

Increased Nectin-4 Levels in Chronic Ketamine Abusers and the Relationship with Lower Urinary Tract Symptoms

Hu-Ming Chang¹, Yu-Li Liu², Ming-Chyi Huang¹

¹ Department of Addiction Sciences, Taipei City Psychiatric Center, Taipei City Hospital, Taipei, Taiwan

² Center for Neuropsychiatric Research, National Health Research Institutes, Miaoli County, Taiwan

Background

Persistent ketamine use causes susceptibility to addiction and bladder toxicity. We examined the association of lower urinary tract symptoms and levels of Nectin-4, a member of the cell adhesion molecules that is essential for maintaining the urothelium barrier in chronic ketamine abusers.

Aims & Objectives

In this study, we aimed to explore the role of Nectin-4 in ketamine-associated LUTS. To achieve this goal, we first compared the blood Nectin-4 levels between treatment-seeking ketamine-dependent patients and healthy controls. Second, we examined the correlation of Nectin-4 levels with clinical symptoms and subjective ratings of LUTS. Third, we evaluated whether the Nectin-4 levels differed between chronic ketamine users with and without LUTS.

Methods

Treatment-seeking patients with KD who voluntarily admitted to an inpatient ward for detoxification were consecutively screened for their eligibility to participate in this study. We measured the plasma levels of Nectin-4 in 88 patients with ketamine dependence and 69 controls. Patients with ketamine dependence were assessed for ketamine use variables, psychological symptoms, and lower urinary tract symptoms.

Results

A total of 157 participants (88 patients with KD and 69 gender-matched controls) were enrolled in the study. All of them reported snorting as the main route of ketamine administration, which is reported to cause more severe LUTS compared with smoking. The patients with KD scored 33.1 ± 33.9 mm on the VAS craving scale, and expressed high levels of ketamine dependence severity, depression and anxiety. The plasma level of Nectin-4 was significantly higher in the patients with KD than in controls ($p < 0.0001$).

The correlations between Nectin-4 levels and the demographics, ketamine use parameters, and clinical variables of patients with KD are presented in Table 2. The level of Nectin-4 was negatively correlated with BMI in patients with KD ($p = 0.045$). Nectin-4 level was not significantly correlated with smoking; ketamine use parameters; VAS for craving; and SDS, BDI, and BAI scores.

To examine the correlation between Nectin-4 level and LUTS in patients with KD, we further divided the patients in two subgroups according to their LUTS: 44 patients with LUTS and 34 without LUTS. We used the Mann–Whitney U test to determine that the Nectin-4 level in patients without LUTS was higher than that in patients with LUTS after adjusting for age, BMI, and smoking ($p = 0.021$).

Discussion & Conclusion

Our results suggest an up-regulation of Nectin-4 following chronic and heavy ketamine use. Patients with ketamine dependence with a compromised upregulation of Nectin-4 are likely to have more severe urinary tract symptoms.