3-26-2015

Low Dose Aspirin: An Effective Chemoprophylaxis for Preventing Venous Thromboembolic Events

Javad Parvizi, MD, FRCS
Rothman Institute, Thomas Jefferson University, Javad.Parvizi@jefferson.edu

Antonia F. Chen, MD, MBA
Rothman Institute, Thomas Jefferson University, antonia.chen@rothmaninstitute.com

Camilo Restrepo, MD
Rothman Institute, Thomas Jefferson University, camilo.restrepo@rothmaninstitute.com

Ronald Huang, MD
Rothman Institute at Thomas Jefferson University, ronald.huang@jefferson.edu

Jenny Cal, BS
Rothman Institute, Thomas Jefferson University, jenny.cal@jefferson.edu

See next page for additional authors

Authors
Javad Parvizi, MD, FRCS; Antonia F. Chen, MD, MBA; Camilo Restrepo, MD; Ronald Huang, MD; Jenny Cal, BS; William J. Hozack, MD; and Jess H. Lonner, MD

Low Dose Aspirin: An Effective Chemoprophylaxis for Preventing Venous Thromboembolic Events

Javad Parvizi MD, FRCS, Antonia F. Chen MD, MBA, Camilo Restrepo MD, Ronald Huang MD, Jenny Cai BS, William J. Hozack MD, Jess H. Lonner MD.

Investigation performed at the Rothman Institute at Thomas Jefferson University, Philadelphia, PA.

INTRODUCTION

The available guidelines, endorsed by Surgical Care Improvement Project (SCIP), have advocated that aspirin (ASA) is a safe and effective strategy for venous thromboembolic events (VTE) prophylaxis following total joint arthroplasty (TJA). The optimal dose of aspirin for this purpose is not known. The first guidelines for prevention of VTE that were issued by the American Academy of Orthopedic Surgeons recommended 325 mg *Bis in die* (twice a day) (bid) for this purpose with the recommendation having a 1C grade (little evidence to support the recommendation). It is known that platelet aggregation inhibition occurs at lower doses. Traditionally, ASA 81mg has been used as a cardio-protective medication. Additionally, all available randomized studies, including the sentinel study on Pulmonary Embolism Prevention (PEP) trial[1-4] have used lower doses of ASA. It was our hypothesis that lower dose aspirin is likely to be as effective as higher dose aspirin while reducing the gastrointestinal side effects associated with the higher dose aspirin.

MATERIALS AND METHODS

We analyzed a cohort of 2,880 primary TJA patients. All patients were treated with post-operative intermittent pneumatic compression while hospitalized. Of these, 2,138 patients with an average age of 64.6 years [Standard desviation (SD) ±10.4] received enteric coated ASA 325mg by mouth, bid for 4 weeks. In the other group, 742 patients with an average age of 64.1 years (SD±12.0) received plain ASA 81mg by mouth bid for 4 weeks. Gender, body mass index (BMI), and comorbidities assessed by the Charlson comorbidity index (CCI) were recorded (Table 1). There was no difference in age, gender, CCI, or BMI between the patient populations. Patients were evaluated for the development of symptomatic VTE in the post-operative period using International Classification of Diseases version 9 (ICD-9) codes, specifically deep vein thrombosis (DVT) and pulmonary embolism (PE). Statistical analysis was performed using Wilcoxon and Fisher's tests.

RESULTS

There was no significant difference in the incidence of VTE between the two groups; 0.1% in the 81mg ASA group (one DVT), compared to 0.2% in the 325mg ASA group (2 DVT and 2 PE). Two episodes of gastrointestinal (GI) bleeding occurred in the 325mg ASA group, compared to none in the 81mg ASA group.

TABLES 1 & 2

		Aspirin 81mg bid	Aspirin 325mg bid	p-value
Age (years) mean (SD)		64.1 (12.0)	64.6 (10.4)	0.295
CCI mode (SD)		3 (± 2)	3 (± 1)	0.082
BMI (kg/m^2) mean (SD)		29.7 (6.2)	29.5 (5.1)	0.738
LOS (days) mean (SD)		1.9 (1.1)	1.9 (2.2)	0.591
Sex	Male	46.2%	45.1%	0.654
	Female	53.8%	54.9%	
Primary THA		40.2%	51.6%	<0.001
Primary TKA		59.8%	48.4%	

Table 1: Demographics and procedures in patients receiving ASA 81mg bid vs. 325mg bid.
mg=milligrams; bid=*Bis in die* (twice a day); SD=Standard deviation; CCI=Charlson comorbidity index; Kg=Kilograms; m^2=Square meter; THA=Total hip arthroplasty; TKA=Total knee arthroplasty.

Complication	ASA 81mg bid (n=742)	ASA 325mg bid (n=2138)	p-value
DVT	1 (0.1%)	2 (0.1%)	0.764
Pulmonary Embolism	0 (0%)	2 (0.1%)	0.405
Gastrointestinal Bleeding	0 (0%)	2 (0.1%)	0.405
Acute Infection	0 (0%)	5 (0.2%)	0.187
90-day Mortality	1 (0.1%)	2 (0.1%)	0.764

Table 2: Complication rates in patients receiving ASA 81mg bid vs. 325mg bid.
mg=milligrams; bid=*Bis in die* (twice a day); DVT=Deep venous thrombosis.

FIGURE 1

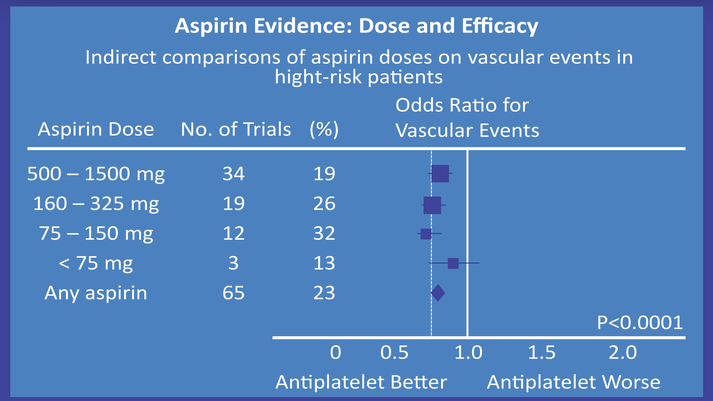

Figure 1: Forest plot from the Antitrombotic Trialists' Combination study[4] depicting the protective effect againts vascular events among different aspirin dosages. Studies using between 75 and 150 mg of aspirin exhibit a greater antiplatelet effect than studies with aspirin regimens in between 160 and 325 mg.
No.=Number; mg=milligrams.

RESULTS

Acute infection rate was also higher in the 325mg ASA group at 5 cases (0.2%) compared to none in the 81mg ASA group. Finally, there were two mortalities in the 325mg ASA group (one in-hospital, one post-discharge) compared to one mortality in the 81mg ASA group (post-discharge).

DISCUSSION

Our ongoing study demonstrates that low dose ASA (81mg bid for four weeks) is as effective of a prophylaxis agent as high dose ASA (325mg) following TJA. This is not surprising as all available literature, including many publications related to VTE prophylaxis following TJA, demonstrate that low dose aspirin has better antiplatelet aggression properties. Continued evaluation of the safety and efficacy of ASA as a prophylactic agent and the comparison of the doses continues at our in our prospective study.

REFERENCES

1. Hovens MM, Snoep JD, Tamsma JT, Huisman MV. Aspirin in the prevention and treatment of venous thromboembolism. *J Thromb Haemost.* 2006 Jul;4(7):1470-5.
2. Antitrombotic Trialists' Combination. Collaborative meta-analysis of randomised trials of antiplatelet therapy for prevention of death, myocardial infarction, and stroke in high risk patients. *BMJ* 2002;324:71–86.
3. Geerts WH, Pineo GF, Heit JA, Bergqvist D, Lassen MR, Colwell CW, Ray JG. Prevention of venous thromboembolism: the Seventh ACCP Conference on antithrombotic and thrombolytic therapy. *Chest* 2004;126: 338S–400S.
4. Antitrombotic Trialists' Combination. http://www.slideshare.net/dhavalshah4424/aspirinandvascular. Accessed 01/21/2015.