Long-term Clinical Experience in CKD Patients with Sevelamer and Lanthanum Carbonate

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Chronic renal failure is associated with disturbances of calcium and phosphate metabolism. Hyperphosphatemia may occur early in the course of chronic kidney disease (CKD) and generally worsens with CKD progression. Early treatment and prevention of hyperphosphatemia is an important goal. Studies have shown that elevated serum phosphorus levels are associated with negative patient outcome in terms of vascular calcification, hospitalization, and mortality.

Hyperphosphatemia in CKD patients can be treated by dietary protein restriction and oral phosphate binders. In patients with end-stage renal disease optimal dialysis efficiency is also required. Calcium-containing phosphate binders can be given in first place but daily amounts in excess of 2.5 g elemental calcium must be avoided because of the reported association between the dose of calcium-containing phosphate binders and vascular calcification. Moreover, calcium-containing phosphate binders generally cannot be administered together with active vitamin D derivatives since this increases the risk of developing hypercalcemia, adynamic bone disease and soft tissue calcification.

Promising new treatment options are the calcium-free, aluminum-free phosphate binders. The administration of sevelamer has been shown, in prospective randomized trials in hemodialysis patients, to reduce the progression of aortic and coronary artery calcification, as compared to calcium-containing phosphate binders[1-3]. We found, using the apolipoprotein E gene knock-out mouse model, that sevelamer treatment led not only to a decrease in the progression of both intima and media calcification of the aorta, but also to a reduction in the progression of atherosclerosis[4]. Whether sevelamer decreases the mortality of CKD patients remains a matter of debate.

Lanthanum carbonate is another possible option in the treatment of hyperphosphatemia. Its efficacy is comparable to that of calcium-containing phosphate binders. A potential problem is that this drug is absorbed from the intestinal lumen and accumulates in various tissues including the liver, bone, skeletal and cardiac muscle, kidney and brain. Although in long-term studies done in dialysis patients no evidence for toxic effects was observed, including the absence of histomorphometric changes in bone, we found a decrease in liver weight in lanthanum-treated uremic rats, as compared to placebo-trated uremic rats[5]. Since our study lasted for only one month and we did not examine hepatic structure and function, further studies are needed to confirm this observation and to see whether it has relevance for the human condition.

Conclusion

An adequate control of hyperphosphatemia in CKD patients is mandatory. Starting treatment

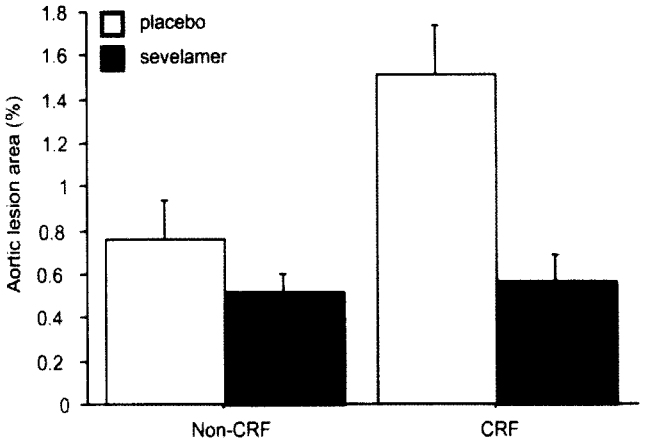

Fig. 1. *Reduction in the progression of aortic atherosclerosis in non uremic (Non-CRF) and uremic (CRF) apoE-/- mice in respone to placebo or sevelamer treatment (Phan et al, ref. 4).*

early during the progression of CKD probably is the best way to achieve this goal, combining the optimal use of established treatment modalities with novel medications. An adequate use of the latter should allow the prevention of parathyroid oversuppression, adynamic bone disease and vascular calcification in CKD patients. Ideally, their use also should improve overall outcome. Finally, it is important to demonstrate that calcium-free, aluminum-free phosphate binders are safe.

References

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