Inosine halts disease progression and also neuroprotective effects of though up-regulation of urate levels in Parkinson's disease

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A population-based cohort study, reported that increased serum urate is thought be a predictor of decreased incidence of Parkinson's disease (PD) and slower progression in early PD. Inosine (hypoxanthine 9-beta-D-ribofuranoside), a precursor of urate, also serves as an extracellular modulatory signal. It has been shown trophic protective effects on neurons and to induce axonal growth following neuronal insult in vivo and in vitro. In this study, at first, we accomplished a single-arm, single-center clinical trial to assess safety issues of inosine oral administration for clinical use of PD patients. After informed consent, ten subjects were given oral inosine medications to maintain a target urate level between 6.0 mg/dl and 8.0 mg/dl for one year. Any adverse events were not shown by the participants that might be required dose adjustment or termination, although uric acid crystalluria was transiently observed in a single subject. An inosine dosage of 1070 (SD = 501) mg/day significantly raises the urate level from 3.5 (0.84) mg/dl at baseline to 6.68 (1.11) mg/dl at the 52nd week. Then, we employed 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine (MPTP)-induced in a murine model of PD to explore insight into the mechanism of inosine in PD. Our HPLC studies on MPTP-treated animals model showed the protective effect of inosine by showing increased contents of dopamine as compared to controls (MPTP, P<0.05). Our flow cytometry analysis also showed that the degeneration of dopaminergic neurons in the substantia nigra were rescued by inosine pretreatment, although no improvement in the motor behavior was observed. To go further, we examined the anti-inflammatory effects of inosine on BV2 cells (murine microglial cell line). Inosine treatments suppressed nitric oxide release in LPS-treated microglial cells, suggesting that the anti-inflammatory effect of inosine. Collectively, our results suggest that inosine induces a neuro-protective of the dopaminergic effect and anti-inflammatory on microglial cells which support further studies to investigate the potential of a diet-based intervention, or at least the combination of such approach, to current treatments in PD.