

BXL-628, A VITAMIN D RECEPTOR AGONIST, RESTORES NERVE-INDUCED CONTRACTIONS IN PROSTATES FROM MICE WITH AUTOIMMUNE PROSTATITIS

Hypothesis / aims of study

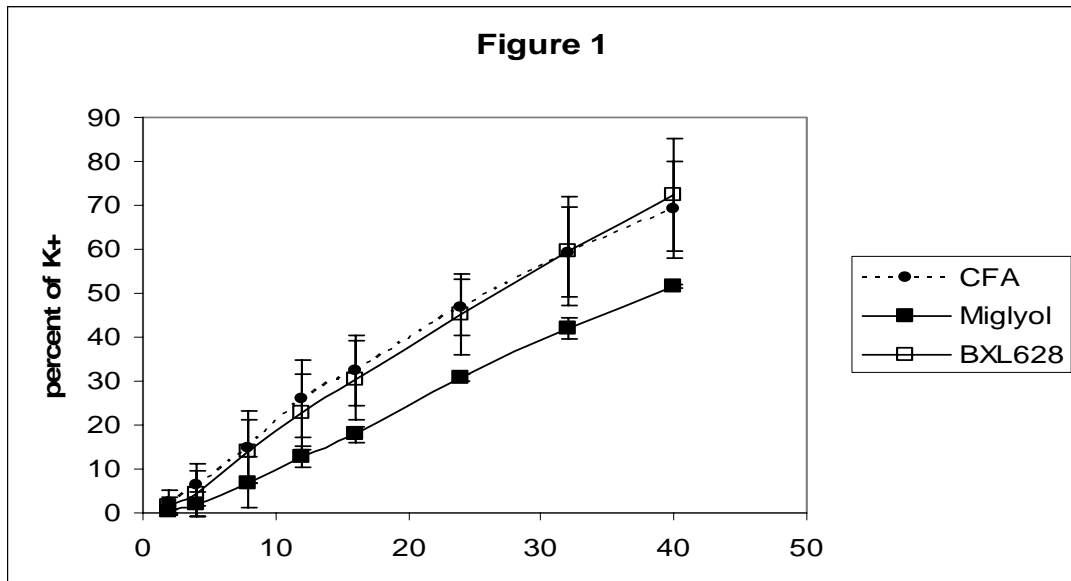
The pathogenesis of non-bacterial chronic prostatitis (CP category III; CP III) / chronic pelvic pain syndrome (CPPS) is proposed to involve immunological, endocrine and neuronal factors. Non-obese Diabetic (NOD) mice have been shown to be susceptible to develop experimental autoimmune prostatitis (EAP), but it is not known if prostates from these mice are functionally different from controls. BXL-628, a vitamin D receptor (VDR) agonist has been shown to inhibit human prostate cell proliferation in vitro and to reduce testosterone-induced prostatic growth in rats. The aim of the present study was to characterize the in vitro function of prostates from NOD mice with and without EAP, and to evaluate if BXL-628 could modify any functional changes in these preparations.

Study design, materials and methods

EAP was induced in NOD mice by injection of mouse prostate homogenate in complete Freund's adjuvant (CFA). Three groups of animals were studied: NOD with and without EAP (controls), and NOD with EAP treated with BXL 628. BXL-628 was administered orally 5 days/week at 100 g/Kg from day 14 to 28 post immunization. Prostates were microsurgically dissected and prepared for functional experiments in tissue baths. General smooth muscle contractility, and nerve-induced contractile responses were assessed in preparations of the ventral and dorsal lobes of the prostates. Statistical comparisons were made by a two-way ANOVA.

Results

There were no differences in body weight, prostate weight, or prostate versus body weight between the three groups of animals: none of the preparations exhibited spontaneous contractile activity. Contractions induced by 124 mM of potassium tended to be increased in preparations of the dorsal prostatic lobe from NOD with EAP (0.99 ± 0.3 mN/mg) when compared to preparations from controls (0.48 ± 0.2 mN/mg), or BXL-628-treated mice (0.62 ± 0.3 mN/mg). Frequency-dependent contractions were obtained in all preparations stimulated electrically. Both dorsal (Figure 1, $p < 0.01$) and ventral prostatic lobes from NOD mice with EAP exhibited significantly lower nerve-induced contractile responses than controls and BXL-628-treated mice. No differences in nerve-induced responses were observed between mice treated with BXL 628 and control animals.



Interpretation of results

Isolated prostatic preparations from NOD mice with EAP exhibit functional alterations suggestive of an increased postjunctional excitability and reduced nerve-mediated contractility. Treatment with BXL 628 of NOD mice with EAP restores contractile responses of prostatic preparations to activation of nerves.

Concluding message

NOD mice with AEP appear to exhibit functional alterations in preparations of prostatic tissue which may be counteracted by systemic treatment with a vitamin D receptor agonist. These findings may represent the basis for a future pharmacological principle to treat non-bacterial chronic prostatitis.