Central Neuropathic Pain Development in Experimental Autoimmune Encephalomyelitis C57BL/6 Mouse Model Induced by QS-21 Adjuvant

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Abstract

Central neuropathic pain (CNP) is considered as a complicated sensory disturbance which many multiple sclerosis (MS) patients suffer from. Although monophasic experimental autoimmune encephalomyelitis (EAE) mouse model is a gold standard model in preclinical research of MS, severe movement deficit could confound pain behaviors evaluation over the disease course. In this study, complete Freund’s adjuvant (CFA) was substituted with an acylated triterpene glycoside saponin adjuvant named quillaja saponin-21 (QS-21) to establish EAE model for CNP development. Twentyfour, 5-7 weeks old female C57BL/6 mice were randomly divided into three groups. Two groups immunized with MOG35-55 peptide emulsified with CFA and QS-21 adjuvant. The last group received PBS as negative control group. Thermal hyperalgesia as a CNP clinical manifestation through hot plate test and clinical signs were assessed for 60 days’ post immunization (p.i). On days 21 and 60 p.i mice were sacrificed and TCD4+, TCD8+, IL-17+ cells in total splenocytes population by flow cytometry and lymphocyte infiltration and demyelination of brain samples by histopathological staining were evaluated. EAE was established in MOG+CFA and MOG+QS-21 groups as mild relapsing-remitting and monophasic models, respectively. Thermal hyperalgesia developed in the bilateral hindpaws on the onset of clinical symptoms in MOG+CFA and MOG+QS-21 groups and it was maintained until study completion in MOG+QS-21 group. TCD4+, TCD8+ and IL-17+ cells population in MOG+QS-21 and MOG+CFA groups increased significantly (P<0.05) on days 21 and 60 p.i compared to PBS group. Although, inflammatory cells infiltration were increased significantly on days 21 and 60 in MOG+QS-21 and MOG+CFA groups, however demyelination was seen on days 21 and 60 only in MOG+CFA group compared to PBS group (P<0.05). QS-21 adjuvant is capable of establishing mild relapsing-remitting EAE model for CNP development with severe neuro-inflammation and no significant demyelination in white matter.

Keywords: Multiple Sclerosis, Experimental Autoimmune Encephalomyelitis, Quillaja Saponin-21, Central Neuropathic Pain, Thermal Hyperalgesia

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