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POSTER ABSTRACTS

113.SICKLE CELL DISEASE, SICKLE CELL TRAIT AND OTHER HEMOGLOBINOPATHIES, EXCLUDING THALASSEMIAS: BASIC AND TRANSLATIONAL

B-Lactam Antibiotic Ceftriaxone As a Potential Therapeutic Intervention for Chronic Pain in Sickle Cell Disease

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Sickle cell disease (SCD) features the presence of complex physiologic changes beyond a simple vasculopathy. Among its most debilitating neurological complications, chronic pain remains a challenging condition with limited effective treatments. Patients with SCD suffer tremendous pain every day. β-Lactam antibiotics have been shown to offer neuroprotection by promoting glutamate transporter GLT1 expression in the nervous system. This study aimed to investigate the effect of ceftriaxone, a prototype beta-lactam antibiotic, on chronic pain in SCD.

In a humanized mouse model of SCD, spontaneous ongoing pain as well as evoked hypersensitivity to mechanical and thermal stimuli were present in mice carrying human sickle hemoglobin, but not non-sickle control littermates. Notably, prominent activation of astrocytes was observed in the spinal cord dorsal horn region in the mice with SCD. As compared with non-sickle littermates, the spinal expression of GLT1 was dramatically decreased in sickle cell mice. Repeated intraperitoneal administration of ceftriaxone effectively attenuated spontaneous pain, mechanical allodynia, and heat hyperalgesia in mice with SCD. We found the pain reversal effect by ceftriaxone (200 mg/kg, *i.p.*, for 7 days) lasted for at least 4 weeks. Correlating with the behavioral manifestations, ceftriaxone significantly deactivated astrocytes and elevated the level of GLT1 in the spinal cord in the mice with SCD.

These findings suggest that ceftriaxone alleviates both non-evoke ongoing pain and evoked pain in SCD by up-regulating spinal GLT1 expression, which highlights the possibility of a new clinical strategy to treat chronic pain in SCD. This study sheds light on the role of astrocyte activation in SCD and lays the foundation for the development of a potential new intervention for chronic pain in sickle cell disease.

Disclosures No relevant conflicts of interest to declare.

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