

Melatonin agonist tasimelteon ameliorates traumatic brain injury induced liver damage in a dose-dependent manner by enhancing IL-10 expressions

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Traumatic brain injury (TBI) is a prevalent neurological disorder with significant morbidity and mortality rates, often leading to systemic inflammatory responses and secondary organ damage. Among the organs affected, the liver is particularly vulnerable, with the inflammatory process following TBI impairing liver function and worsening disease progression. Despite existing treatments, there remains a need for effective therapies to mitigate organ damage in the aftermath of TBI. Melatonin, a neurohormone known for its anti-inflammatory and antioxidant properties, has shown potential as a therapeutic agent for reducing such damage. Tasimelteon (TASI), a melatonin agonist, binds to melatonin receptors and exhibits similar biological effects. However, limited research exists on the protective effects of TASI against TBI-induced liver damage, and its potential dose-dependency remains unclear. This study aimed to investigate the impact of TASI on the inflammatory response in traumatic secondary liver injury (TSLI) induced by TBI, specifically evaluating the role of anti-inflammatory cytokine interleukin (IL)-10 levels. Forty Wistar Albino male rats were divided into four groups: sham, TSLI (trauma induced by dropping a 50 g weight from a height of 80 cm to create 0.2 N severity according to Newton's law), TASI-1 (TSLI+TASI 1 mg/kg, ip) and TASI-10 (TSLI+TASI 10 mg/kg, IP). After 48 hours, rats were sacrificed under anesthesia and the liver tissues were collected for histopathological and immunohistochemical examination. The TSLI group exhibited moderate hyperemia, mild hemorrhages, inflammatory cell infiltrations, and necrosis, along with increased IL-1 β , TNF- α , and decreased IL-10 expression levels compared to the sham group. Treatment with TASI significantly reversed these findings in both TASI-treated groups. Our results suggest that TASI, a melatonin agonist, effectively attenuates inflammatory liver damage induced by TBI in a dose-dependent manner by increasing IL-10 levels. However, these positive effects should be further explored in future studies.

Keywords: Head trauma, Liver, Tasimelteon, Pathology, Inflammation