

Drug lowers body's 'set point' to control hyperparathyroidism in dialysis patients

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A medication called cinacalcet—an important part of treatment to control high levels of parathyroid hormone (PTH) in patients receiving dialysis for end-stage renal disease (ESRD)—works by resetting the balance between calcium and PTH levels, according to a study in the November *Journal of the American Society of Nephrology* (JASN).

Cinacalcet is one of a family of drugs called calcimimetics. "In hemodialysis patients, the use of calcimimetics decreases the set point of the PTH-calcium curve, which means that PTH secretion by cells is suppressed at low or normal calcium levels," comments Mariano Rodriguez, MD, PhD, of Nephrology Service, Hospital Universitario Reina Sofia in Cordoba, Spain.

Dr. Rodriguez and colleagues studied responses to cinacalcet treatment in nine patients with ESRD receiving long-term hemodialysis to replace lost kidney function. All patients had high levels of PTH, or secondary hyperparathyroidism—a frequent complication of kidney disease that is mainly caused by low calcium levels. Hyperparathyroidism can lead to weakening of the bones and other problems, including cardiovascular disease.

The researchers assessed the "PTH-calcium curve," which reflects the way PTH levels respond to calcium levels, by comparing blood samples obtained during dialysis performed at low and high calcium levels. The study took advantage of a new test that provides more complete information on the dynamics of PTH secretion.

Treatment with cinacalcet led to significant reductions in the patients' blood phosphorus levels. Their levels of PTH before dialysis were also decreased.

Cinacalcet also led to a reduction in the set point of the PTH-calcium curve. This occurred because cinacalcet made parathyroid cells more sensitive to calcium.

The study provides important new information on how cinacalcet and other calcimimetic drugs work to reduce PTH levels. Normally, low calcium levels cause cells to increase secretion of PTH. After cinacalcet treatment, PTH secretion doesn't increase even when calcium levels are low. Cinacalcet doesn't just lower calcium and PTH levels in the short term, the new results suggest—it changes the interaction between calcium and PTH levels in the long term.

Secondary hyperparathyroidism is a common and potentially serious problem in patients with kidney disease. Calcimimetic drugs like cinacalcet provide a valuable new treatment option. "Nowadays the calcimimetics are an essential tool in the treatment of secondary hyperparathyroidism," says Dr. Rodriguez. "With these drugs, the need for surgery to remove the parathyroid gland (parathyroidectomy) is markedly decreased."

The results provide nephrologists with new insights into the way cinacalcet works to control PTH levels in ESRD patients with hyperparathyroidism. "High PTH levels and the excess of calcium in blood are easy to control with calcimimetics," Dr. Rodriguez adds.

The study was limited by the lack of data on the effects of cinacalcet in patients on peritoneal dialysis, although there are no reasons to believe that results would have been different in peritoneal dialysis patients. In addition, the patients in the study were not taking vitamin D, another

effective treatment for hyperparathyroidism. "It would have been interesting to evaluate the combined effect of calcimimetics and vitamin D on the set point of the PTH-calcium curve," says Dr. Rodriguez.

Source: American Society of Nephrology

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