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EDITORIAL OPEN ACCESS

Risk of hemorrhagic stroke from aspirin use: Does risk outweigh the benefit?

Fatai Kunle Salawu, Zira Gyhi Vandi

Aspirin has been widely used to prevent myocardial infarction and ischemic stroke but some authors have suggested that it increases the risk of hemorrhagic stroke. The first randomized controlled trial of aspirin in the prevention of vascular events was conducted in South Wales in 1974 [1]. Since then overviews of numerous trials [2, 3] have established aspirin in cardiovascular disease, as the most thoroughly and the most highly cost-effective drug available in clinical practice. Aspirin is now a standard part of both the early and the long-term management of coronary thrombosis. Aspirin was introduced as an analgesic and antipyretic agent in the late 1890s. However, it is only during the past two decades that attention has been focused on the therapeutic effect of aspirin on cardiovascular disease [4]. A number of large randomized controlled clinical trials have demonstrated that aspirin treatment reduces the risk of subsequent myocardial infarction and ischemic stroke among patients with a wide range of pre-existing cardiovascular diseases [5–10]. A study suggested that aspirin treatment reduces the risk of non-fatal myocardial infarction in healthy individuals [11, 12]. Aspirin is now being used for primary and secondary prevention of cardiovascular disease in the general population [13–15]. Several studies have suggested that aspirin increases the risk of hemorrhagic stroke [5–12]. It should be used with caution in individuals, who are at high risk of hemorrhagic stroke, e.g., hypertensive patients with a low level of serum cholesterol [16, 17]. Although aspirin therapy has been well documented to reduce the incidence of myocardial infarction in those who are at relatively high risk, its benefits have not been well documented in healthy persons who are younger than 50 years [11, 12]. Thus, aspirin treatment may not be recommended to such persons for the purpose of primary prevention of cardiovascular disease. There is overwhelming evidence that aspirin reduces cardiovascular disease morbidity and mortality in patients with ischemic heart disease or stroke. A meta-analysis of randomized controlled trials involving 16 trials with 55,462 participants and 108 hemorrhagic stroke cases revealed aspirin use was associated with an absolute reduction of 97 cardiovascular deaths per 10,000 persons, 137 myocardial infarction events per 10,000 persons and 39 ischemic stroke events per 10,000 persons. Even in healthy populations older than 50 years in western countries, the absolute risk reduction of myocardial infarction and ischemic stroke is much higher than that of hemorrhagic stroke [18]. Therefore, the overall benefit of aspirin use on myocardial infarction and ischemic stroke almost certainly overcomes the potential risk of hemorrhagic stroke in such groups.

There are several possible mechanisms by which aspirin could increase the risk of hemorrhagic stroke. Aspirin selectively acetylates the hydroxyl group of a single serine residue at position 529 within the polypeptide chain of platelet prostaglandin G/H synthase 1, causing irreversible loss of its cyclooxygenase activity [4, 19]. This results in decreased conversion of arachidonate to prostaglandin G_2 and ultimately of prostaglandin H_2 and thromboxane A_2, which are important mediators in platelet aggregation and thrombi formation. Platelets are exquisitely sensitive to aspirin. A dosage of only 30 mg/day effectively eliminates the synthesis of thromboxane A_2. The minimum dosage of aspirin in the trials that were included in the meta-analysis by He et al. was 75 mg/day which is higher than this threshold [20]. Several trials failed to include data on stroke subtypes, while some of the trials were conducted in the late 1970s or early 1980s, when computed tomography might have been routinely used for the diagnosis of stroke.

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There is little doubt wheter the use of aspirin in the primary and secondary prevention of cardiovascular events and stroke slightly increases the risk of serious bleeding, or not but this risk is outweighed by its beneficial effect.

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Keywords: Aspirin, Coronary thrombosis, Hemorrhagic stroke

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Fatai Kunle Salawu – Substantial contributions to conception and design, Acquisition of data, Analysis and interpretation of data, Drafting the article, Revising it critically for important intellectual content, Final approval of the version to be published

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