Angiotensin II shows promise in helping critically ill patients with low blood pressure

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Sixty years after Cleveland Clinic researchers first isolated the role of angiotensin II in controlling blood pressure, a new international study led by Cleveland Clinic researchers shows that the compound can safely improve blood pressure among critically ill patients who are experiencing life-threatening hypotension, or low blood pressure.

The research - led by Ashish Khanna, M.D., an intensivist and anesthesiologist in Cleveland Clinic's Center for Critical Care - will be published online by the *New England Journal of Medicine*, in conjunction with the American Thoracic Society's special session on clinical research.

"Vasodilatory shock - in which a patient's blood pressure drops and blood vessels dilate - is a serious concern for ICU patients. When the condition is not responsive to high-dose vasopressors like norepinephrine and vasopressin, it is associated with high mortality, with more than half of these patients dying within 30 days," Dr. Khanna said. "We found that angiotensin II is an effective intervention for these patients, significantly increasing blood pressure in this life-threatening situation. The drug was safe and well-tolerated and also showed a trend to decreased mortality, though this did not achieve clinical significance."

The study enrolled 321 patients - 163 treated with angiotensin II and 158 with placebo - who were experiencing vasodilatory shock and had received high doses of conventional vasopressors.

Angiotensin II significantly improved hypotension (low blood pressure) - increasing mean arterial pressure at 3 hours - compared with placebo; nearly 70 percent of angiotensin II-treated patients (114 of 163) saw improved blood pressure compared with 23 percent of the placebo group (37 of 158 patients).

The trial was conducted in 75 intensive care units across nine countries in North America, Australia and Europe.

Angiotensin II was first isolated at Cleveland Clinic in the 1950s by Irvine Page, M.D., who discovered that the substance in blood causes blood vessels to constrict and blood pressure to rise. Along with co-researcher F. Merlin Bumpus, Ph.D., Page synthesized the peptide in 1957, helping to shape medicine's understanding of blood pressure and heart disease. For the first time, high blood pressure was viewed as a condition that could be treated, by blocking the body's production on angiotensin II.

In this new research, the goal was to raise blood pressure in critically ill patients in vasodilatory shock by providing exogenous Angiotensin II. It is the first and largest phase III randomized controlled trial of stable, synthetic human angiotensin II.

It was conducted under a special protocol assessment with the US Food and Drug Administration, which considers an uncompleted Phase III trial's design, clinical endpoints, and statistical analyses acceptable for FDA approval.

Provided by Cleveland Clinic

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