Activation of Ŭ7 nicotinic acetylcholine receptor ameliorates zymosan-induced acute kidney injury in BALB/c mice

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Abstract

Zymosan, a natural compound, provokes acute peritonitis and multiple organ dysfunction that affects the kidney, beside other organs via exaggerated inflammatory response. The aim of the present study is to test the role of cholinergic anti-inflammatory pathway (CAP) in alleviating acute kidney injury (AKI) induced by zymosan in BALB/c mice, using galantamine, a cholinesterase inhibitor, known to act via Ŭ7 nicotinic acetylcholine receptor (Ŭ7 nAChR) to stimulate CAP. Galantamine verified its anti-inflammatory effect by elevating acetylcholine (ACh) level, while abating the interleukin-6/ janus kinase 2 (Y1007/1008)/ signal transducer and activator of transcription 3 (Y705) (IL-6/ pY(1007/1008)-JAK2/ pY705-STAT3) inflammatory axis, with a consequent inhibition in suppressor of cytokine signaling 3 (SOCS3). This effect entails also the nuclear factor-kappa B (p65)/ high mobility group box protein-1/ (NF-əB (p65)/ HMGB-1) signaling pathway. Furthermore, the reno-curattive effect of galantamine was associated by a reduction in plasma creatinine (Cr), cystatin (Cys)-C, IL-18, and renal neutrophil gelatinase-associated lipocalin (NGAL), as well as an improved histopathological structure. Blocking the Ŭ7 nAChR by methyllycaconitine abolished the beneficial effect of galantamine to document the involvement of this receptor and the CAP in the amelioration of AKI induced by zymosan.

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