Effects of Perioperative Acetyl Salicylic Acid on Clinical Outcomes in Patients Undergoing Craniotomy for Brain Tumor

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OBJECTIVE: **To evaluate the safety of continuing acetyl salicylic acid (ASA) in patients undergoing brain tumor resection. Many patients are on antiplatelet agents that are withheld before elective neurosurgical procedures to reduce bleeding risk. Cessation of ASA in patients with cardiovascular disease is associated with a known increased risk of thrombotic events, especially in patients with coronary stents.**

METHODS: **The medical records of patients who underwent surgical resection of a brain tumor at the University of Florida from 2010 to 2014 were evaluated. The patients were separated into groups based on preoperative ASA use and whether or not it was stopped before surgery. Patients were evaluated for thrombotic complications, postoperative hemorrhage, estimated blood loss, length of hospital stay, and discharge disposition.**

RESULTS: **Of the 452 patients analyzed, 368 patients were not on chronic ASA therapy, 55 patients had their ASA discontinued before surgery, and 28 patients were continued on ASA perioperatively. The patients on preoperative ASA were comparable on all collected demographic variables. There were no statistical differences detected between the groups for outcomes including bleeding complications, need for reoperation, or thrombotic complications.**

CONCLUSIONS: **In this analysis, perioperative low dose ASA use was not associated with increased risk of perioperative complications.**

INTRODUCTION

The management of antiplatelet agents is a serious therapeutic dilemma in neurosurgical patients. The devastating and potentially fatal sequelae of a hemorrhagic complication from a craniotomy are well-known (16). Therefore, most neurosurgeons commonly stop the administration of all antiplatelet agents several days before elective cranial surgery. An increasing number of patients are taking chronic low dose acetyl salicylic acid (ASA) (9, 10) because it has been shown to have a clear benefit in secondary prevention of cardiovascular events and possible benefit in primary prevention as well (4). In addition, patients with coronary stents are often on dual antiplatelet therapy with ASA and another agent. The American College of Cardiology/American Heart Association guidelines (14) recommend uninterrupted dual antiplatelet therapy with ASA plus a thienopyridine (clopidogrel, prasugrel, or ticagrelor) for 6 weeks after bare metal stent placement and 12 months after drug-eluting stent (DES) placement to prevent stent thrombosis. Thereafter, ASA should be continued lifelong in most patients to prevent late stent thrombosis.

In most cases, patients with brain tumors need timely surgical treatment that cannot be delayed to meet these antiplatelet guidelines. If antiplatelet therapy is continued during surgery, the risk of a hemorrhagic complication may increase (5, 17). Of patients who suffer a postoperative hemorrhage, more than half will die or live with severe disability (17). Therefore, almost uniformly, patients with brain tumor on ASA will have their ASA stopped before surgical resection. This strategy potentially decreases the risk of postoperative hemorrhage, but increases the risk of thrombotic cardiovascular events. At present, little evidence exists to inform the management of neurosurgical patients on antiplatelet agents.

Key words
- Acetyl salicylic acid
- Antiplatelet therapy
- Aspirin
- Brain tumor
- Neurosurgery
- Perioperative complications

Abbreviations and Acronyms
ASA: Acetyl salicylic acid
DES: Drug-eluting stent
EBL: Estimated blood loss
POISE-2: PeriOperative ISchemic Evaluation-2

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Citation: World Neurosurg. (2015) 84, 1:41-47.
http://dx.doi.org/10.1016/j.wneu.2015.02.016

Journal homepage: www.WORLDNEUROSURGERY.org

Available online: www.sciencedirect.com

Table 1. Demographic Data Based on Perioperative ASA Management

	Overall (n = 452)	No ASA (n = 369, 81.6%)	Cont ASA (group 1) (n = 28, 6.2%)	Discont ASA (groups 2 & 3) (n = 55, 12.2%)	*P* Value
Age (years)					Overall: <0.0001 Cont vs. Discont: 0.407
Mean (SD)	56.9 (15.7)	54.6 (16.0)	65.9 (8.2)	67.5 (9.7)	
Median (range)	60 (1—92)	56 (1—92)	67 (42—84)	68 (38—88)	
Deceased (n, %)	100 (22.1)	71 (19.2)	9 (32.1)	20 (36.4)	Overall: 0.008 Cont vs. Discont: 0.810
Female (n, %)	228 (50.6)	196 (53.3)	12 (42.9)	20 (36.4)	Overall: 0.044 Cont vs. Discont: 0.636
CCI					Overall: <0.0001 Cont vs. Discont: 0.541
Mean (SD)	5.6 (2.6)	5.3 (2.5)	6.7 (2.1)	7.0 (2.3)	
Median (range)	5 (1—13)	5 (1—13)	6 (3—11)	7 (2—13)	
CAD (n, %)	47 (10.4)	22 (6.0)	7 (25.0)	18 (32.7)	Overall: <0.0001 Cont vs. Discont: 0.614
PVD (n, %)	27 (6.0)	20 (5.4)	4 (14.3)	3 (5.5)	Overall: 0.154 Cont vs. Discont: 0.219
Stent (n, %)	17 (3.8)	6 (1.6)	4 (14.3)	7 (12.7)	Overall: <0.0001 Cont vs. Discont: 1
CABG (n, %)	8 (1.8)	3 (0.8)	1 (3.6)	4 (7.3)	Overall: 0.005 Cont vs. Discont: 0.658
Stroke (n, %)	37 (8.2)	25 (6.8)	5 (17.9)	7 (12.7)	Overall: 0.041 Cont vs. Discont: 0.528
VTE (n, %)	26 (5.8)	20 (5.4)	3 (10.7)	3 (5.5)	Overall: 0.446 Cont vs. Discont: 0.400

The *P* values are shown for overall comparisons as well as comparisons between patients who had aspirin continued (Cont) and those who had it discontinued (Discont).
ASA, acetyl salicylic acid; CCI, Charlson comorbidity index; CAD, coronary artery disease; PVD, peripheral vascular disease; CABG, coronary artery bypass graft surgery; VTE, venous thromboembolism.

Quantifying the risks associated with continuing or discontinuing antiplatelet agents in the perioperative period is critical. The purpose of this study is to evaluate the safety of continuing ASA in patients undergoing brain tumor resection by comparing outcomes in patients who were kept on ASA perioperatively with patients whose ASA was discontinued before surgery.

METHODS

Patients, Inclusion/Exclusion Criteria, and Study Variables

Institutional Review Board approval was obtained at the University of Florida. Admissions of patients with brain tumors to University of Florida Health between 2010 and 2014 were identified using the neurosurgery billing database and the following *International Classification of Diseases, 9th Revision* (22) codes: 191.0-.9, 225.0-.2, 225.9, 198.3, 192.1, 239.6, 237.1, 237.5-.6, and 227.3-.4. From the list obtained, patients who underwent a supratentorial or infratentorial craniotomy for tumor or meningioma were analyzed (CPT codes 61510, 61512, 61518, and 61519). A retrospective chart review was conducted using the EPIC electronic medical records system.

The patients were separated into groups based on the treating neurosurgeon. The regular practice pattern of 2 of the neurosurgeons (Surgeons 1 and 2) was to continue ASA for certain patients during surgery who were believed to be low risk for a hemorrhagic complication based on tumor size and location. These patients were compared with patients treated by 2 other surgeons (Surgeons 3 and 4) who routinely stopped ASA before surgery. Patients who were on preoperative ASA were classified into 3 groups: 1) ASA continued; group 1 (Surgeons 1 and 2); 2) ASA discontinued before surgery; group 2 (Surgeons 1 and 2); 3) ASA discontinued before surgery; group 3 (Surgeons 3 and 4).

The data collection tool included the following primary end points: thrombotic complications (myocardial infarction, pulmonary embolism, deep vein thrombosis, or ischemic stroke), postoperative hemorrhage, estimated blood loss (EBL), and length of hospital stay. Other collected variables included age, gender, specific pathologic diagnosis, comorbidities (as per the Charlson Comorbidity Index (6)), vital status, date of tumor resection surgery and/or cardiac stent placement, discharge disposition (home, subacute nursing home, acute rehabilitation facility, correctional facility, or death), reason for reoperation (if applicable), details of other perioperative anticoagulant or antiplatelet use, and history of pulmonary embolism, deep vein thrombosis, stroke, coronary artery bypass graft, cardiac stent