MedicalXpress

Investigational urate elevation does not appear to raise hypertension risk

November 9 2018

A study from a group of Massachusetts General Hospital (MGH) investigators may reduce the concern that elevating levels of urate, an approach being investigated to treat several neurodegenerative disorders, could increase the risk of hypertension. The study authors—several of whom previously conducted a phase 2 trial finding that the drug inosine safely elevated urate levels in patients with early Parkinson disease—are reporting their most recent findings in *EBioMedicine*, an open-access journal published by *The Lancet*.

"Our study does not support a hypertensive effect from urate elevation," says Xiqun Chen, MD, Ph.D., of the MGH Department of Neurology, lead author of the EBioMedicine report. "It also highlights the need for a more careful evaluation of urate-lowering treatments being investigated to treat hypertension."

Animal studies have suggested that the antioxidant urate could have neuroprotective effects, and observations in human patients —associations between naturally higher urate levels and reduced risk of developing Parkinson disease or slower disease progression—led to initiation of the two-year, phase 2 SURE-PD clinical trial, led by MGH neurologist Michael Schwarzschild, MD, Ph.D., senior author of the current study. The encouraging results of that trial, which enrolled 75 newly diagnosed Parkinson disease patients with relatively low urate levels, led to the initiation of the larger SURE-PD Phase 3 trial, which is currently underway.

But because significant evidence has suggested that higher urate is associated with hypertension, the team took a closer look at any potential effects on blood pressure among participants in the phase 2 SURE-PD trial. Among all three groups of participants—those receiving doses producing mild or moderate urate elevation or those receiving a placebo—there were no significant differences in blood pressure readings taken before, during or after the 18- to 24-month study period.

Those findings were further supported by experiments in mouse models genetically engineered to have either reduced urate or mild or moderate urate elevation. Those studies found no association of altered urate levels with significant differences in blood pressures between any of the genetically engineered mice and genetically unaltered control animals. In addition, the use of blood-pressure-manipulating agents had similar effects both on animals with elevated urate and on the controls, adding additional support to a lack of connection between urate levels and blood pressure.

"Together with the original report on the SURE-PD trial, this study provides strong evidence that long-term administration of oral inosine can be generally safe in patients with early Parkinson disease." says Chen, who is an assistant professor of Neurology at Harvard Medical School (HMS). "Although those SURE-PD participants were otherwise healthy with no obvious cardiovascular or renal disease, these findings may not be generalized to all patients. More studies are needed to definitively determine the role of urate in hypertension—including the potential of the urate-lowering drugs currently being investigated. Meanwhile, we are taking advantage of the current phase 3 inosine trial to monitor any possible risks of urate elevation in a larger group of patients."

More information: Xiqun Chen et al, Dissociation between urate and blood pressure in mice and in people with early Parkinson's disease,

EBioMedicine (2018). DOI: 10.1016/j.ebiom.2018.10.039