Antithrombotic Medication Use and Misuse Among Patients with Intracranial Hemorrhage: A 16-Year, Lebanese, Single-Center Experience

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OBJECTIVE/BACKGROUND: **The use of antithrombotic medication (ATM) frequently is reported in patients with intracranial hemorrhage (ICH) and is associated with increased mortality. Unfortunately, ATMs sometimes are prescribed and/or used inappropriately. We sought to determine the rate of ATM misprescription/misuse among patients with ICH in a single-center retrospective study.**

METHODS: **All patients admitted with ATM-related ICH in 1998–2014 were included. Charts were reviewed and demographic, clinical, and radiologic variables were recorded. The type of ATM, dose, and duration of treatment were analyzed critically. The adequacy of ATM prescription/use was assessed in light of the recommendations and guidelines of the American Heart Association, American Stroke Association, and French National Authority for Health, in effect at the time of admission.**

RESULTS: **A total of 106 patients with mean age 68 years were identified. Aspirin (53.8%) was the most commonly used drug, followed by oral anticoagulants (31.1%) and clopidogrel (22.6%). In only 80 patients (75.5%), the use of ATM was in line with contemporary guidelines. In the remaining 26 (24.5%), the use of ATMs was inappropriate, including bad drug combination, wrong dose, poor indication, wrong drug class, and/or incorrect treatment duration.**

CONCLUSIONS: **In this Lebanese cohort of patients with ICH, the 24.5% rate of ATM misprescription and/or misuse is highly alarming and the origin of this problem is likely multifactorial. Immediate measures should be undertaken, and efforts should be focused on regaining tight control of ATM prescription and fulfillment, ensuring good patient education, and offering more vigilant oversight on physician licensure.**

INTRODUCTION

Antithrombotic medications (ATMs), including antiplatelet agents (APAs) and oral anticoagulants (OACs), are being used increasingly for the primary and secondary prevention of thromboembolic events in patients at high cardiovascular risk, largely driven by the increasing life expectancy and aging population.[1-3] Intracranial hemorrhage (ICH) is the most serious complication of ATM use, with mortality rates ranging from 28% to 65%.[4-7] Thus, the importance of the judicious use of ATM prescriptions to minimize the risk of ICH and other serious hemorrhagic complications, particularly in the setting of an aging population, cannot be overemphasized. Several studies and a recent systematic review of the literature have revealed a high rate of underprescription/underuse of ATMs in patients with atrial fibrillation[8-13]; however, to the best of our knowledge, the rate of ATM misprescription/misuse among patients with ICH has not been studied previously. For this reason, we sought to analyze the adequacy of ATM prescription and use in a large cohort of patients presenting with ICH.

MATERIALS AND METHODS

All patients who were admitted and managed in our tertiary referral medical center for either spontaneous or traumatic ICH between December 1998 and February 2014 and who were

Key words
- Anticoagulant
- Antiplatelet
- Antithrombotic
- Intracerebral hemorrhage
- Intracranial hemorrhage
- Subarachnoid hemorrhage

Abbreviations and Acronyms
APA: Antiplatelet agent
ATM: Antithrombotic medication
ICH: Intracranial hemorrhage
INR: International normalized ratio
OAC: Oral anticoagulant

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receiving ATMs at the time of admission were included in this retrospective observational study. Medical charts were reviewed, and demographic, clinical, and radiologic data were recorded, including age, sex, type of ICH, mechanism, location, etiology, type(s) and dose(s) of ATM, and duration of ATM use. The appropriateness of ATM prescription/use in each patient was determined in light of the recommendations and guidelines of the American Heart Association, American Stroke Association, and French National Authority for Health, that were in effect at the time of the patients' admission.[14-16] This study was approved by the university's ethics committee. Statistical analyses were performed with PASW Statistics for Windows, version 18.0 (SPSS Inc., Chicago, Illinois, USA).

RESULTS

During the study period, a total of 800 patients with ICH were admitted and managed in our center. Of those, 106 (13.3%) were receiving ATMs at the time of admission (Figure 1). These were 64 men and 42 women with a mean age of 68 years (range 23–102 years). ICH was spontaneous in 91 patients (85.8%) and traumatic in 15 (14.2%). The location was intraparenchymal (with or without intraventricular extension) in 65 (61.3%), subarachnoid in 34 (32.1%), subdural in 6 (5.7%), and epidural in 1 (0.9%). Etiology of spontaneous cases ($n = 91$) was as follows: idiopathic in 53 (58.2%), hemorrhagic conversion of an infarct in 18 (19.8%), tumor in 5 (5.5%), aneurysm in 4 (4.4%), arteriovenous malformation in 4 (4.4%), cerebral venous or dural sinus thrombosis in 2 (2.2%), and other in 5 (5.5%).

Aspirin was the most commonly used ATM, in 57 patients (53.8%), either alone or in combination with clopidogrel or an OAC, followed by OACs (acenocoumarol or warfarin) in 33 (31.1%) and clopidogrel in 24 (22.6%) (Table 1). ATMs were most commonly prescribed for secondary prevention: stroke in 57 (53.8%) and cardiac disease in 49 (46.2%). Only 11 patients (10.4%) were receiving ATMs for primary prevention (Table 2). The use of ATM was in line with contemporary guidelines in only 80 patients (75.5%). In the remaining 26 (24.5%), the use of ATMs was either unjustifiable or inappropriate: bad drug combination in 13 (50%), wrong dose in 5 (19.2%), poor indication in 3 (11.5%), wrong drug class in 3 (11.5%), and incorrect treatment duration in 2 (7.7%). Interestingly, 5 patients (19.2%) were undertreated. Of 33 patients on OACs, 5 (15.2%) had a labile, poorly controlled international normalized ratio (INR) before ICH (Table 3). The rate of ATM misprescription/misuse was fairly constant throughout the study period, ranging from 20% to 67%, although a 0% rate was observed in 6 calendar years (2002, 2004, 2007, 2008, 2013, 2014) during which only 2–3 patients/year were admitted with ATM-related ICH (Figure 2).

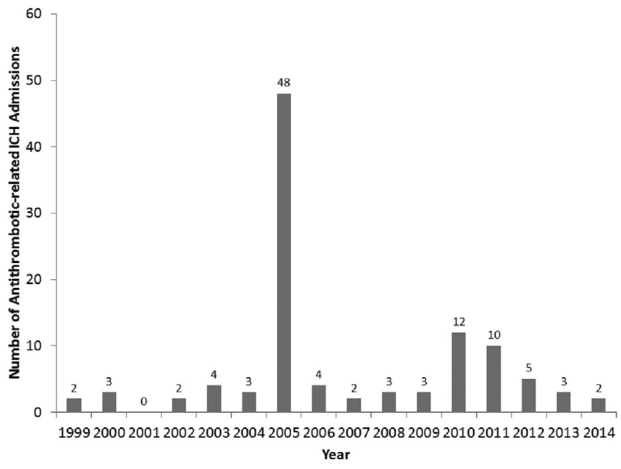

Figure 1. Distribution of antithrombotic-related intracranial hemorrhage (ICH) admissions throughout the study period (1998–2014).

Table 1. Types of ATMs Used

Drug	*n* (%)
Aspirin	47 (44.3%)
OAC (acenocoumarol, warfarin)	30 (28.3%)
Clopidogrel	17 (16%)
Aspirin + clopidogrel	7 (6.6%)
Aspirin + acenocoumarol	3 (2.8%)
Enoxaparin	1 (0.9%)
Other	1 (0.9%)

ATM, antithrombotic medication; OAC, oral anticoagulant.

DISCUSSION

In this 16-year retrospective review, we have found that nearly one quarter of Lebanese patients presenting to our center with antithrombotic-related ICH were not receiving ATMs properly. Although the majority of those were overtreated, close to 20% were undertreated and still developed ICH. To the best of our knowledge,

Table 2. Indications for ATM Use

Indication	*n* (%)
Ischemic stroke	41 (38.7%)
Coronary artery disease	21 (19.8%)
Atrial fibrillation or flutter	16 (15.1%)
Heart valve disease	12 (11.3%)
Primary prevention	11 (10.4%)
Transient ischemic attack	10 (9.4%)
Extra/intracranial atherosclerotic disease	5 (4.7%)
Peripheral artery disease	2 (1.9%)
Cerebral venous or dural sinus thrombosis	1 (0.9%)
Other	3 (2.8%)

ATM, antithrombotic medication.