

ELEVATED SERUM IMMUNOGLOBULIN E AND BLADDER EOSINOPHILS INFILTRATION SUGGEST HYPERSENSITIVITY MIGHT CONTRIBUTE TO THE PATHOGENESIS OF KETAMINE CYSTITIS

Hypothesis / aims of study

The number of ketamine related cystitis (KC) is increasing, but the pathogenesis of KC is still unclear. Previous studies revealed bladder mast cell and eosinophil cell increased infiltration in patients with KC. Mast cell and eosinophil in tissue usually suggested hypersensitivity. This study investigated the possibility of hypersensitivity as pathogenetic mechanism of KC.

Study design, materials and methods

KC patients were investigated for MBC, serum immunoglobulin (Ig) E, IgG, IgM, drug abuse history, and pain VAS. Patients who continued to use ketamine in the most recent month preceding hospitalization were considered current drug abusers. Bladder biopsies were obtained for evaluation of mast cell and eosinophil. Bladder specimen was graded by the inflammation and eosinophil infiltration on a 4-point scale (0: none, 1: mild, 2: moderate, and 3: severe). Patients with interstitial cystitis/bladder pain syndrome (IC/BPS), acute bacterial cystitis and normal controls were also investigated for serum IgE, IgM and IgG. Mann-Whitney U test for non-parametric data was used to compare serum IgE among groups.

Results

Twenty patients with KC, 13 IC/BPS, 15 acute bacterial cystitis and 10 healthy controls were enrolled. The mean serum IgE level in KC patients was significantly higher in KC group (447.3±611 IU/mL) than that in IC/BPS (113.2±145.2 IU/mL), acute bacterial cystitis (80.4±85.1 IU/mL) and controls (74.8±98.4 IU/mL). The mean VAS pain score of KC patients with serum IgE >200 IU/mL was significantly greater than that of KC patients with serum IgE <200 IU/mL (8.2±1.1 vs. 4.4±2.2, p=0.001) (Table 1). MBC was significantly smaller in KC patients with higher IgE. The patients with recently use of ketamine had higher serum IgE. The patients with severe or moderate bladder eosinophil infiltration had greater mean VAS, higher serum IgE, and smaller MBC (Table 1). In addition, serum IgE and VAS were significantly correlated ($r^2=0.318$, p=0.01) (Fig.1).

Interpretation of results

The KC patients had higher serum IgE than the patients with IC/BPS, acute bacterial cystitis and normal controls. The bladder biopsy specimen also showed eosinophil infiltration in almost every patients. The serum IgE and submucosal eosinophil is correlated with clinical symptoms. These evidences suggest hypersensitivity might be the pathogenesis of KC.

Concluding message

Elevated serum IgE level and eosinophil infiltration in bladder specimen suggest hypersensitivity might contribute to the pathogenesis of KC.

Table 1. Symptoms and serum immunoglobulin levels in different subgroups

| | Abuse duration | Symptom duration | VAS (scale) | CBC (mL) | MBC (mL) | IgE (IU/mL) | IgM (IU/mL) | IgG (IU/MI) |
|---------------|----------------|------------------|-------------|------------|-------------|-------------|-------------|--------------|
| IgE>200(n=11) | 70.9±43.3 | 23.1±17.3 | 8.2±1.1 | 63.0±25.8 | 139.1±64.1 | 790.8±649.9 | 114.6±54.3 | 1086.6±257.3 |
| IgE<200(n=9) | 48.7±19.5 | 17.2±11.8 | 4.4±2.2 | 99.2±77.9 | 314.4±274.3 | 27.5±17.8 | 103.4±31.6 | 970.9±315.4 |
| P value | 0.333 | 0.457 | 0.001 | 0.424 | 0.027 | 0.000 | 0.849 | 0.253 |
| Current use | | | | | | | | |
| Yes (n=14) | 57.9±39.1 | 18.6±16.3 | 7.7±1.7 | 58.2±24.4 | 148.6±60.4 | 579.1±673.4 | 121.4±47.8 | 1056.4±242.7 |
| No (n=6) | 68.0±28.1 | 24.7±11.7 | 3.7±1.6 | 128.5±81.5 | 380.0±323.4 | 139.8±285.1 | 81.9±19.2 | 983.5±383.8 |
| P value | 0.424 | 0.218 | 0.002 | 0.029 | 0.084 | 0.039 | 0.025 | 0.172 |
| Eosinophil | | | | | | | | |
| 2-3 (n=8) | 75.8±39.4 | 24.0±17.0 | 8.3±0.9 | 59.3±27.9 | 128.8±48.2 | 794.9±699.5 | 105.2±39.7 | 975.6±129.6 |
| 0-1 (n=9) | 58.0±30.0 | 18.6±11.8 | 4.7±2.5 | 93.8±79.5 | 308.9±277.4 | 192.3±502.3 | 99.9±30.1 | 958.4±316.3 |
| P value | 0.430 | 0.651 | 0.009 | 0.360 | 0.039 | 0.004 | 0.700 | 0.287 |

CBC: cystometric bladder capacity, MBC: maximal bladder capacity, VAS: visual analog scale.

Eosinophil infiltration grading: 0: none, 1: mild, 2: moderate, and 3: severe.

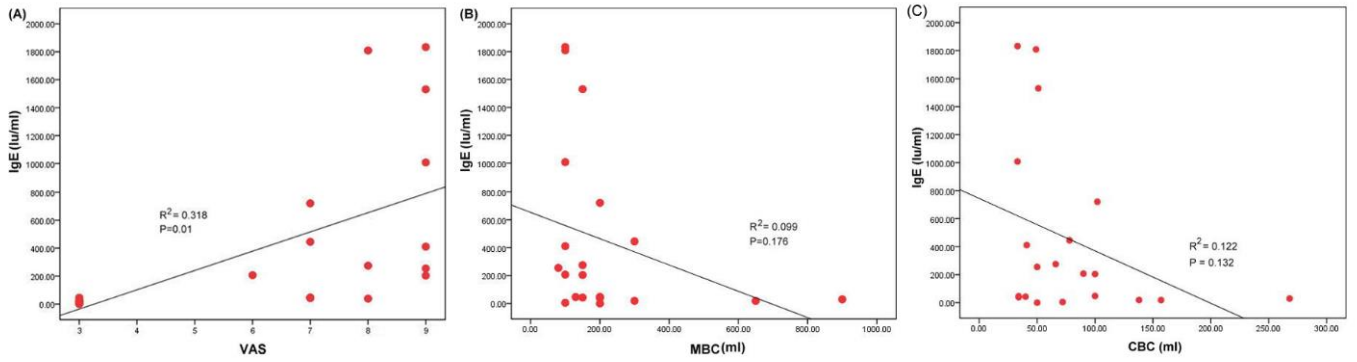


Fig. 1. Correlations of (A) visual analog scale for pain (VAS) and serum IgE levels and (B) maximum bladder capacity (MBC) and serum IgE levels (C) cystometric bladder capacity. (CBC) and serum IgE levels in patients with ketamine cystitis.

Disclosures

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