DIABETIC NEPHROPATHY

Paricalcitol lowers residual albuminuria in type 2 diabetes

The addition of paricalcitol (a selective activator of the vitamin D receptor) to treatment with renin–angiotensin–aldosterone system (RAAS) inhibitors reduces albuminuria in patients with type 2 diabetes, according to the results of the randomized, controlled VITAL study.

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RAAS inhibitors such as angiotensin-converting-enzyme (ACE) inhibitors and angiotensin-receptor blockers (ARBs) are known to reduce renal and cardiovascular mortality in individuals with diabetes, but even with such treatment, residual renal and cardiovascular risks can remain high. As increased residual albuminuria is associated with increased renal risk, additional strategies are needed to reduce this risk. The VITAL study was initiated after a *post hoc* analysis of a randomized trial investigating use of paricalcitol for lowering parathyroid hormone levels in patients with chronic kidney disease

showed that paricalcitol was associated with an increased likelihood of reduction in dipstick-measured proteinuria.

The VITAL study involved patients who had type 2 diabetes and albuminuria and were on ACE inhibitors or ARBs. Dick de Zeeuw and co-workers randomly assigned patients to 24 weeks of daily treatment with placebo ($n=93$), 1 μg paricalcitol ($n=93$), or 2 μg paricalcitol ($n=95$). The change in geometric mean urinary albumin-to-creatinine ratio (UACR) between baseline and the last measurement taken during treatment was -3% in the placebo group and -16% in the combined paricalcitol groups, with a between-group difference of -15% . Use of the higher paricalcitol dose was associated with greater reductions in UACR (between-group differences compared with placebo: -11% in the 1 μg group and -18% in the 2 μg group). The proportion of patients who achieved a decrease in UACR of $\geq 15\%$ between baseline and the last measurement during treatment was significantly higher in patients on 2 μg paricalcitol doses than in patients on placebo (55% versus 40%; $P=0.038$) but the researchers did not find a statistically significant difference in this

proportion between the 1 μg group (52%) and placebo. de Zeeuw *et al.* found that the treatment effect of a daily 2 μg dose of paricalcitol seemed to be present regardless of the degree of RAAS inhibition. The frequency of adverse events was similar in paricalcitol and placebo groups. Three deaths occurred, all in the 2 μg paricalcitol group, but none of the deaths were deemed to be related to the study drug. Hypercalcemia incidence was similar in all groups.

“The most interesting finding was that paricalcitol worked best [in terms of albuminuria reduction] in patients with high sodium intake in their diet,” states de Zeeuw. “This finding is all the more interesting given that these people respond worst to ACE inhibitor and ARB therapy.” de Zeeuw hopes that a future trial will examine hard outcomes associated with the long-term use of vitamin D analogues.

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Original article de Zeeuw, D. *et al.* Selective vitamin D receptor activation with paricalcitol for reduction of albuminuria in patients with type 2 diabetes (VITAL study): a randomised controlled trial. *Lancet* 376, 1543–1551 (2010)