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THE TH1/TH2/TH17/TREG CELLS IMBALANCE IN PATIENTS WITH KETAMINE CYSTITIS

Hypothesis / aims of study

Chronic ketamine use may cause ulcerative cystitis and bladder dysfunction, commonly referred to ketamine cystitis (KC). The pathogenesis of KC has recently been linked to an immune response to ketamine but has not yet been definitively established. This study proposes a novel immune mechanism to explain the irreversible bladder damage caused by KC.

Study design, materials and methods

Twenty-six KC patients and 24 healthy volunteers were included in this study. Demographic, clinical and serological data were retrospectively assessed. Each KC patient was interviewed and a histological analysis was run on urothelial samples to determine the severity of inflammation. Plasma cytokines levels of TH1 (IL-2, IFN-γ), TH2 (IL-4, IL-5), TH17 (IL-6, IL-17) and Treg (TGF-ß) were measured by enzyme-linked immunosorbent assays (ELISA). Flow cytometry was used to assess the population of TH1, TH2 and TH17 in CD4+ T cells.

Results

Serum IgE was significantly higher in KC patients (261.59 ± 56.03 IU/ml). KC patients were found to have significantly higher levels of IL-6 ($p < 0.05$) and IFN-γ ($p < 0.001$), and significant reduction of TGF-b levels, but comparable levels of IL-2 and IL-4 compared to control patients. KC patients also had significantly higher counts of TH1, TH2, and TH17 cells than healthy volunteers ($p = 0.0001$).

Interpretation of results

- IL-6, a cytokine that promotes the development of TH17 cells, is higher in KC patients than in healthy subjects suggesting that the balance between TH17 and TH1 responses as well as IL-6 production is dysregulated in KC, resulting in reinforced feedback that increases IL-1□ and IL-17 production from CD4+ T cells. This increase may contribute to disease pathogenesis.
- Significant lower concentration of TGF-□3 in the KC group may explain the impaired healing capability of the bladder epithelial lining in chronic KC patients.
- IL-6 derived from APCs may initiate IL-4 production in naive CD4+ T cells, thereby polarizing these cells into TH2 cells

Concluding message

The immune response of KC may begin with the differentiation of TH17 and continue by alternating between high expression of TH1 and TH2. Suppression of TREG cells may aggravate chronic inflammation in KC patients. The imbalance of TH1, TH2, TH17 and TREG may involve the pathogenesis of KC.

Disclosures

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