ABSTRACT

Neuroprotective Role of Erythropoietin in Reducing The Rate of Subventricular Zone Effacement by Inhibiting Microglial Activation and Reactive Astrocyte in Hydrocephalus

Wihasto Suryaningtyas

Purpose: To elucidate the potential role of Erythropoietin (EPO) as a neuroprotective agent against reactive astrogliosis and reducing the thinning rate of subventricular zone (SVZ) in kaolin-induced hydrocephalic rats.

Method: Thirty-six ten-week-old Sprague-Dawley rats were used in this study. Hydrocephalus was induced with 20% kaolin suspension injected into the cistern of thirty rats and leaving the six rats as normal group. The hydrocephalic rats were randomly divided into hydrocephalic and treatment group. The treatment group received daily dose of recombinant human erythropoietin (rhEPO) from day-7 to day-21 after induction. The animals were sacrificed at 7 (only for hydrocephalic group) and 14 or 21 (for both groups) days after induction. Brain was removed and was prepared for histological analysis by hematoxylin and Eosin staining as well as immunohistochemistry for 4-HNE, β-catenin, GFAP, Iba-1 and Ki-67.

Results: Immunohistochemical analysis showed that animals treated with rhEPO had a reduced astrocyte reactivity displayed by lower GFAP expression. Hydrocephalic rats received rhEPO also displayed reduced microglial activation shown by lower Iba-1 protein expression. Exogenous rhEPO exerted its protective action in reducing astrogliosis by inhibiting lipid peroxidation that was documented in this study as lower expression of 4-HNE than non-treated group. Expression of β-catenin was also reduced following the pattern of 4-HNE. The SVZ thickness was progressively declining in hydrocephalus group, while the progression rate could be reduced by rhEPO.

Conclusion: Erythropoietin inhibited lipid peroxidation, and reactive astrogliosis in hydrocephalic animal model. The reduced thinning rate of SVZ demonstrated that EPO also had effect in reducing the hydrocephalus progressivity. Further research is warranted to explore its efficacy and safety to use in clinical setting.

Keyword: Hydrocephalus, Erythropoietin, Subventricular zone, Astrogliosis