Plasma Urate in REM Sleep Behavior Disorder

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ABSTRACT

Background: Rapid eye movement (REM) sleep behavior disorder (RBD) is associated with a high risk of developing Parkinson's disease (PD). Higher urate levels are associated with a lower risk of PD. We conducted a study to evaluate plasma urate levels in patients with RBD and their role in the development of PD.

Methods: We evaluated plasma urate levels in a cohort of 24 patients with idiopathic RBD. Patients were divided into 2 groups according to the presence or absence of PD. Other known markers of the risk of developing PD, such as olfaction testing, and substantia nigra (SN) hyperechogenicity, were evaluated in the 2 groups.

Results: No differences were observed regarding age, years of evolution of the RBD, SN hyperechogenicity, or plasma urate levels between the 2 groups. In patients without PD, there was a positive correlation between years of evolution of RBD and the levels of uric acid ($R^2 = 0.88$). Patients without PD and those who had more than 5 years of RBD exhibited higher levels of uric acid than patients with PD ($P = 0.02$).

Conclusions: Higher levels of plasma urate were associated with a longer duration of RBD without converting to PD. Future prospective studies would be needed to confirm this finding. Disorder Society.

Key Words: REM sleep behavior disorder; urate; Parkinson's disease; premotor manifestations

Rapid eye movement (REM) sleep behavior disorder (RBD) is a parasomnia characterized by abnormal behavior during REM sleep. Recent studies suggest that over 50% of individuals with idiopathic RBD will develop Parkinson's disease (PD) or dementia.[1,2] Previous studies have identified several potential biomarkers of the onset and progression of PD.[3] In particular, hyperuricemia has been associated with a lower risk of PD onset and progression.[4,5] However, there is no information regarding urate levels in patients with RBD and their implication in the development of PD in this population. We conducted a study to evaluate plasma urate levels in patients with RBD and their role in the development of PD.

Patients and Methods

All patients were evaluated at the Sleep Center of the Neurology Department of the Pontificia Universidad Catolica de Chile between 2000 and 2011. Individuals who met the diagnostic criteria of RBD,[6] including undergoing nocturnal polysomnography, and who did not use uric-acid–modifying drugs were included in this study. The study protocol was approved by the Ethics Committee of the institution, and each patient provided written, informed consent.

First, we performed a clinical screening using a validated RBD questionnaire.[7] For the diagnosis of PD, the London Brain Bank criteria were used. In addition, olfaction was evaluated using the Sniffin' Sticks test.[8] Substantia nigra (SN) hyperechogenicity was assessed using transcranial ultrasonography performed as previously described.[9] Uric acid concentration was assessed in triplicate experiments (Roche Modular Analytics Enzymatic Colorimetric Test; Roche Diagnostics, Mannheim, Germany). Data were analyzed using IBM SPSS Statistics 20.0 software (IBM, Armonk, NY). The Fisher's exact test and the Mann–Whitney test were used as appropriate.

Results

Twenty-four patients (20 men) met the diagnostic criteria for RBD. Two groups were established: individuals with PD (11 patients) and without PD (13 patients). There were no differences between the 2 groups regarding sex, age, RBD duration, scores in the RBD questionnaire, SN hyperechogenicity, Sniffin' Stick test scores, or levels of uric acid.

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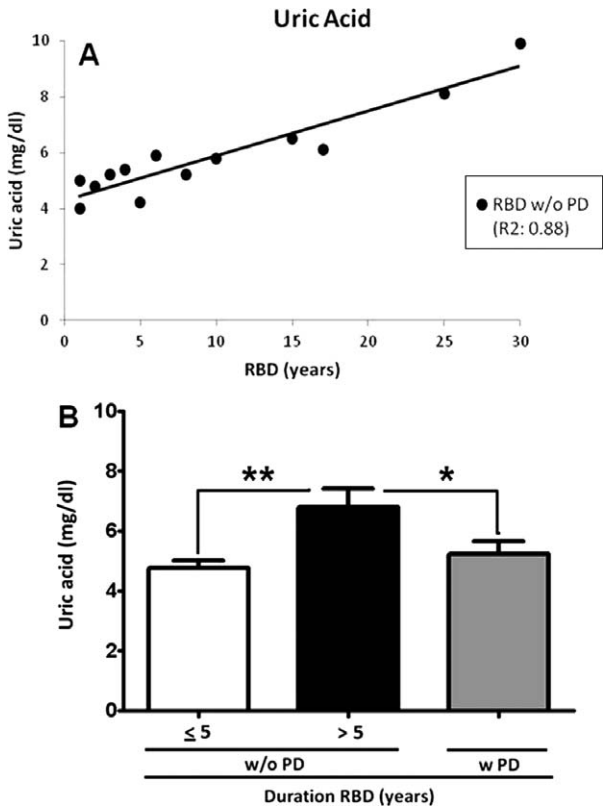

FIG. 1. Correlation between uric acid levels and the evolution over time of rapid eye movement (REM) sleep behavior disorder (RBD) is illustrated. (**A**) In patients who had RBD without Parkinson's disease (w/o PD), a close correlation was observed between the years of RBD evolution and plasma uric acid levels (correlation coefficient [R^2], 0.88). (**B**) Higher plasma uric acid concentrations were observed in patients who had more than 5 years of RBD (7 patients) compared with those who had less than 5 years of RBD (6 patients) and patients with PD (w PD) (11 patients). Double asterisks indicate $P = 0.007$; single asterisk, $P = 0.02$.

There was a positive correlation between the levels of uric acid and the time of evolution of RBD without PD (13 patients; $R^2 = 0.88$) (Fig. 1A). This correlation was unaffected by correction for age. Patients without PD and with more than 5 years of RBD (7 patients) exhibited higher levels of uric acid than patients with less than 5 years of disease evolution (6 patients; $P = 0.007$) and patients with PD (11 patients; $P = 0.02$) (Fig. 1B). There was no correlation between RBD duration and uric acid levels in the PD group ($R^2 = 0.03$). Moreover, an analysis of the hyperechogenicity area and olfaction test scores revealed an absence of other correlations.

Discussion

Our study demonstrated higher levels of plasma urate in individuals who had a longer duration of RBD without converting to PD, suggesting that urate may act as a modifying factor in the progression of neurodegeneration in patients with RBD. According to this observation, plasma urate levels may be a useful marker for the evaluation of the risk of conversion to PD in patients who have newly diagnosed RBD. Because of methodological limitations (small sample size, cross-sectional design), our results should be considered as preliminary, and future prospective studies would be needed to confirm this finding.

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