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# New Approach May Help Dialysis Patients Fight Anemia

***A new drug called FG-2216 can stimulate production of the hormone erythropoietin (EPO) in dialysis patients -- possibly offering a new approach to treatment of kidney disease-related anemia, according to a study appearing in an upcoming issue of the Journal of the American Society of Nephrology (JASN).***

Anemia is a major problem in patients with kidney disease. It is caused by low production of EPO, which has been assumed to result from damage to the kidney cells that produce EPO. "Our study clearly shows that this may not be the case, and that the kidneys of patients on dialysis retain significant ability to produce erythropoietin," comments Wanja M. Bernhardt, MD (Department of Nephrology, University hospital Erlangen, Germany). "Renal anemia seems to result from disturbed regulation rather than lost production capacity of the hormone."

The study evaluated an experimental drug called FG-2216. FG-2216 is a prolyl-hydroxylase inhibitor that stabilizes hypoxia-inducible transcription factor (HIF) -- the "master switch" that normally tells the body to produce EPO in response to low oxygen levels. EPO stimulates production of oxygen-carrying red blood cells.

Treatment with FG-2216 significantly increased EPO production in dialysis patients, as well as in healthy people with normal kidneys. The greatest increase in EPO production occurred in dialysis patients whose kidneys were still present, but no longer functioning.

FG-2216 also stimulated EPO production in dialysis patients who had no kidneys. (Their kidneys had been removed at surgery for cancer or other diseases.) The increase in EPO production in patients without kidneys was almost as high as in people with normally functioning kidneys. In the patients without kidneys, FG-2216 apparently stimulated production of EPO by the liver.

**Take-home message:** The results question the conventional wisdom that dialysis-related anemia occurs because patients with advanced kidney disease can no longer make their own EPO. "Our results confirm that both the liver and the kidneys retain a significant production capacity for erythropoietin in end-stage renal disease patients," says Bernhardt.

Currently, patients with dialysis-related anemia receive EPO replacement therapy with drugs called erythropoiesis-stimulating agents (ESAs). Despite almost two decades of use, there remains an ongoing controversy related to the safety, appropriate clinical use, and in particular high costs of ESAs. If the new results are borne out by future studies, then using prolyl-hydroxylase inhibitor such as FG-2216 to help the body make its own EPO might provide a new alternative to ESAs.

The preliminary study evaluated only the response to a single dose of FG-2216. Although there were no adverse effects, the results and long-term safety of activation of HIF by prolyl-hydroxylase inhibitors remain unclear. Further study will also be needed to find out why HIF is apparently not stabilized in response to decreased oxygen concentrations in patients with kidney disease but responds to treatment with prolyl-hydroxylase inhibitors.

Study co-authors include James Chou, Kai-Uwe Eckardt, Volkmar Gunzler, Roland Schmieder, Paul Scigalla, and Michael Wiesener.