

PARKINSON DISEASE

Higher urate means less clinical decline in PD

Patients with Parkinson disease (PD) who have raised levels of urate in their serum or cerebrospinal fluid at diagnosis experience slower rates of clinical decline, according to a new study. “This finding builds on recent epidemiological data that showed that healthy individuals with higher urate levels have a lower risk of developing PD,” comments senior author Michael Schwarzschild (MassGeneral Institute for Neurodegenerative Disease, Boston, MA, USA). Schwarzschild adds that laboratory studies have shown that urate is a major antioxidant as well as the end product of purine metabolism in humans, and that it can prevent dopaminergic cell degeneration in culture models of PD.

The current study mined a database and biospecimen repository from DATATOP (Deprenyl and Tocopherol Antioxidant Therapy of Parkinsonism), a clinical trial involving 800 patients with PD that

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was conducted over 20 years ago. The hazard ratio (HR) for patients reaching the primary end point originally specified by DATATOP—the start of levodopa therapy—decreased with increasing baseline serum urate concentrations. The HR for the highest quintile compared with the lowest was 0.64 (95% CI 0.44–0.94). “These results strongly substantiate our findings from an independent cohort from PRECEPT, another large clinical trial, which also showed that higher serum levels of urate were predictive of a favorable outcome based on clinical and neuroimaging measures of disease progression,” explains Schwarzschild.

Given that urate seems to be a predictor of the risk and progression of typical PD,

urate or one of its determinants might prove to be neuroprotective in PD. “There is now a convergence of laboratory, epidemiological and clinical data to suggest that higher—but still normal—levels of urate, may slow the course of PD”, notes Schwarzschild.

The researchers have now begun a major phase II trial of inosine to elevate urate levels in patients with early untreated PD. Schwarzschild, who is directing SURE-PD (Safety of URate Elevation in PD), reports that this trial is being conducted under an Investigational New Drug application to the FDA and is intended to set the stage for a larger ‘disease modification’ trial of inosine in PD.

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Original article Ascherio, A. *et al.* Urate as a predictor of the rate of clinical decline in Parkinson disease. *Arch. Neurol.* doi:10.1001/archneurol.2009.247