The Effect of Valproic Acid Therapy on the Glial Scar Formation after Acute Spinal Cord Injury Following by Motor Vehicle Traffic Crashes

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Abstract

Motor vehicle traffic crashes (MVTCs) are important cause of traumatic spinal cord injury (SCI). SCI is a devastating condition, with loss of sensory, motor, and autonomic function. Inflammatory reaction following a SCI contributes substantially to secondary effects. A biochemical event in that process is gliosis. Valproic acid (VPA) is a histone deacetylase inhibitor and has potent anti-inflammatory properties. The aim of the present study was to examine optimum dose of VPA on gliosis and axonal regeneration sought to functional recovery after acute SCI. Rat models received daily intraperitoneal injections of different doses (150, 200, 300, 400 and 500 mg/kg), at time points (2, 6, 12 and 24 h) after SCI or sham surgery. Spinal cord was examined histologically for glial fibrillary acid protein (GFAP) expression, three month after surgery. Spinal cord sections were stained with silver impregnation to assess demyelination, and axonal regeneration. The injured spinal cord was then examined histologically, including quantification of cavitation. The immunohistochemical evaluation were done with immunofluorescent and immunoperoxidase techniques 12 weeks post-surgery. The expression of GFAP in the untreated group had the highest immunofluorescence while it decreased in the VPA treated group (300 mg/kg delivered at 12 h post-injury, P<0.05). The cavity volume in the VPA treated group significantly reduced compared to control (saline-injected) group (P<0.05). There were few axons could be noticed in the untreated group while the treated group showed many axons in the regenerating spinal tissues. Quantitative analysis showed that there is a dose dependent decrease in the relative intensity of the GFAP fluorescent at 300 mg/kg (12 h). In conclusion, this result suggest VPA reduces inflammatory reaction-induced in SCI.

Keywords:

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