156

Tsai Y[1], Lee C[2], Jhang J[2], Jiang Y[3], Kuo H[2]

1. *Department of Urology, Taipei Tzu Chi Hospital, Buddhist Tzu Chi Medical Foundation, New Taipei, Taiwan,* ***2.*** *Department of Urology, Buddhist Tzu Chi General Hospital and Tzu Chi University, Hualien, Taiwan,* ***3.*** *Department of Urology, Buddhist Tzu Chi General Hspital and Tzu Chi University, Hualien, Taiwan*

IMMUNOHISTOCHEMISTRY STUDY OF KETAMINE RELATED CYSTITIS – A CORRELATION WITH CLINICAL CHARACTERISTICS WITH UROTHELIAL DYSFUNCTION AND CHRONIC INFLAMMATION

Hypothesis / aims of study

Ketamine related cystitis (KC) is a recently emergent bladder disease characterized by severe bladder irritative symptoms, bladder pain, small voided volume and upper urinary tract deterioration after long-term ketamine abuse. The changes of the bladder histology have not been well elucidated to explain the disease progression of this disease. In this study, we compared the urothelial dysfunction, chronic inflammation and expressions of sensory proteins in the bladder urothelium and tried to correlate these parameters with the clinical characteristics.

Study design, materials and methods

The bladder mucosa biopsies from 29 patients (17 men and 12 women, mean age 25.4±4.3 years) with KC and 10 controls (all women, mean age 50.5±9.6 years) were collected for immunohistochemistry study (IHC) of the urothelial dysfunction and sensory protein expressions. Patients with KC were divided according to the clinical characteristics as severe KC and mild KC. The IHC study of the urothelial dysfunction included TUNEL for urothelial apoptosis, mast cell activities for inflammation, E-cadherin and zonula occludin-1 (ZO-1) expressions for urothelial cell junction function. Functional protein expressions including muscarinic receptors M2, M3, TRPV-1, TRPA-1 and TGF-beta were also assessed. The urothelial dysfunction and functional protein expressions were compared between KC and control bladders and between severe and mild KC bladders.

Results

The TUNEL, mast cell activity, M3 and TGF-beta expressions were significantly increased in KC bladder than in the controls (Table 1), indicating a significantly higher inflammatory process in the KC bladders. Significantly decreased E-cadherin and ZO-1 expressions ere also noted in KC bladders, which explained the urothelial dysfunction and defective barrier function in KC bladders (Fig. 1). Increased M3 expression in KC bladders correlated with a higher incidence of detrusor overactivity. The increased TGF-beta expression further linked the contracted bladder and decrease of bladder capacity (Fig. 2).

Interpretation of results

Significantly increased inflammation, increased urothelial apoptosis and decreased junctional protein expression were noted in KC bladders. These IHC results correlated with severe bladder pain, irritative sympoms and reduced bladder capacity in severe KC bladders

Concluding message

Inflammation leading to urothelial dysfunction and upregulation of M3 receptors were evident in KC bladder and causes bladder symptoms.

Table 1. The urothelial dysfunction between KC and control bladders

	Normal (N=10)	Ketamine Cystitis (N=29)	P-value
TUNEL	0.08 ± 0.26	3.63 ± 2.38	0.000
Mast cell	1.25± 1.15	8.75 ± 5.69	0.000
E-cadherin	42.41 ± 16.73	13.86 ± 15.74	0.000
ZO-1	11.02 ± 5.66	3.64 ± 4.77	0.000

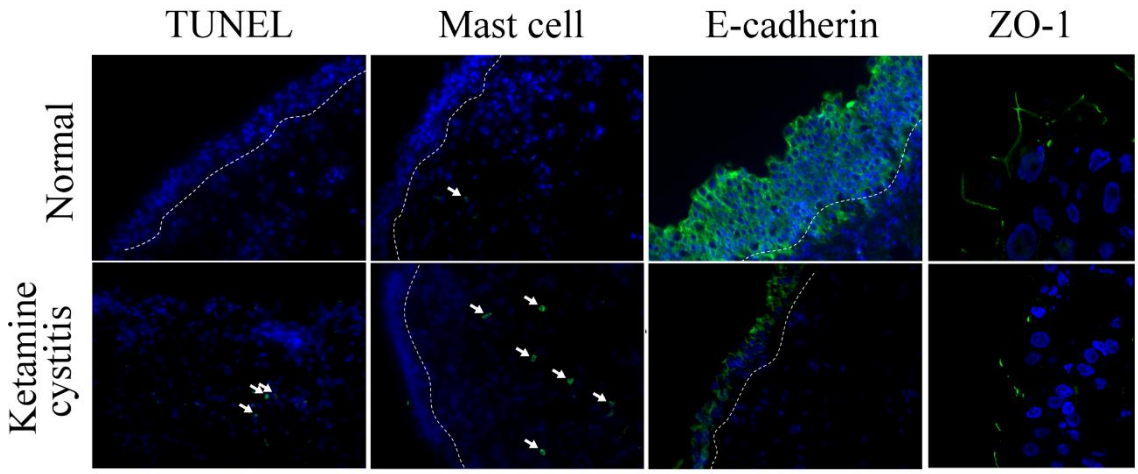

Fig. 1. Increased apoptotic cell count, increased mast cell activity, decrease E-cadherin, and decrease ZO-1 expression in the urothelium of ketamine cystitis compared with the control.

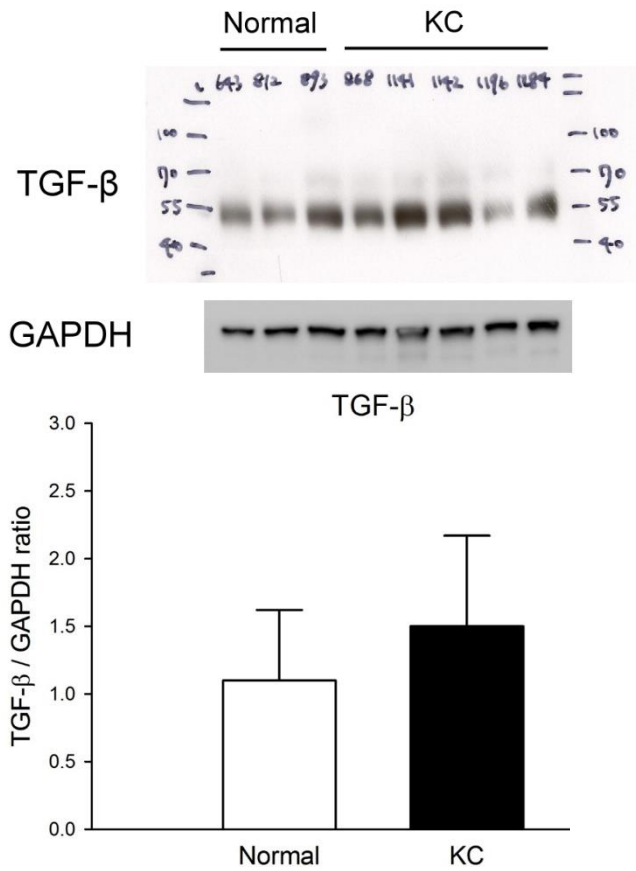

Fig. 2. The TGF-beta expressions in KC bladders compared with the controls.

Disclosures
Funding: NONE **Clinical Trial:** No **Subjects:** HUMAN **Ethics Committee:** Research Ethics Committee of Buddhist Tzu Chi General Hospital **Helsinki:** Yes **Informed Consent:** Yes