Glatiramer acetate is safe for a virus-induced demyelinating disease model

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Abstract

[Objective] Multiple sclerosis (MS) is an inflammatory demyelinating disease of the central nervous system (CNS) associated with autoimmunity and/or viral infections. While most disease-modifying drugs (DMDs) for MS suppress disease activities by regulating uncontrolled immune responses (immunopathology), DMDs potentially inhibit anti-viral immune responses, leading to CNS viral reactivation and demyelination.

[Background] In this study, we aimed to determine the efficacy and safety of GA in the Théller’s virus model to assess whether GA can be effective in MS without causing PML. We used SJL/J mice, a mouse model of MS, to study the effects of GA on viral immune responses in the CNS.

[Methods] GA was administered to MS-infected SJL/J mice, and their immune responses were monitored through clinical scores, immunohistochemistry, and quantification of viral loads.

[Results] GA treatment enhanced the ratio of Foxp3+ / Il17a+ without increasing viral loads.

[Conclusions] GA could be safe for MS patients and were not effective in suppressing viral immunity.

References, Grants, & COI

References

- Marrot et al., J. Autoimmun., 2014, doi:10.1016/j.jaut.2014.05.005
- Takeda Neuroimmunology Investigator-Initiated Program
- KAKENI from the Japan Society for the Promotion of Science
- Science Research Promotion Fund from the Promotion and Mutual Aid Corporation for Private Schools of Japan
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Background

Multiple sclerosis (MS)

- Inflammatory demyelinating disease in the CNS
- Caused by interactions among autoimmunity, viral infection, and genetic factors
- Approximately 20,000 patients in Japan with the ratio of women to men of 3:1

Viral infection

- Epstein-Barr virus and human herpesvirus 6 etc.

Autoimmunity

- Genetic factors
- GWAS: Susceptibility genes

Disease-modifying drug (DMD)

- Has immunomodulatory effects
- Suppresses MS activities by regulating anti-myelin immune responses
- Potentially inhibits anti-viral immune responses
- Risk factor of CNS viral reactivation syndromes, such as progressive multifocal leukoencephalopathy

Théller’s murine encephalomyelitis virus (Théller’s virus)

- Used as a viral model of MS
- Infects neuronal cells after intracerebral injection
- Causes acute encephalitis
- Causes chronic demyelination in the CNS due to direct lytic infection (viral pathology) and anti-viral immune responses (immunopathology)

Glatiramer acetate (GA) & Gap in knowledge

- Used as a DMD for MS, COPAXONE
- Has anti-inflammatory effects: 1) Enhances interleukin (IL)-4 and IL-10 production 2) Increases regulatory T cells expressing the transcription factor Foxp3
- Effective in MS without causing PML

Aim & Methods

[Objective] To determine the efficacy and safety of GA in the Théller’s virus model

[Methods] GA treatment enhances the ratio of Foxp3/Il17a without increasing viral loads

GA treatment does not suppress immune responses to Théller’s virus

GA treatment induces immune responses to GA

GA treatment enhances regulatory but not pro-inflammatory cytokine production

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