MedicalXpress

Study supports possible role of urate in slowing Parkinson's disease progression

October 12 2009

By examining data from a 20-year-old clinical trial, a research team based at the MassGeneral Institute for Neurodegenerative Diseases (MGH-MIND) and Harvard School of Public Health (HSPH), has found evidence supporting the findings of their 2008 study - that elevated levels of the antioxidant urate may slow the progression of Parkinson's disease. The report - which will appear in the December 2009 *Archives of Neurology* and has been released online - analyzed blood and cerebrospinal fluid samples from participants in a 1980s trail of potential Parkinson's medications, confirming the previous study's findings in a totally different group of patients.

"These results were critically important. Only now we can be reasonably sure that the slower rate of progression in patients with higher concentrations of urate is real and not a chance occurrence," says Alberto Ascherio, MD, DrPh, of HSPH, the new study's lead author.

Parkinson's disease - characterized by tremors, rigidity, difficulty walking and other symptoms - is caused by destruction of brain cells that produce the neurotransmitter dopamine. The 2008 study, which investigated the observation that healthy people with elevated but still normal urate levels have a reduced risk of developing Parkinson's, found an association between higher blood urate levels and slower disease progression in 800 participants from a previous clinical trial.

To follow up that finding, the current study reviewed information from a much earlier trial that had investigated whether the drug deprenyl, now

an established treatment for Parkinson's, or doses of vitamin E would slow disease progression. The researchers analyzed samples of both blood and cerebrospinal fluid from 800 participants in the DATATOP study, conducted by the Parkinson's Study Group at centers across the U.S. and Canada, to find any association of urate levels with how quickly recently diagnosed patients progressed to the point where they needed to begin standard drug therapy.

Confirming the results of the 2008 study, they found that participants with the highest blood urate levels had a 36 percent less chance of needing to begin treatment during the two-year study period than did those with the lowest urate levels. Similar results were seen for urate levels in the cerebrospinal fluid. Also echoing last year's results, the association of urate levels with risk was robust in men but less clear in women, which may reflect the fact that few women have the high natural urate levels associated with risk reduction.

"Since cerebrospinal fluid circulates in and around the brain, the association with urate CSF levels strengthens the possibility that urate has a protective influence on the cells that degenerate in Parkinson's disease," says Michael Schwarzschild, MD, PhD, of MGH-MIND, the study's senior author. "Urate is a major antioxidant and it can protect brain cells in the lab, which makes this a compelling possibility; but we don't yet know if it's urate itself or some urate-determining factor that helps people with Parkinson's."

One unexpected observation was that the association of urate levels with disease progression was not seen in DATATOP trial participants who had received vitamin E, also a powerful antioxidant that had no effect on disease progression in the original study. The researchers speculate that vitamin E might block urate's effects or that the elevated doses in the DATATOP trial might have had a pro-oxidant effect, possibilities that need further investigation.

With the support of the Michael J. Fox Foundation, Schwarzschild and Ascherio, along with Parkinson Study Group colleagues from across the country, are conducting a multicenter Phase 2 trial at 10 centers. Enrolling 90 recently diagnosed patients, the SURE-PD trial will investigate whether treatment with the urate precursor inosine can safely increase urate levels with a goal of slowing disease progression. More information on this trial is available at http://www.pdtrials.org/en/browse/all/view/259.

"Because elevated urate levels have known health risks, including gout and kidney stones," Schwarzschild stresses, "urate elevation should only be attempted in the context of a closely monitored clinical trial in which potential benefits and risks are carefully balanced."

More information: *Arch Neurol.* 2009;66[12] doi:10.1001/archneurol.2009.247

Source: Massachusetts General Hospital (news : web)