ABSTRACT

Effect of $ACTH_{4-10}PRO^{8}GLY^{9}PRO^{10}$ Administration towards Proinflammatory Mediators TLR, NF-kB, IL-8, TNF-α, and Neutrophil on Acute Compression of the Spinal Cord (An Experimental Study on Sprague-Dawley Rat Spinal Cord Injury Model)

Muhammad Faris

Background: Acute spinal cord injury (SCI) is a devastating traumatic event often followed with decreased quality of life, making it as a significant public health burden. $ACTH_{4-10}PRO^{8}$-GLY^{9}-PRO^{10} (Met-Glu-His-Phe-Pro-Gly-Pro) is a synthetic analogue of a short ACTH fragment with augmented neuroactivity and known anti-inflammatory properties. Studies had shown intranasal administration of $ACTH_{4-10}$ were able to reach the central nervous system with higher tissue concentration and longer duration compared to intravenous administration. Its effect on SCI model is postulated via melanocortin receptor but its direct mechanism still unknown.

Methods: This experimental study was done on SCI model of Sprague-Dawley rat. TLR, NF-kB, IL-8, and TNF-α were observed using immunohistochemistry staining as inflammatory markers. Neutrophil was observed using Hematoxylin Eosin staining. Sham group for this study was done using normal saline. Spinal cord of rat model was observed on 3- and 6-hours following injury. Statistical analysis was done using ANOVA with Bonferoni correction for normal data distribution. Kruskal Wallis followed by non-parametric Mann-Whitney U test were used for abnormal data distribution.

Result: TLR, NF-kB, IL-8, and TNF-α expression along with neutrophil count showed significant decrease on 3 hours and 6 hours observation in ACTH4-10 treated group compared to normal saline treated croup ($p < 0,05$). TLR-2, NF-kB, and IL-8 are able to be regulated in ACTH treated group down to control level showing no significant difference during 6 hours observation.

Conclusion: ACTH4-10 intranasal administration significantly reduced inflammation cytokines expression of acute SCI animal model. It may supressed secondary tissue damage from inflammation cascade. ACTH4-10 might be beneficial in SCI cases to regulate over-expression of inflammation modulators.

Keywords: Spinal cord injury, ACTH, inflammation, TLR, NF-kB, IL-8, TNF-α, and Neutrophil