Rupatadine prevents histamine-induced gene expression of B1 and B2 bradykinin receptors in the rat paw

B Kokkas¹, D Molyva¹, K Kalokasidis³, A Tsartalis¹, C Poulios², H Dedi¹, A Goulas¹,²

¹Aristotle University of Thessaloniki Medical School, Department of Pharmacology, Greece, ²Aristotle University of Thessaloniki Medical School, Department of Anatomical Pathology, Greece, ³Aristotle University of Thessaloniki Medical School, 2nd Department of Dermatology, Papageorgiou Hospital, Greece

Introduction/Aim: The gene expression of B1 and B2 bradykinin receptors is known to be induced by a variety of proinflammatory stimuli, such as activators of Toll-like receptors, cytokines, platelet-activating factor (PAF) and kinins. In many instances this upregulation was shown to be dependent on or facilitated by TNF action and neutrophil migration. In this study we examine the effect of histamine on bradykinin receptor gene expression, in the rat paw. The effect of rupatadine, a second generation antihistamine and PAF receptor antagonist, was also examined.

Methods: Hydrochloric histamine (5mM, in 100 µl normal saline) was injected in the hind paw of Wistar rats and, three hours later, the animals were sacrificed and their paw tissue excised and either immediately frozen for RNA extraction or added to a solution of formalin for histopathological examination. Gene expression of the B1 and B2 bradykinin receptors as well as the H1 histamine receptor was assessed by reverse transcription followed by real-time PCR. Rupatadine fumarate, dissolved in DMSO (20 mg/kg), was administered intraperitoneally, 1 hour prior to histamine injection into the paw.

Results: Under our experimental conditions, a statistically significant increase of gene expression was recorded for all three receptors, which was prevented to a significant extent by the administration of rupatadine. Histamine induced considerable lymphocyte but not neutrophil infiltration, which was similarly prevented by rupatadine.

Conclusions: Histamine is able to stimulate a neutrophil–independent induction of the B1 and B2 bradykinin, as well as the H1 receptor gene expression, in the rat paw. Rupatadine, administered systemically prior to histamine is able to prevent this effect, an observation which may be of use when considering future uses for this drug.