Letter to the editor: “Urothelial barrier dysfunction: cause or outcome of ketamine-induced voiding dysfunction”

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TO THE EDITOR: Ketamine-induced cystitis was first reported by Shahani et al. in 2007 (6). Clinical presentations of this entity is characterized by lower urinary tract symptoms (LUTS), such as frequency, urgency, gross hematuria, and bladder pain (2, 6). The underlying mechanisms are still unelucidated in ketamine-induced cystitis, and the approaches to therapy include cessation of ketamine, medicine relieving symptoms, and surgical interventions.

Bladder barrier dysfunction is a possible mechanism in the pathogenesis of ketamine-induced cystitis. Bladder mucosa ulceration and urothelial denudation could be easily found in these patients, and intravesical treatment with mucosa-protective agents was also verified to relieve patients’ symptoms (7). These indicated bladder urothelial barrier dysfunction might be a potential contributor to the pathogenesis of ketamine-induced cystitis. Bladder tissue samples from ketamine abusers or animal models showed downregulating expressions of E-cadherin, which was a cell adhesion molecule (3, 4). Some researchers also revealed that the expression of tight junction proteins (zonula occludens-1, claudin-4) were obviously downregulated in ketamine-induced animal models (1, 4). These results pointed out that the urothelial barrier was disrupted in ketamine-induced cystitis to some extent. So, urothelial barrier dysfunction may be involved in the pathogenesis of ketamine-induced cystitis, after which secondary injuries caused by inflammation or potassium leakage would accelerate voiding dysfunction (1, 2).

However, a recent study conducted by Rajandram et al. (5) didn’t support previous opinions about the role of urothelial barrier function in ketamine-induced cystitis. In this study, urothelial permeability and urothelial structure are intact in the ketamine group (5). The authors held the viewpoint that urothelial barrier dysfunction might be caused by bladder stress and overactivity of mechanotransduction from accumulated ketamine and its metabolites in urine, and urothelial barrier dysfunction wasn’t the reason or direct pathogenesis of voiding dysfunction (5). This research might arrive at a conclusion that urothelial barrier dysfunction may be an outcome of ketamine-induced voiding dysfunction. We think this is just a preliminary result, and dynamic monitoring of urothelial barrier function and structure would provide more convincing conclusions. In addition, animal models of different species and suitable doses according to ketamine concentration in serum and urine should also be taken into consideration.

According to previous research, the role of bladder barrier function in the pathogenesis of ketamine-induced cystitis is still under investigation. Further studies will provide more information to reveal the precise mechanisms about urothelial barrier dysfunction in ketamine abusers. However, urothelial barrier dysfunction is still a potential factor to promote voiding dysfunction. We think urothelial barrier dysfunction is a stage in the pathogenesis of ketamine-induced cystitis, although the precise mechanisms need to be further investigated. Therefore, we recommend intravesical mucosa-protective agents as one of the indicated protocols in dealing with ketamine-induced cystitis currently.

DISCLOSURES

No conflicts of interest, financial or otherwise, are declared by the authors.

AUTHOR CONTRIBUTIONS

Z.W. provided conception and design of research; Z.W. drafted manuscript; L.W. and L.-f.L. analyzed data; Y.-m.H. and Z.-y.T. edited and revised manuscript.

REFERENCES


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