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Over-the-counter analgesic powder use in patients presenting with intracerebral hemorrhage
A case series

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Abstract
Introduction: Over-the-counter (OTC) analgesics including aspirin-containing powder formulations (BC Powder, Goody's Powder) (ACPFs) are commonly utilized in the United States. While the ACPFs have been associated with upper gastrointestinal bleeding, we describe a case series of patients presenting with intracerebral hemorrhage (ICH) within 24 hours of ingestion.

Methods: We reviewed all ICH patients presenting to a comprehensive stroke center from September 1, 2014 through June 30, 2016 to identify patients who reported taking BC Powder or Goody’s Powder within 7 days of their stroke. Baseline characteristics, medication use, stroke risk factors, clinical imaging, and laboratory testing were reviewed retrospectively.

Results: Of 334 patients admitted with ICH during the study period, 6 (2%) reported use of OTC analgesic powders within 1 week of their index stroke. All had consumed at least 1 packet within 24 hours of their ICH. All patients were African American and all except 1 patient were females. Three patients had no identified traditional stroke risk factors and 3 other patients had evidence of mild hypertension history.

Conclusions: Over-the-counter analgesic powders containing high doses of aspirin including BC Powder and Goody’s Powder may contribute to ICH in patients with no or minimal risk factors. Providers should inquire about the use of these powders in ICH patients particularly among African Americans.

Abbreviations: ACPF = aspirin-containing powder formulation, AVF = arteriovenous fistula, AVM = arteriovenous malformation, COX1 = cyclooxygenase-1, CTA = computed tomography angiography, ICH = intracerebral hemorrhage, MRA = magnetic resonance angiography, NANSAIDs = nonaspirin nonsteroidal antiinflammatory drugs, NSAIDs = nonsteroidal antiinflammatory drugs, OTC = over-the-counter, PG = prostaglandin.

Keywords: intracerebral hemorrhage (ICH), nonsteroidal antiinflammatory drugs (NSAIDs), over-the-counter (OTC)

1. Introduction

Over-the-counter (OTC) drugs are widely used in the United States. A prior study of medication use patterns in the United States found that more than 80% of American adults used at least 1 OTC or prescription drug each week.[1] The most frequently utilized medications include OTC analgesics with 17% to 23% of the population using these in the preceding week.[1] Chronic OTC analgesic use is also frequently used in the elderly population for pain relief.[2,3]

OTC analgesics commonly include acetaminophen, nonsteroidal antiinflammatory drugs (NSAIDs) including aspirin, ibuprofen, and naproxen- and powder formulations (BC Powder, Goody’s Powder). Adverse effects including increased upper gastrointestinal (GI) bleeding tendency is a commonly reported adverse effect of the use of NSAIDs.[2] Cyclooxygenase (COX) inhibition by NSAIDs leading to interference with protective prostaglandins (PGs) contributes to upper GI bleeding.[2] Aspirin and nonaspirin nonsteroidal antiinflammatory drugs (NANSAIDs) also affect systemic hemostasis by inhibiting platelet COX.[4] Platelet COX-1 enables conversion of arachidonic acid into thromboxane A2 which mediates platelet aggregation; inhibition of COX-1 thereby leads to increased bleeding time.[2,4] Aspirin is an irreversible inhibitor while NANSAIDs reversibly inhibit COX-1 which lead to differential pharmacodynamics relevant to COX-1 blockade. Risks of bleeding with aspirin or NANSAIDs are enhanced with use of large doses, concomitant use of alcohol, anticoagulants or by presence of comorbidities like liver disease, renal failure, and coagulopathies.[1] Hemorrhagic stroke has been associated with use of aspirin previously.[5–7] This may be attributed to impaired primary hemostasis as a result of platelet inhibition when an imbalance between thromboxane and prostacyclin occurs.[4,8]

In this study, we evaluated the frequency of recent OTC analgesic powder use with BC Powder (Aspirin 845 mg, Caffeine 65 mg) and Goody’s Powder (Aspirin 320 mg, Acetaminophen...
We identified patients with ICH who had consumed OTC analgesic powders within 1 week of their index stroke and who had been evaluated for hemorrhagic stroke. Patients who presented with ICH were those who presented with a new focal neurological deficit due to bleeding into the brain. The most common indication for use of analgesic powders was for headaches, which were being used for at least 7 days and up to 6 months before ICH presentation. All patients had taken at least 1 packet of the OTC analgesic powder daily for at least 1 week before the stroke. Brain imaging showed evidence of an acute ICH in all patients, suggesting that the use of analgesic powders had preceded the onset of ICH.

### Results

During the 24-month study period, 334 patients were admitted to the hospital with ICH and 6 patients (2%) had documented use of OTC analgesic powders (BC Powder, Goody Powder) within 1 week of their index stroke. All patients had utilized at least 1 packet of the OTC analgesic powder daily for at least 1 week before the stroke. Brain imaging showed evidence of an acute ICH in all patients, suggesting that the use of analgesic powders had preceded the onset of ICH.

### Discussion

We identified patients with ICH who had consumed OTC analgesic powders within 1 week of their index stroke and who had been evaluated for hemorrhagic stroke. Patients who presented with ICH were those who presented with a new focal neurological deficit due to bleeding into the brain. The most common indication for use of analgesic powders was for headaches, which were being used for at least 7 days and up to 6 months before ICH presentation. All patients had taken at least 1 packet of the OTC analgesic powder daily for at least 1 week before the stroke. Brain imaging showed evidence of an acute ICH in all patients, suggesting that the use of analgesic powders had preceded the onset of ICH.

### Table 1

<table>
<thead>
<tr>
<th>Patient no.</th>
<th>Stroke type</th>
<th>Stroke location</th>
<th>Age</th>
<th>Sex</th>
<th>Race</th>
<th>Stroke risk factors</th>
<th>Powder type used</th>
<th>Reason for powder use</th>
<th>Powder amount</th>
<th>Last use of powder before stroke</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 (YW)</td>
<td>ICH</td>
<td>Basal ganglia</td>
<td>56</td>
<td>Female</td>
<td>African American</td>
<td>None</td>
<td>BC Powder</td>
<td>Joint pains</td>
<td>50 packets in 30 d</td>
<td>Within 24 h of the stroke</td>
</tr>
<tr>
<td>2 (MS)</td>
<td>ICH</td>
<td>Cerebellum</td>
<td>70</td>
<td>Female</td>
<td>African American</td>
<td>Diabetes (A1c 9.4), HTN, OSA</td>
<td>Goody Powder</td>
<td>Headache</td>
<td>Daily packet use for 14 d</td>
<td>Within 24 h of the stroke</td>
</tr>
<tr>
<td>3 (B)</td>
<td>ICH</td>
<td>Basal ganglia</td>
<td>39</td>
<td>Female</td>
<td>African American</td>
<td>None</td>
<td>Goody Powder</td>
<td>Chronic headaches</td>
<td>Daily packet use for 15 d</td>
<td>Within 24 h of the stroke</td>
</tr>
<tr>
<td>4 (SA)</td>
<td>ICH</td>
<td>Basal ganglia</td>
<td>63</td>
<td>Male</td>
<td>African American</td>
<td>HTN (mild concentric LVH)</td>
<td>Goody Powder, BC Powder</td>
<td>Intermittent headache</td>
<td>Daily packet use of both powders for 6 mo</td>
<td>Within 24 h of the stroke</td>
</tr>
<tr>
<td>5 (JR)</td>
<td>ICH</td>
<td>Occipital lobe</td>
<td>46</td>
<td>Female</td>
<td>African American</td>
<td>None</td>
<td>Goody Powder</td>
<td>Intermittent headache</td>
<td>Daily packet use for 1 wk</td>
<td>Within 24 h of the stroke</td>
</tr>
<tr>
<td>6 (MB)</td>
<td>ICH</td>
<td>Basal ganglia</td>
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<td>Female</td>
<td>African American</td>
<td>HTN (mild LVH)</td>
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**Notes:**
- HTN: hypertension
- ICH: intracerebral hemorrhage
- LVH: left ventricular hypertrophy
- OSA: obstructive sleep apnea
- A1c: hemoglobin A1C
- HTN: hypertension
- Cerebellum: cerebellum
- Basal ganglia: basal ganglia
- Occipital lobe: occipital lobe
- Chronic headaches: chronic headaches
- Intracerebral hemorrhage: intracerebral hemorrhage
- Hypertension: hypertension
- Left ventricular hypertrophy: left ventricular hypertrophy
- Obstructive sleep apnea: obstructive sleep apnea


Medicine

2016; Caffeine 32.5 mg, Potassium 60 mg) in patients presenting with ICH.

In this case series, we retrospectively reviewed all ICH patients presenting to Emory University Hospital from September 1, 2014 through June 30, 2016 with documentation of BC Powder and Goody Powder use within 7 days of their index stroke. Hemorrhagic stroke was confirmed with noncontrast CT and thorough examination and brain imaging with and without contrast. BC Powder was used in patients with a history of ICH and Goody Powder was used in patients with a history of ICH. A nonsurgical strategy of acute blood pressure control in combination with avoidance of antithrombotic use was used to treat ICH patients.

Data were collected from patients' electronic medical records including demographics, past medical history, secondary causes of bleeding if any, medication history, clinical evaluation, diagnostic testing including laboratory results, brain imaging, and cerebral vascular imaging. The study was approved by the Emory institutional review board.

### 4. Discussion

We identified patients with ICH who had consumed OTC analgesic powders within 1 week of their index stroke and who had been evaluated for hemorrhagic stroke. Patients who presented with ICH were those who presented with a new focal neurological deficit due to bleeding into the brain. The most common indication for use of analgesic powders was for headaches, which were being used for at least 7 days and up to 6 months before ICH presentation. All patients had taken at least 1 packet of the OTC analgesic powder daily for at least 1 week before the stroke. Brain imaging showed evidence of an acute ICH in all patients, suggesting that the use of analgesic powders had preceded the onset of ICH.

### Table 1

Patient baseline characteristics, risk factors, and analgesic powder use.

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- A1c: hemoglobin A1C


Medicine

2016; Caffeine 32.5 mg, Potassium 60 mg) in patients presenting with ICH.
The principal components of one BC Powder packet are aspirin (845 mg) and caffeine (63 mg) while one Goody’s Powder packet consists of aspirin (520 mg), acetaminophen (260 mg), caffeine (32.5 mg), and potassium (60 mg). Previously, results from a randomized clinical trial for primary prevention of cardiovascular disease with 325 mg of daily aspirin among healthy male physicians demonstrated increased risk of hemorrhagic stroke (relative risk 2.14, 95% CI, 0.61–4.57, P = .06). A meta-analysis incorporating 16 trials involving aspirin treatment for myocardial infarction and ischemic stroke prevention involving 108 hemorrhagic stroke cases demonstrated a significant absolute risk increase in hemorrhagic stroke of 12 events per 10,000 persons (95% CI, 5–20; P < .001). A meta-analysis involving nine trials of aspirin with different doses (50–500 mg daily or every other day) used for 3.6 to 10.1 years showed an increased risk for hemorrhagic stroke by about 30% regardless of dose.

Both these OTC analgesic powder formulations contain caffeine. Previous studies have suggested that caffeine-containing medications may also be associated with an increased risk of both subarachnoid and intracerebral hemorrhage (ICH). The proposed mechanism involves caffeine’s effect of elevating systemic arterial blood pressure. An acute increase in blood pressure may lead to loss of cerebral blood flow autoregulation and disruption of the blood brain barrier resulting in a possible subarachnoid or ICH. While there is stronger evidence for high doses of aspirin and their association with ICH, the presence of caffeine in these OTC analgesic powder formulations increasing the propensity of an ICH warrants further investigation.

In our case series, all ICH patients using these analgesic powders were African American. In comparison to Caucasians, African Americans have twice the incidence of ICH due to higher risk of hypertension and drug abuse. In our analysis however we excluded all patients who had evidence of moderate or severe HTN and also patients who had positive urine drug screen. Whether the use of these OTC analgesic powders (BC Powder and Goody’s Powder) by African Americans is more common due to directed marketing efforts or due to other factors is less clear. A previous study did demonstrate the use of certain NSAID products, including BC Powder and Goody’s Powder, to be twice as common in African Americans as compared to Caucasians.

5. Conclusion

OTC analgesic powders such as BC Powder and Goody’s Powder may be associated with increased risk of hemorrhagic stroke in African Americans who have minimal to no stroke risk factors, likely due to their formulations containing high amounts of aspirin. Providers should inquire about the use of these powders in ICH patients particularly among African Americans.

Author contributions

Conceptualization: Fadi Nahab.

Data curation: Brittain Davis, Fadi Nahab, Ghada A. Mahmoud, Laura Henriquez, Syed Ali Raza.

Formal analysis: Ghada A. Mahmoud, Laura Beth Durm, Syed Ali Raza.

Methodology: Fadi Nahab.

Supervision: Fadi Nahab.

Writing – original draft: Ghada A. Mahmoud, Syed Ali Raza.

Writing – review & editing: Fadi Nahab, Haseeb Rahman.

References