

Oral presentation

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

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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 β 1 (TGF- β 1), 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- β 1 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- β 1 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.