by assessing nephrology practices throughout Europe. ENP, the European Nephrology Portal, is the latest new initiative of ERA-EDTA, where 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 relating to renal issues that actively interacts with the European Parliament. For more information, please visit www.era-edta.org