

Alterations in the systemic inflammatory milieu as a result of cerebral aneurysm treatment: Does modality dictate inflammatory response?

J Mocco MD MS; Aqeela Afzal PhD; Brain Hoh MD; Edward W. Scott PhD; E. Sander Connolly MD
Vanderbilt University, University of Florida, Columbia University

VANDERBILT UNIVERSITY
MEDICAL CENTER



Introduction

Subarachnoid hemorrhage (SAH) afflicts 30,000 people in the United States every year. Additionally, as SAH frequently results in devastating neurologic injury and affects a relatively young patient population, it produces a disproportionate burden on society. (1) A significant portion of this morbidity results from cerebral vasospasm. (2)

There are two accepted modalities for the treatment of ruptured aneurysms, open surgical clipping and endovascular coiling. There currently exists substantial debate as to which modality is superior in any given ruptured aneurysm. However, it has been suggested in a well designed prospective trial that post-subarachnoid hemorrhage cerebral vasospasm occurs more frequently in patients who have undergone clipping than coiling. (3) Cerebral vasospasm has been demonstrated to be, at least in part, a pro-inflammatory disease.(2,4) Therefore, some preliminary efforts have been made to determine whether inflammatory modulation is associated with the observed difference in the occurrence of cerebral vasospasm in clipped versus coiled patients.

In an effort to establish a clearer determination of whether there is a difference in systemic inflammatory responses to the two different treatment modalities, we examined the inflammatory profiles of unruptured, electively treated aneurysms. Unruptured aneurysm patients undergo the same exact procedures as re-ruptured patients, however, they are not burdened with the large amount of concomitant disease and injury.

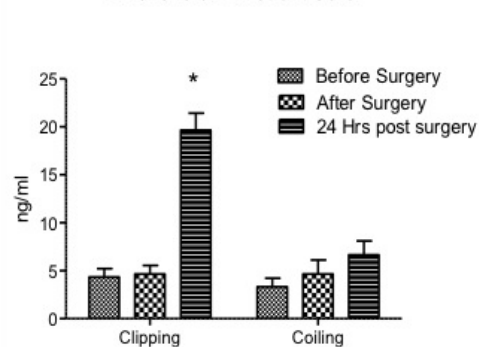
Methods

IRB approval to obtain samples from patients who elect to have surgical or endovascular intervention for an unruptured aneurysm was obtained. Samples were collected prior to surgery, immediately following surgery and 24 hours post surgery. Blood was collected into a serum separator tube and allowed to clot. The blood was spun in a centrifuge, the serum removed, aliquoted and frozen till the time of the assays. Serum samples were assessed using ELISA for IL-6, IL-8. Each sample was assessed in triplicate and concentrations read from standard curves of the purified proteins.

Results

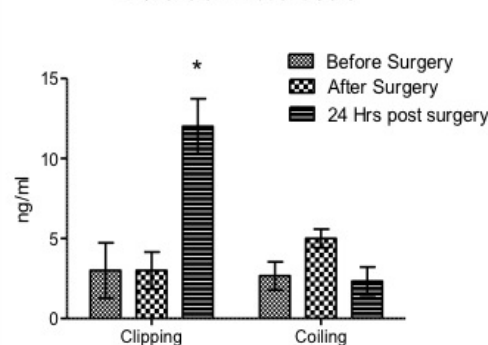
Analysis demonstrated significantly elevated levels of both cytokines in clipped aneurysm patients compared to endovascularly coiled patients. These data demonstrate that the human body experiences a more robust inflammatory response following open surgical clipping, as compared to endovascular coiling.

IL-6 levels in Patient Sera



Serum was collected from 20 patients; 10 patients underwent an elective clipping surgery and 10 patients underwent an elective coiling surgery. Serum samples were obtained before, after and 24 hours after the surgery. Patients that underwent a clipping procedure showed significantly elevated levels of IL-6 in the 24 hours post surgery samples.

IL-8 levels in Patient Sera



Serum was collected from 20 patients; 10 patients underwent an elective clipping surgery and 10 patients underwent an elective coiling surgery. Serum samples were obtained before, after and 24 hours after the surgery. Patients that underwent a clipping procedure showed significantly elevated levels of IL-8 in the 24 hours post surgery samples.

Conclusions

70% of SAH patients suffer radiographic cerebral vasospasm and in 40-50% of these patients, the spasm results in clinical neurologic deficit. These findings may suggest that particular inflammatory cascades could potentially contribute to the observed differences in vasospasm rates across endovascular versus surgical cohorts, possibly leading to the identification of key mediators in the pathophysiologic cascade resulting in cerebral vasospasm. This research may help delineate critical differences in patient milieu following open surgical clipping versus endovascular coiling, differences that may indicate key mediators in the pathophysiologic cascade that leads to cerebral vasospasm.

References

1. Ferro, JM., et al. Update on Subarachnoid haemorrhage. *J. Neurol.* 2008; 255:465.
2. Chaichana, KL., et al. Role of inflammation (leukocyte-endothelial cell interactions) in vasospasm after subarachnoid hemorrhage. *World Neurosurg.* 2010; 73 (1):22-41
3. Macdonald, RL., et al. CONSCIOUS-1 investigators. Clazosentan to overcome neurological ischemia and infarction occurring after subarachnoid hemorrhage (CONSCIOUS-1): randomized, double-blind, placebo-controlled phase 2 dose-finding trial. *Stroke.* 2008; 39(11):3015-21
4. Mocco, J., et al. Rise in serum soluble intercellular adhesion molecule-1 levels with vasospasm following aneurysmal subarachnoid hemorrhage. *J Neurosurg.* 2002; 97(3):537-41.