Proceedings of the British Pharmacological Society at http://www.pA2online.org/abstracts/Vol16Issue1abst064P.pdf

Blocking kinin B1 receptors reduces neointimal formation after vascular injury in mice

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Kinin B1 receptors mediate leukocyte recruitment, cytokine and chemokine production, smooth muscle cell proliferation, and driving injury-induced tissue remodeling. This study aimed to investigate the role of kinin B1 receptors in neointimal formation. Vascular injury was induced in right carotid artery of Male Balb-c mice by an angioplasty guide wire. Mice were randomly assigned to receive the treatment of vehicle (0.1% Natrosol, p.o., b.i.d.) or kinin B1 receptor antagonist BI113823 (30 mg/kg, p.o., b.i.d.) for 4 weeks. Four weeks later, denuded carotid artery and plasma samples were collected for biochemical and histochemical analysis. The role of kinin B1 receptors on mouse carotid arterial smooth muscle cell outgrowth and proliferation was studied in vitro. Injured vessels from BI113823 treated mice show reduced neointima formation, with a reduction of intima-to-media ratio by 73%, and vascular stenosis by 58% compared to vehicle treated mice. Macrophage infiltration, smooth muscle cell proliferation and collagen content in the lesions were also reduced by BI113823 treatment. Furthermore, BI113823 treatment group had lower level of cytokines TNF-α, and IL-1β, and reduced expression of kinin B1 and B2 receptors, MMP-2, and MMP-9. In addition, BI113823 treatment significantly inhibited mouse carotid arterial smooth muscle cell outgrowth and proliferation in vitro. Kinin B1 receptor blockade with BI113823 inhibits macrophages infiltration and smooth muscle cell proliferation, and reduces neointima formation following vascular injury.