ORAL TREATMENT WITH A VITAMIN D3 ANALOGUE SHOWS ANTI INFLAMMATORY EFFECTS AND REDUCES BLADDER OVERACTIVITY IN RODENT MODELS OF CHRONIC CYSTITIS

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INTRODUCTION AND OBJECTIVE: Vitamin D analogues possess anti-inflammatory effects and improve histological signs and clinical symptoms in animal models of inflammatory bowel disease and psoriasis. In this study we investigated the effects of a vitamin D3 analogue (BXL628) in two well established animal models of chronic cystitis; the mouse model of allergic cystitis and rat model of cyclophosphamide (CYP) induced cystitis.
METHODS: BALB/c female mice were sensitized by injection of chicken ovalbumin (Sigma OVA, grade V, 10 µg/mouse), followed by a slow intravesical instillation of 150 µl of OVA. The levels of inflammatory markers in the bladder were evaluated and compared between mice receiving oral BXL628 or sham treatment. Chronic cystitis was induced in female Wistar rats by three intraperitoneal injections of CYP (75 mg/kg in three days intervals). The bladder function was assessed *in vivo* in freely moving animals using continuous intravesical infusion (10 mL/hour) with recording of the intravesical pressure and voided volume.
RESULTS: Intravesical OVA injection resulted in edema of the submucosa, massive infiltration of both the submucosal and muscle layers by eosinophils, lymphocytes, basophils and mast cells and local and systemic signs of mast cell activation as evidenced by increased expression and release of mast cell proteases (MMCP-1, MMCP-2, MMCP-4). The oral administration of BXL628 at a dose that did not cause hypercalcemia resulted in a significant reduction of bladder inflammation as evidenced by diminished leukocyte infiltration and decreased expression of mast cell proteases. Functionally the treatment group showed significant increase in bladder capacity and decrease in both number and amplitude of non-voiding bladder contractions (NVBC). The cystometric data are summarized in the following table.
CONCLUSIONS: Oral treatment with vitamin D3 analogue BXL628 exerts anti-inflammatory and desirable functional effects on the urinary bladder in two distinct animal models of chronic bladder inflammation. Vitamin D analogues represent a new promising therapeutic option for interstitial cystitis.

Group	Capacity(mL)	Voiding pressure (cm H_20)	Number of NVBC	Amplitude of NVBC
Sham treated	1.2 ± 0.1	103.6 ± 4.1	21.8 ± 4.0	16.8 ± 1.9
BXL628 treated	2.1 ± 0.1	90.5 ± 3.1	8.3 ± 1.9	13.6 ± 1.3