Commencing antiplatelet therapy in older people after an acute ischaemic stroke

Each year an estimated 150,000 people in the United Kingdom suffer an acute stroke. Of these, approximately one-third are due to recurrent cerebrovascular events. Ischaemic stroke accounts for 85% of first ever strokes, and older persons are at greatest absolute risk of stroke and other occlusive vascular disease. Antiplatelet therapy is key to the secondary prevention of stroke, reducing the risk of serious occlusive vascular events by about one quarter in high-risk patients [1], but treatment is not without risk. Regular aspirin use causes a wide spectrum of adverse gastrointestinal effects, ranging from an inability to tolerate the drug because of dyspepsia with endoscopically normal mucosa, to symptomatic and asymptomatic lesions such as erosions and ulcers, and is associated with a 2-fold increased risk of upper gastrointestinal bleeding or perforation. The degree of gastrointestinal damage sustained during treatment is related to the dose of aspirin [2], with a comparable bleeding risk to clopidogrel when used in long-term secondary prevention [3].

The body maintains its gastromucosal integrity through a number of inherent mechanisms designed to oppose internal and external aggressive factors. With increasing age, arterial blood supply to the stomach reduces and gastric epithelial cell turnover diminishes. Prostaglandin levels in the gastric mucosa decrease and the production of bicarbonate and mucus by the gastric epithelium also decreases. As a consequence, the integrity of the gastric mucosal surface becomes impaired and progressively susceptible to damage by factors that can overwhelm the stomach’s protective barriers [4].

As a result of these changes, older people are much more susceptible to adverse events. Combined with this susceptibility, advanced age is also a major risk factor for complicated ulcer disease, which itself is associated with a high mortality. These factors are a regular consideration when starting...
older people on antiplatelet therapy and recent guidelines acknowledge this risk by recommending that patients with aspirin-associated dyspepsia are routinely started on prophylactic proton pump inhibitors (PPIs) [5]. There are additional factors however that further compound the situation and may predispose to gastrointestinal intolerance.

The prevalence of Helicobacter pylori increases with age and affects over 75% of the older population in some areas of the United Kingdom [6]. H. pylori, in addition to aspirin and non-steroidal anti-inflammatory drug (NSAID) ingestion, is an established cause of gastroduodenal ulceration. Much of our understanding of the interaction between H. pylori and NSAIDs derives from studies of patients with rheumatological diseases. The evidence from these studies is conflicting and few have looked specifically at aspirin and H. pylori. Even less is known regarding the interaction of H. pylori with dipyridamole or clopidogrel. There is no current consensus as to who should be investigated and treated for H. pylori eradication before commencing antiplatelet therapy. Recent evidence suggests that aspirin naive patients potentially have the most to gain from H. pylori eradication treatment prior to commencing therapy [7] but such an approach has not been evaluated in stroke patients and is likely only to be considered in patients with symptomatic dyspepsia. There is uncertainty, therefore, as to which patients are most at risk of aspirin-associated dyspepsia and how this can best be prevented or managed.

Acute stroke induces major physiological responses. For gastric mucosa already contending with the physiological changes of ageing, H. pylori infection and initial high-dose aspirin treatment, the increased risk of gastroduodenal ulceration associated with a major stress response may be the final insult. The effect of stress on the gastric mucosa of patients admitted to intensive care units has been shown to increase the risk of gastrointestinal haemorrhage. In patients with severe head trauma this risk increases, occurring in up to 75% of patients [8], but there are limited data on the incidence of gastrointestinal haemorrhage following an acute stroke. Davenport et al. reported the frequency of gastrointestinal haemorrhage after an acute stroke in 607 patients to be 3% [9]. Stroke severity and age were both significant risk factors for gastrointestinal haemorrhage.

Following an acute stroke dysphagia is a frequent symptom, affecting up to 50% patients, and associated with short- and long-term difficulties maintaining hydration or nutrition. There is little information upon the effect of acute starvation on the incidence of peptic ulcer disease. When a cohort of rats was starved for 7 days all developed gastric ulceration [10]. Acute starvation also significantly enhanced the gastric mucosal damage induced by NSAID treatment in rats [11]. When starvation was combined with a stress event, the increase in severity of ensuing ulcerations directly corresponded to the duration of starvation [12]. Compounded by the stress effect of an acute stroke, it could be presumed that suboptimal nutritional management, in addition to the commencement of antiplatelet therapy, could produce conditions ripe for the development of complicated peptic ulcer disease. Even enhanced nutritional support, via nasogastric or percutaneous endoscopic gastrostomy tube, has, however, been shown to increase significantly the risk of gastrointestinal haemorrhage [13].

Individuals who are malnourished after an acute stroke have a worse outcome in terms of survival and disability at 6 months. Malnutrition, in the form of acute weight loss, can adversely affect the body’s natural gastrointestinal defence mechanisms and may contribute to the onset and severity of haemorrhage in NSAID-induced gastric ulcers [14]. At the other extreme, obesity is also known to increase significantly the risk of developing gastroduodenal ulcers [15].

Much more work is needed to develop and guide safe prescribing of antiplatelet therapy in the setting of an acute ischaemic stroke. Advancing age, stroke severity, concurrent H. pylori infection, malnutrition and acute starvation are all factors potentially conspiring to cause gastrointestinal upset, even before antiplatelet therapy is added to the equation. These factors are implicated not only in acute bleeding but also long term, occult blood loss. Antiplatelet therapy is the mainstay of acute treatment and long-term prevention for ischaemic stroke but we need to further our understanding of the acute pathophysiological changes occurring in the gastrointestinal tract following stroke, the influence of potential risk factors and the implications these have for clinical care.

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References


