¿Es el agente o el nivel de presión arterial lo que influye en la protección renal de las nefropatías crónicas?

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Hypertension is not only an important presenting feature of renal disease and, together with proteinuria, probably a major factor contributing to progression, but also a significant determinant of morbidity and mortality among hemodialysis patients.

Over the last decade, a number of trials have been performed to assess the degree of BP reduction needed to achieve reno-protection. The results of the Modification of Diet in Renal Disease (MDRD) Study clearly showed that stricter BP control was capable of slowing CRI progression, compared with BP control that was usual for that time. The patients with higher levels of baseline proteinuria received greater benefits from being assigned to a low BP target. Over recent years it has become clear that not all anti-hypertensive agents are equally effective in slowing CKD progression, and that some have an additional reno-protective effect that seems at least partially independent of BP reduction and is probably linked to their capacity of halting some of the pathogenic mechanisms involved in renal damage. Indeed, several clinical trials have shown that drugs blocking the renin-angiotensin system are more effective in reducing CKD progression compared with other anti-hypertensive drugs in diabetic and non-diabetic nephropathies. However, in the majority of large trials, target and achieved BP values were constantly higher than those nowadays recommended. Moreover, the BP values were often lower in the experimental groups (ACE-I or ATIIRA) compared with the control groups and BP values during 24 hours were not recorded.

Although this effect seems to be partially independent of blood pressure (BP) reduction, it is still unclear whether these drugs are really superior to other anti-hypertensive agents when the BP values recommended by the present guidelines are actually achieved. This is particularly true when considering that, in published trials, target and achieved blood pressure values were constantly higher than those nowadays recommended. Furthermore, in the majority of these studies, patients treated with ACE-inhibitors (ACE-I) or Angiotensin II receptor antagonists (ATIIRA) achieved lower BP values than those in control groups and BP values during 24 hours were not recorded. A secondary analysis of the AIPRI data, which has taken into account both the effects of SBP and DBP, at baseline and during follow-up, on the risk of developing the primary composite end-point showed that proteinuria values at baseline and throughout follow-up were the main factors related to the renal outcomes (each g per day greater levels of proteinuria at baseline was associated with an increase of 39% in the relative risk for the primary end-point, each g per day greater levels of proteinuria during follow-up was associated with an increase in the relative risk of 35%). DBP at baseline (relative risk increase of 6% for each mmHg increase) and SBP changes from baseline throughout follow-up (relative risk increase of 3% for each mmHg increase) were also independently related to the primary end-points. When all of these co-variates were considered, a trend towards independent reno-protection by ACE-I was still present, but without statistical significance (relative risk reduction of 20%). However, the regression lines of the control and benazepril groups were parallel (P 0.326) and significantly different ($P < 0.001$), possibly indicating that the anti-proteinuric effect of ACE-I was independent of the BP control achieved.

In conclusion, the reno-protective effect of these agents (ACE-I, ATIIRA) is partially independent of a better BP control. However, caution should be paid in attributing true biological reno-protective properties to drugs just basing on statistical adjustments of BP values, although robustly performed, without being aware of what those BP values actually reflect.