Intracerebral hemorrhage (ICH) is a life-threatening condition characterized by bleeding within the skull. Intracerebral hemorrhages can be secondary to a traumatic event such as a traumatic brain injury (TBI), or from non-traumatic causes such as arteriovenous malformations, ruptured aneurysms, tumors, or cerebral amyloid angiopathy. Several risk factors for non-traumatic ICH have been identified including hypertension (systolic blood pressure greater than 160 mmHg), African American ethnicity, decreased low-density lipoprotein levels, increasing age, anticoagulant or antiplatelet medication use, and low triglyceride levels.1

In ICH, a hematoma is formed in the area of the injured vasculature. The presence of this hematoma has several adverse effects on the cerebral tissue and brain as a whole. The addition of the hematoma to the fixed volume of the cranial cavity leads to increased intracranial pressure (ICP). The increase in ICP can lead to a lack of perfusion as systemic blood pressure must be able to overcome the increased pressure gradient in the cranial cavity. Cerebral tissue exposure to blood components leads to tissue damage due to inflammation, free radical formation, and direct cell toxicity due to blood degradation products.1 Expansion of the hematoma in ICH has been shown to be a common occurrence. Clinical trials have demonstrated that hematoma expansion occurs in 71.8% to 73.9% of ICH. An increase in ICH volume is associated with mortality. A meta-analysis performed by Davis et al. found that mortality was significantly related to the increase in hematoma volume in ICH patients. For every 10% increase in hematoma volume, the hazard ratio increased by 5% (HR 1.05, 95% CI: 1.03, 1.08; p<0.001).1

A common complication in the acute phase of ICH is fever. Fever in this patient population may have multiple etiologies ranging from infection to damage to the hypothalamus. A temperature ≥ 37.5°C was found in 91% of ICH patients in a study performed by Schwartz and colleagues, demonstrating the high prevalence of fever in this disease state.3 The presence of fever in these patients is not benign. In subarachnoid hemorrhage (SAH) patients, fever has been associated with an increased mortality rate, severe disability, and cognitive impairment.4 Typical management strategies are shown below:

Non-pharmacologic methods: cooling blanket, fan, ice pack
Pharmacologic methods: acetaminophen, diclofenac

Non-steroidal anti-inflammatory drugs (NSAIDs) are not typically used for fever control in the ICH population due to their antiplatelet effects via cyclooxygenase-1/2.1* Additionally, the safety of NSAIDs use in ICH patients is poorly described in the literature. A study performed by Cormio et al. in 2011 found that patients treated with clofibrate-induced fever in controls and SAH patients. The study found a significant decrease in the duration of fever in patients treated with diclofenac-induced fever. Importantly, there were no cases of new onset intracranial hemorrhage in either the diclofenac-induced fever group, or the control group.2

To determine the safety of post-bled NSAID use in ICH patients and to lead to an increase in hematoma volume or to clinically significant rebleeding. Establishing the safety of NSAIDs in this patient population could identify an additional fever control agent.

Methods

• Retrospective chart review of cases who presented with non-traumatic subarachnoid hemorrhage (SAH) as identified via a database review
• Patients were assigned to the case group if received an NSAID medication for fever control during their hospital admission and had a 24-72 hour post-exposure computed tomography (CT) scan of the head
• Patients were assigned to the control group if did not and NSAID medication for fever control during their hospital admission and had a 24-72 hour follow-up CT head scan
• Neurosurgical resident physicians and nurse practitioners reviewed baseline and follow-up CT imaging
• The study timeframe was January 1st 2013 through December 31st 2015

Inclusion Criteria

• Diagnosed with non-traumatic SAH within 48 hours of onset via CT head
• History of coagulation disorder
• Patients initiated on antiplatelet therapy during admission
• Patients initiated on a low-dose heparin protocol whose PTT is found to be ≥ 60 seconds

Exclusion Criteria

• History of benign hematologic disorders
• Patients initiated on aspirin, clopidogrel, or warfarin during admission

Primary Outcome

• Progression of ICH on CT imaging 24-72 hours after NSAID administration

Secondary Outcomes

• In hospital mortality
• ICU/Hospital length of stay

References


Disclosures

Authors of this presentation have no滚滚 to disclose concerning possible financial or personal relationships with commercial entities that may have direct or indirect interest in the subject matter of this presentation.

Data Collection

• NSAIDs for fever control
• No NSAIDs for fever control
• 24-hour post-exposure CT head
• 24-hour post-exposure CT head

Statistical Analysis

• Descriptive statistics will be used to characterize demographic data
• Categorical outcomes (progression of ICH and in-hospital mortality) will be analyzed using chi-squared tests or Fisher’s exact test
• Continuous outcomes (change in hematoma volume, ICU length of stay, and hospital length of stay) will be analyzed using Student’s t-test or Wilcoxon rank sum test

Limitations

• This study is not without limitations.
• The retrospective nature of this study could lead to missing data points.
• The timing of follow-up CT studies will not be standardized across patients following the receipt of NSAIDs.
• Different NSAID medications and dosages could have different antiplatelet effects, and thus cause different amounts of hematoma progression and growth.
• Neurosurgical intervention due to hematoma progression will be affected by the practice patterns of different neurosurgery practitioners.