Clin-IQ Project

Clinical Question: In adults with coronary artery disease or at high risk of stroke, does taking 81 mg of aspirin daily result in improved outcomes compared to those taking 325 mg aspirin per day?

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Answer: **No**

Level of Evidence for the Answer: **A** or B or C

Search Terms: aspirin 81 mg vs aspirin 325 mg; CAD and aspirin; stroke and aspirin

Date Search was Conducted: September 2012

Inclusion and Exclusion Criteria:

Inclusion Criteria: Published reviews/meta-analysis and clinical research trials that compare low to high dose aspirin in patients with CAD and/or at risk of stroke.

Exclusion Criteria: Trials or reviews that only include a subgroup, such as men aged 40 and over were not included.

Summary of the Issues: (word count=200-300)

Aspirin, or acetylsalicylic acid (ASA) has been used for a multitude of indications ranging from fevers to spondyloarthropathies. Aspirin, however, is best known for its cardiovascular uses. There have been numerous published trials and recommendations regarding the use of 'low versus high dose' aspirin, for both the primary and secondary prevention of cardiovascular events as well as strokes and acute coronary syndromes (ACS). Dosing, then becomes important as one must consider the side effects and benefits to maximize the outcome of taking aspirin to prevent cardiovascular disease (CVD) and or strokes while minimizing

gastrointestional bleedin

Summary of the Evidence: (word count=500-700)

What is then the optimal dose of aspirin, when considering decreased platelet aggregation while sustaining coronary artery vasodilatation with minimal gastrointestinal toxicities? To properly evaluate this question, it is important to take into account several important considerations. This includes methods of ingestion, adequate acetylation of platelet function for ACS treatment and cardiovascular disease prevention while also managing adverse effect.

In regards to method of ingestion, different techniques and types of pills can influence Aspirin's effectiveness. Aspirin absorption and the onset of anti-platelet activity are significantly shortened by chewing or drinking solubilized aspirin with maximum inhibition of platelets achieved within 20-30 minutes compared to 60 minutes found with swallowing a whole pill. In a study of 18 volunteers, chewing an 81mg, 162mg or 325mg aspirin pill led to maximal inhibition of platelet function in 15 minutes with only the 162mg and 325mg doses. This rapid administration of aspirin by chewing tablets with a minimum dose of 162mg was found to be beneficial with treating ACS but found no advantage for chronic coronary artery disease (CAD)prevention. [6] In another study, evaluating the acute antiplatelet effects of 40mg, 100mg, 300mg, and 500mg doses of aspirin, the 300mg and 500mg doses were found to achieve equal levels of platelet inhibition 2 hours following ingestion. Enteric coated pills have not shown to be effective with protecting gastric mucosa, but they have been shown to significantly limiting aspirin's platelet inhibition[7].

Current published data show that dosage of 50 to 1500 mg per day is an effective antithrombic agent. In the Antithrombotic Trialists' Collaboration of Antiplatelet Therapy (ATC) trl, low dose aspirin (75-150 mg/day) was shown to be an effective regimen, suggesting that 75

mg/day should be the minimum effective daily dose. Doses greater than 300 mg/day were noted to cause more GI side effects. It is, however, safe to say that if GI toxicities were not a concern, low dose aspirin (75-162) and high dose aspirin (>162 mg/day), as in the BRAVO and CURE studies showed, may be used,as there were no significant difference in preventing the incidence of myocardial infarction, or stroke.

In a trial from the Dutch TIA study group, a significant benefit of higher dosages of aspirin up to 1300 mg was not found, with the lowest event rates realized among patients randomized to the low dose group. In this trial, 3131 individuals were randomized to receive either 283mg/d or 30mg/d of aspirin following a TIA or stroke. After a mean of 2.6 years of follow-up, the combined end point of vascular death, MI, or stroke was similar in the 2 groups (14.7% for 30mg/d vs 15.2% for 283 mg/d; hazard ratio, 0.91; 95% confidence interval [CI], 0.76-1.09[8].

Evaluating the dose of aspirin for adverse effects appears to be mostly focused in regards to gastrointestional bleeding. Kaufman et al found that treatment with 75 mg/d dosage of aspirin was associated with an odds ratio of 2.3 for a bleeding ulcer (95% CI, 1.2-4.4), whereas 300 mg/d increased the odds ratio to 3.9 (95% CI, 2.5-6.3). They also found that enteric coated or buffered aspirin preparations do not appear to influence the risk of major bleeding in the upper GI tract.[9]

Table/Figure/Graph

Table 1. Risk of hospitalization for bleeding ulcer associated with aspirin prophylaxis

Aspirin dose	Odds Ratio (OR)	95% CI
75 mg	2.3	1.2-4.4
150 mg	3.2	1.7-6.5
300 mg	3.9	2.5-6.3

Table 2. Combined end point of vascular death, myocardial infarction or stroke after 2.6 years follow up was similar in both groups.

Aspirin Dose	% Death from vascular, MI or stroke
30 mg daily	14.7
283 mg daily	15.2

Aspirin is the most commonly used drug throughout the world. While it has been shown to be safe for the general public, its vast use predisposes the general population to risks even at low doses. Multiple studies have shown that there is an increased risk with high dose aspirin without improvement in efficacy. This research further suggests no improved outcomes with doses larger than 81mg except in situations needing acute platelet inhibition commonly found in ACS which recommend chewing 160-325mg of aspirin. The best antiplatelet regimen currently supported by clinical data is the daily use of 81 mg for cardiovascular disease prevention with the least associated gastrointestinal bleeding.

Reference List (1-2 review articles, 2 evidence articles):

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ischemic attack. PubMed, 2008. (Accessed Sept 7, 2012, a thttp://guidelines.gov/content.aspx?id=12950#Section420)

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