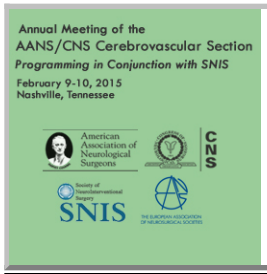

Estrogen Therapy for Cerebral Vasospasm and Delayed Cerebral Ischemia Secondary to Aneurysmal Subarachnoid Hemorrhage

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Introduction

Cerebral vasospasm (CV) remains the leading cause of delayed morbidity and mortality following aneurysmal subarachnoid hemorrhage (SAH). However, increasing evidence supports etiologies of delayed cerebral ischemia (DCI) other than CV. Estrogen, specifically 17ß-estradiol (E2), has potential therapeutic implications for ameliorating the delayed neurological deterioration which follows aneurysmal SAH.

Methods

We review the causes of CV and DCI and examine evidence for E2-mediated vasodilation and neuroprotection.

Results

E2 potentiates vasodilation by activating endothelial nitric oxide synthase (eNOS), preventing increased inducible NOS (iNOS) activity caused by SAH, and decreasing endothelin-1 production. E2 provides neuroprotection by increasing thioredoxin expression, decreasing c-Jun N-terminal kinase activity, increasing neuroglobin levels, preventing SAH-induced suppression of the Akt signaling pathway, and upregulating the expression of adenosine A2a receptor. The net effect of E2 modulation of these various effectors is the promotion of neuronal survival, inhibition of apoptosis, and decreased oxidative damage and inflammation.

Conclusions

E2 is a potentially potent therapeutic tool for improving outcomes related to post-SAH CV and DCI. However, clinical evidence supporting its benefits remains lacking. Given the promising preclinical data available, further studies utilizing E2 for the treatment of patients with ruptured intracranial aneurysms appear warranted.

Learning Objectives

By the conclusion of this session, participants should be able to 1) Describe the importance of successfully treating aneurysmal SAH-induced cerebral vasospasm and delayed cerebral ischemia, 2) Discuss, in small groups the mechanisms by which estrogen therapy prevents vasoconstriction and provides neuroprotection in the setting of aneurysmal SAH, and 3) Identify an effective treatment for aneurysmal SAH-induced cerebral vasospasm and delayed cerebral ischemia.

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