Intact urothelial barrier function in a mouse model of ketamine induced voiding dysfunction

Retnagowri Rajandram, Teng Aik Ong, Azad Hassan Abdul Razack, Bryce MacIver, Mark Zeidel, Weiqun Yu
American Journal of Physiology - Renal Physiology Published 24 February 2016 Vol. no. DOI: 10.1152/ajprenal.00483.2015

Abstract

Ketamine is a popular choice for young drug abusers. Ketamine abuse causes lower urinary tract symptoms, with the underlying pathophysiology poorly understood. Disruption of urothelial barrier function has been hypothesized to be a major mechanism for ketamine cystitis, yet the direct evidence of impaired urothelial barrier function is still lacking. To address this question, 8-week old C57BL/6J female mice were injected intraperitoneally with 30mg/kg/day ketamine for 12 weeks to induce ketamine cystitis. Spontaneous voiding spot assay showed that ketamine treated mice had increased primary voiding spot (PVS) numbers, and smaller PVS size than control mice (p < 0.05), indicating a contracted bladder and bladder overactivity. Consistently, significantly increased voiding frequency was observed in ketamine-treated mice on cystometrograms (CMGs). These functional studies indicate that ketamine induces voiding dysfunction in mice. Surprisingly, the urothelial permeability in
ketamine treated mice was not changed when measured using an Ussing chamber system with isotopic urea and water. Mouse urothelial structure was also not altered, and intact umbrella cell structure was observed by both transmission and scanning electron microscopy. Furthermore, immunostaining and confocal microscopy confirmed the presence of well-defined distribution of ZO-1 in the tight junctions and uroplakin in the umbrella cells. In conclusion, these data indicate that ketamine injection induces voiding dysfunction in mice, but does not necessarily disrupt mouse bladder barrier function. Disruption of urothelial barrier function may not be the major mechanism in ketamine cystitis.