Correlation of transient receptor potential cation channel subfamily V proteins in patients with different clinical severity of ketamine cystitis

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INTRODUCTION

The abuse of ketamine can injure the bladder and cause ketamine cystitis (KC), which was first documented in a case report in 2007 [1]. KC patients often suffer from increased voiding frequency, urgency, pain, and decreased capacity. It is known that the bladder contractile activity is controlled by the sensory and motor nerve within the mucosa layer. However, the specific identity of the mechanical sensor is not clear yet. Transient receptor potential (TRP) channels expressed in the lower urinary tract are thought to be involved in the physiological and pathological function of the bladder [2]. Here we are interested in the roles of transient receptor potential cation channel subfamily V (TRPV) in the pathophysiology of KC.

AIMS OF STUDY

To investigate the roles of TRPV proteins in the pathogenesis of KC patients using the correlation of these proteins with the severity of clinical symptoms.

STUDY DESIGN, MATERIALS AND METHODS

Bladder tissues from 12 patients with severe KC, and 12 patients with mild KC, and 4 asymptomatic control (AC) subjects were analyzed. All patients with severe KC underwent videourodynamic study followed by augmentation enterocystoplasty to increase bladder capacity. Patients with mild KC received conservative treatment after cystoscopic hydrodistention. Bladder specimens were retrieved from partial cystectomy in severe KC, and from bladder biopsies in mild KC. Western Blot was used to examine the expression level of TRPV proteins in severe KC, mild KC and control. The Pearson test was used for correlations between these protein expression level and the clinical characteristics.

RESULTS

Table 1 Clinical characteristics and Western blot analysis of TRPV proteins in severe KC, mild KC and control.

	Control	Mild	Severe	P value
Clinical Characteristics				
Number	4	12	12	
Sex (F:M)	2:2	2:10	5:7	
Age	55.0 ± 4.2	28.2± 4.9	27.4 ± 5.2	
CBC		138.8 ± 50.5	48.9 ± 12.2	0.001
MBC		333.3 ± 68.3	127.5 ± 82.2	0.003
VAS		2.2 ± 1.5	7.5 ± 2.3	0.002
dPdet/dt		3.1 ± 1.1	5.3 ± 2.9	0.076
Western Blot				
TRPV1 /GADPH	0.08 ± 0.04	0.25 ± 0.27	0.91 ± 0.55	0.13 (C vs M) 0.004 (C vs S) 0.002 (S vs M)
TRPV4 /GADPH	0.04 ± 0.02	0.06 ± 0.05	0.23 ± 0.20	0.762 (C vs M) 0.045 (C vs S) 0.005 (S vs M)

Smaller bladder capacity, larger visual analogue scale and dPdet/dt were observed in the severe KC patients than in the mild KC patients. Compared with mild KC patients and control subjects, the expression of TRPV1 and TRPV4 were significantly increased in the bladder of severe KC patients.

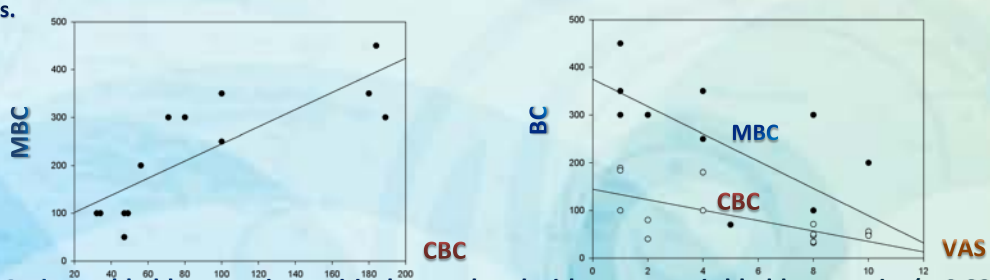

Figure 1. Maximum bladder capacity positively correlated with cystometric bladder capacity (r=0.82, p<0.001) and bladder capacity negatively correlated with VAS (r=-0.75, p=0.002 for MBC and r=-0.68, p=0.005 for CBC)

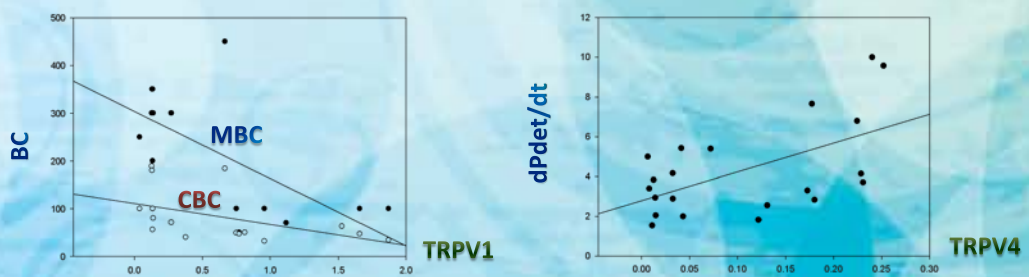

Figure 2. Bladder capacity negatively correlated with TRPV1 (r=-0.66, p=0.01 for MBC and r=-0.48, p=0.06 for CBC) and dPdet/dt positively correlated with TRPV4 (r=0.56, p<0.008)

Interpretation of results

This study demonstrated that the etiology of KC might be correlated with TRPV1 and TRPV4.

Conclusion

Increased TRPV1 and TRPV4 expression are seen in bladder form severe KC patients. TRPV1 may contribute to the pathophysiology of pain and TRPV4 may contribute to the pathophysiology of bladder capacity in KC patients.

Reference

1. Shahani R, Streutker C, Dickson B, Stewart RJ (2007) Ketamine associated ulcerative cystitis: a new clinical entity. Urology 69:810–812.
2. Merrill L, Gonzalez EJ, Girard BM, Vizzard MA (2016) Receptors, channels, and signalling in the urothelial sensory system in the bladder. Nat Rev Urol. 13:193-204.