Aspirin as a Promising Agent for Decreasing Incidence of Cerebral Aneurym Rupture

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See related article, pages 3156–3162.

Approximately 2% of the general population harbor saccular intracranial aneurysms (IAs), lesions that are largely asymptomatic unless they rupture and produce a subarachnoid and/or intracerebral hemorrhage. The natural history of unruptured IAs, especially their propensity to bleed once discovered, remains controversial. Moreover, there is a poor understanding of several factors that may lead to IA rupture. One factor that has recently gained attention is the hypothesis that inflammation of the vessel and/or aneurysm wall may contribute in some way to a higher likelihood of rupture. However, data supporting the clinical relevance of this hypothesis are lacking. In the present submission, Hasan and colleagues use data from the International Study of Unruptured Intracranial Aneurysms (ISUIA) to indirectly address this issue. The ISUIA database likely comprises the most extensive retrospective and prospective database on patients harboring unruptured IAs and contains clinical outcome as well as extensive demographic information. The authors have proposed that if inflammation is related to IA rupture risk, then this risk would be reduced in patients who are taking anti-inflammatory agents.

The authors used data from the prospective untreated cohort in the ISUIA database (n = 1691 cases) to assess whether aspirin use and frequency of use were associated with occurrence of IA rupture. Of these patients, 58 had a proven aneurysmal subarachnoid hemorrhage (SAH) during a 5-year follow-up and were matched against 213 control subjects. The risk of SAH was analyzed based on the frequency of aspirin use. The data suggested a trend for a protective effect of aspirin use such that those patients who used aspirin ≥3 times per week had a lower OR for SAH than those who did not use aspirin. Patients who used aspirin less than once a month and those who used it up to 2× per week also had lower ORs for SAH. The authors thus concluded that frequent aspirin use may confer a protective effect for risk of IA rupture.

The possibility that reducing inflammation may reduce hemorrhage risk is intriguing but unproven. The data currently presented are at best an indirect indication in support of this hypothesis. It is unclear whether the use of aspirin actually affected inflammation in the patients in question, because the data set, by its nature, did not include other measures/biomarkers of inflammation. By the same token, it is unclear whether other actions of aspirin such as a reduction in platelet aggregation that may affect the turbulence of blood flow in an aneurysm may have played a role in affecting hemorrhage risk.

Moreover, patients who routinely use aspirin must have been doing so for reasons other than their aneurysm. Such reasons may include transient ischemic attack prevention, myocardial infarction prevention, arthritis, or even on the assumption that aspirin intake is healthy, suggesting a patient population that is more closely attentive to their medical well-being. The size of the current cohort is insufficient to adequately match patients in the various groups according to known medical comorbidities. Thus, although it is intriguing to believe that aspirin may reduce the incidence of aneurysm SAH due to an anti-inflammatory action, it may simply be that aspirin intake is more frequent in those patients who also have better blood pressure control, use statins, and have a better awareness of the deleterious effects of smoking, etc. The authors did use multivariable regression approaches to examine these issues. However, in this underpowered data set, these analyses do not exclude these alternative explanations. Nonetheless, given the relative paucity of demographic data and longitudinal prospective follow-up on patients with unruptured IAs, the authors’ findings remain most intriguing, and I hope that they may pursue them further in future studies.

As a final word of caution, the association of reduced odds of sustaining an aneurysmal SAH with increased aspirin use should not, at this stage, be interpreted as a suggestion that aspirin use is of overall clinical value in patients with IAs. Whereas the morbidity of a SAH is often severe, it may be compounded if the bleeding patient also has an impairment of platelet function. Thus, the possibility of a more adverse clinical outcome in the event of a SAH should be weighed against the possibility of a reduced likelihood of a SAH.

Disclosures

M.T. is president and CEO of NoNO Inc, a company dedicated to the development of neuroprotectants discovered in his academic laboratory.
References


**Key Words:** aneurysms ■ antiplatelet Rx ■ aspirin ■ cerebrovascular accident ■ hemorrhage ■ inflammation ■ intracranial aneurysm ■ outcomes ■ SAH ■ subarachnoid hemorrhage
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