**Small Changes in Blood Acidity May Affect CKD Patients’ Health**

Very small changes in pH levels in the blood may affect renal calcium reabsorption and parathyroid hormone (PTH) secretion, new research suggests. The findings, which are published in the *Journal of the American Society of Nephrology*, could have important implications for the health of patients with chronic kidney disease (CKD).

“In CKD, calcium and phosphate lost from the bone can end up in the walls of the blood vessels and in other soft tissues, causing potentially serious complications,” said senior author Donald Ward, PhD, of the University of Manchester, in the UK. “The key protein that controls our blood calcium levels is the calcium-sensing receptor, and what we have found is that the mild acidity, or acidosis, that is often seen in CKD is sufficient to impair this protein from working properly.”

In their efforts to uncover the health effects that patients with CKD experience due to the excess release of calcium and phosphate from the bones, Ward and his team found that in both human embryonic kidney cells and bovine parathyroid cells, slightly decreasing the extracellular pH from 7.4 to 7.2 rapidly inhibited intracellular calcium mobilization through the calcium-sensing receptor, whereas raising extracellular pH to 7.6 increased responsiveness to extracellular calcium. “It was known before that large changes in acidity—larger than would normally be seen in human blood—could affect calcium-sensing receptor activity,” Ward said. However, what we have found here is that even relatively mild increases in blood acidity, similar to those commonly seen in CKD, could also inhibit the receptor in cell experiments in our laboratory.”

Also, pH elevation suppressed PTH secretion from human parathyroid cells, while acidosis increased PTH secretion. The findings suggest that acid-base disturbances may affect the control of parathyroid function and calcium metabolism. While other pH-sensitive membrane proteins may also be involved, the extracellular pH changes had no effect in cells lacking the calcium-sensing receptor, or incubated in low extracellular concentrations of calcium.

Because metabolic acidosis and secondary hyperparathyroidism are both common consequences of CKD, the study’s results point to a mechanistic link between the two. Also, the observation that raising extracellular pH promotes calcium-sensing receptor–mediated suppression of PTH secretion points to a new therapeutic strategy for treating secondary hyperparathyroidism in CKD.

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**CKD Prevalence Stable, but Higher in Older Adults, Report Says**

The US prevalence of end stage renal disease (ESRD) continues to increase, but the rate of new cases may be leveling off. Meanwhile, mortality among patients on dialysis or with a kidney transplant continues to decline. Those are among the key findings of the recently released 2014 US Renal Data System Annual Data Report.

The report also finds that the prevalence of chronic kidney disease (CKD) has remained relatively stable, but continues to increase in the Medicare population. The 2014 report on the “state of kidney disease” in the United States was released by the US Renal Data System (USRDS) Coordinating Center, based at the University of Michigan in partnership with Arbor Research Collaborative for Health. Rajiv Saran, MD, is director of the USRDS Coordinating Center and associate director of the University of Michigan’s Epidemiology and Cost Center.

**World Kidney Day 2015**

Themed “Kidney Health for All,” WKD highlights CKD challenges such as poor water, unhealthy food and beverage choices, and literacy.
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receptor function. What distinguishes this paper from previous work is that not only does it demonstrate an effect of extracellular pH on calcium-sensing receptor signaling and PTH release, but it demonstrates that in human parathyroid tissue, changes in extracellular pH within the physiologic range are capable of causing measurable changes in PTH secretion,” said R. Tyler Miller, MD, who was not involved in the study and is the vice chair of medicine at UT Southwestern Medical Center and chief of medicine at the Dallas VA Medical Center. “The paper also demonstrates that the effect of pH is on the receptor, not the cells or other components of the experimental system.”

The calcium-sensing receptor is expressed in a variety of tissues and organs including the kidney, brain, intestine, bone, and skin where extracellular pH could also affect its function.

Miller noted that other work indicates that alterations in human pH that occur with kidney disease, high altitude, and possibly with diets of varying composition can alter metabolism, muscle mass, and bone structure, but the mechanisms for these effects are unclear. Also, the physiologic effects of PTH are complicated and involve not just the level of PTH, but also the frequency of its release. “A long-term effect of pH on parathyroid function via PTH release is a reasonable possibility for some of the physiologic consequences of altered extracellular pH,” Miller said. “Precisely how PTH secretion is affected by extracellular pH will be interesting and valuable to learn as well as determining how pH and PTH secretion relate to long-term nutrition, body composition, and bone biology.”

Ward stressed that additional studies are needed before any clinical applications might be realized. “Firstly, we would need to confirm that this effect is true not only in human cells in the laboratory, but also in live patients. However, if confirmed, then this might reveal a novel mechanism by which acidosis and bone mineral changes might be related in CKD patients,” he said.

Article: “Pathophysiologic Changes in Extracellular pH Modulate Parathyroid Calcium-Sensing Receptor Activity and Secretion via a Histidine-Independent Mechanism” http://jasn.asnjournals.org/content/early/2015/01/01/ASN.2014070653.long