High Prevalence of Aspirin Resistance In Migraineurs
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Background
Migraineurs have platelet hyporeactivity, which may impair their ability to respond to aspirin, a scaffold for effective antiplatelet therapy for reducing the risk of stroke in women and MI in men. Aspirin resistance results in a suboptimal platelet inhibitory response to aspirin treatment manifested by high post-treatment platelet reactivity (HPPR) using an in vitro function platelet assay. This condition is linked to an increased risk of stroke and MI. Although aspirin is the cornerstone of migraine headache therapy, there is limited evidence for its efficacy of aspirin for stroke prevention in migraineurs. Aspirin resistance refers to an inadequate platelet inhibitory response to aspirin treatment manifested by high post-treatment platelet reactivity (HPPR) using an in vitro function platelet assay and has been attributed to limited and inconsistent thromboxane A2 (TXA2) inhibition. Migraineurs have platelet hyperaggregability, which may partially explain their increased risk for stroke and myocardial infarction (MI), particularly in those with aura.

Methods

Design: Single-group, prospective, intervention study approved by the Swedish Medical Center (SMC) Institutional Review Board. Non-probability, consecutive sampling was used to enroll migraineurs from SMC and the University of Washington Headache Clinic.

Target Population: Subjects aged 18-70 years, established diagnosis of active migraine, or with current or uncontrolled head pain as evidenced by recent neurological evaluation using International Headache Society (IHS) criteria and having ≥5 migraines in the 12 months prior to enrollment.

Methods: Underwent a 14-day washout period of aspirin, NSAIDs, and supplements that affect platelet function, followed by a 2-day ex-vivo platelet function test. Subjects were disqualified if they were receiving medications, such as anticoagulants, that may affect platelet function. Demographic, migraine frequency, and comorbidity data were obtained by medical history and/or self-report. Migraine burden and disability were assessed by the Migraine Disability Assessment (MIDAS) and Headache Impact Test (HIT-6), respectively. Subjects were categorized by aura status and migraine subgroups (episodic vs. chronic vs. medication-overuse headache) based on IHS criteria. Platelet reactivity was measured pre- and post-treatment using the VerifyNow® Aspirin Assay (Accumetrics, San Diego, CA), which measures platelet aggregation in whole blood following acetylcysteine stimulation. Results are expressed as aspirin reactive units (ARU) and range from 0-700. Subjects who had baseline ARU ≥500 were excluded due to potential underlying platelet dysfunction or non-adherence to treatment. Following aspirin treatment, subjects with ARU ≥500 were categorized as having aspirin resistance (ARU) as reported by a prior study.

Results

Prevalence of High Post-Treatment Platelet Reactivity (Primary Endpoint): Twelve (24%, 95% CI 12-36%) of subjects, all female, had HPPR post-treatment and were classified as aspirin resistant. Using the more stringent manufacturers’ ARU criterion of ≤250 as an indication of therapeutic platelet inhibition, 4 subjects (8%) had inadequate platelet inhibition (ARU ≥250). Among the 11 subjects with ARU ≥500, 3 had ARU ≥600 following aspirin treatment for 14-21 consecutive days. Eleven of these subjects (90%) also had HPPR. The association between HPPR and inadequate PPI was highly significant (Figure 1; p < 0.001).

Prevalence of Percent Platelet Inhibition (Secondary Endpoint): Twelve subjects (24%) had PPI <60% following aspirin treatment for 14-21 consecutive days. Eleven of these subjects (90%) also had HPPR. The association between HPPR and inadequate PPI was highly significant (Figure 1; p < 0.001).

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Table 1. Baseline demographics and migraine data. Subjects were grouped according to ARU (≤400 and ≤400). ARU = aspirin reactive units.

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