Cerebrospinal Fluid Research

Oral presentation

Effect of rhHB-EGF on the expression of hydrocephalus-related genes *in vitro*

Joon W Shim*[1], Andrew Dudley[2], Michael Klagsbrun[2], Sandra Smith[2] and Joseph R Madsen[1]

Address: [1]Department of Neurosurgery, Children's Hospital Boston and Harvard Medical School, 300 Longwood Avenue, Boston, MA 02115, USA and [2]Vascular Biology Program, Children's Hospital Boston and Harvard Medical School, 300 Longwood Avenue, Boston, MA 02115, USA

Email: Joon W Shim* - joon.shim@childrens.harvard.edu

* Corresponding author

from 52nd Annual Meeting of the Society for Research into Hydrocephalus and Spina Bifida
Providence, RI, USA. 11–14 June 2008

Published: 3 February 2009

Cerebrospinal Fluid Research 2009, **6**(Suppl 1):S5 doi:10.1186/1743-8454-6-S1-S5

This abstract is available from: http://www.cerebrospinalfluidresearch.com/content/6/S1/S5

Background

Heparin binding epidermal growth factor like growth factor (HB-EGF) is a member of the epidermal growth factor family. The role of HB-EGF in cardiovascular disease such as atherosclerosis has been well-reported but its pertinence to cerebrovascular disease including hydrocephalus is unknown. In our laboratory human HB-EGF transgenic mice have been observed to demonstrate communicating hydrocephalus. The goal of this study was to find any difference in expression of three genes in vascular-lining cells under varying concentration of this growth factor.

Materials and methods

Two cell groups of murine microvascular endothelial and non-endothelial cell were exposed to 10, 100, and 1000 ng/ml of recombinant human HB-EGF (rhHB-EGF). Cellular response to rhHB-EGF was examined by quantitative real time reverse transcription polymerase chain reaction focusing on mRNA expression of vascular endothelial growth factor (VEGF), transforming growth factor β1 (TGF-β1), and tumor necrosis factor α (TNF-α), that may be associated with hydrocephalus. Also, VEGF protein levels in the culture supernatants of these cells to rhHB-EGF were measured by enzyme linked immunosorbent assay.

Results

The results indicated that VEGF mRNA was significantly increased by 3–5 fold in endothelial cells treated with rhHB-EGF relative to the untreated control ($p < 0.05$). As compared to the control, mRNA expression of TNF-α in endothelial cells was significantly increased by 3, 9, and 13 fold at 12 h following 10, 100, and 1000 ng/ml of rhHB-EGF treatment, respectively ($p < 0.05$). Also, TGF-β1 mRNA in non-endothelial cells was significantly elevated by 4, 6, and 7 fold at 24 h following introduction of 10, 100, and 1000 ng/ml of rhHB-EGF, respectively ($p < 0.05$). When exposed to rhHB-EGF, VEGF protein levels in the conditioned media of endothelial cells were detectable but those in non-endothelial groups were undetectable over 1–6 h period.

Conclusion

These data demonstrated that rhHB-EGF led to induction of VEGF and TNF-α in microvascular endothelial cells and upregulation of TGF-β1 in non-endothelial cells from murine origin. Our findings support a hypothesis that human HB-EGF could activate multiple mouse genes reportedly linked to hydrocephalus and that it is worthwhile to assay these factors in cerebrospinal fluid of animal models for hydrocephalus.