Withdrawal of Antithrombotic Agents and the Risk of Stroke

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Background and Purpose: Antithrombotic medications are effective for ischemic stroke prevention, but stoppage of these medications is associated with an increased risk of thromboembolism. The frequency of antithrombotic withdrawal in the general population is unknown. Methods: We conducted a random phone sample of 2036 households in the Greater Cincinnati metropolitan area, representative of the stroke population by age, sex, and race, to determine the frequency of antithrombotic medication use and stoppage by physicians for medically indicated procedures. Results: Sixty-two percent of survey respondents reported that they were on an antithrombotic medication. Ten percent of participants reported that they had stopped taking their medication within the past 60 days for a medically indicated intervention. Of those who stopped taking the medication, it was more common for persons taking an anticoagulant to stop their medication (20%) than those taking an antiplatelet agent (9%). Colonoscopies and orthopedic surgeries were the most common reasons for withdrawal of antiplatelet agents, whereas orthopedic and vascular surgeries were the most common reason for withdrawal of anticoagulants. Conclusions: Recommended discontinuation of antithrombotic medication for surgical or diagnostic procedures is common practice for persons in the community representative of a stroke population. Because stoppage of these medications is associated with an increased risk of thromboembolic stroke, further clinical trials are needed to determine best management practices in this setting. Key Words: Ischemic stroke—thromboembolism—antithrombotic—anticoagulant antiplatelet—withdrawal—discontinuation—survey.

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Introduction

Ischemic stroke is the fourth leading cause of death and also a major cause of adult disability in the United States.¹ Antiplatelet and anticoagulant medications are effective for primary and secondary prevention of ischemic stroke.^{2,3}

Antithrombotic medications are often stopped for several days in preparation for a surgical or diagnostic procedure, the rationale for stoppage being to minimize the risk of hemorrhage associated with the procedure. The exact strategy for stoppage of antithrombotics depends on the procedure to be performed and the risks and benefits of stopping the medication. In general, the international normalized ratio should be at a subtherapeutic level of

1.3-1.5 before surgery can be performed on a patient taking warfarin,⁴ meaning that warfarin is usually stopped at least 4 days before the procedure to allow clotting factors to increase.⁹ After the procedure, warfarin is restarted, generally within 12-24 hours of the procedure; it takes about 3 days for the international normalized ratio to return to therapeutic levels.¹⁰ Platelets have a life span of approximately 7 days, so antiplatelet agents are generally stopped 5-7 days before planned surgery, and then restarted as soon as possible after the procedure.

However, withdrawal of antithrombotic medications also carries a risk of thromboembolism. Perioperative strokes, defined as occurring within 30 days of a surgical procedure, are rare but carry a significantly higher morbidity and mortality than nonperioperative strokes. 11,12 In addition, several studies have demonstrated that strokes occurring after antithrombotic withdrawal have been associated with a higher morbidity and mortality than strokes in patients who were still taking antithrombotic medication.^{13,14} Kim et al¹⁴ demonstrated that patients with warfarin withdrawal preoperatively had significantly worse outcomes compared to patients who were still taking warfarin when the stroke occurred. Early neurological deterioration occurred more frequently, and these patients had a lower frequency of favorable outcomes. Thus, physicians must carefully weigh the risks (increased risk of thromboembolic events) and benefits (decreased risk of bleeding) when deciding if and when to withdraw antithrombotic medications. Yet, frequency of the decision to withdraw antithrombotic medications in the general population is not well characterized.

We report a population-based telephone survey of adults representative of the ischemic stroke population with respect to age, sex, and race that addressed the frequency of discontinuation of antithrombotic medication due to medical intervention.

Methods

In 2011, households with a telephone or cell phone in the Greater Cincinnati metropolitan area were randomly sampled via a phone survey to assess the prevalence of risk factors of ischemic stroke and knowledge of stroke risk factors. The Greater Cincinnati and Northern Kentucky regions include 2 counties in southern Ohio and 3 counties in Northern Kentucky that border the Ohio River. This region contains an essentially biracial population of 1.3 million. Survey respondents were contacted by telephone using random-digit selection of telephone numbers. Cell phone numbers were included to account for the growing number of cell phone-only households. While landline interviews were conducted with a randomly selected household member, cell phone interviews were conducted with the person answering the phone.

In comparison to the 2010 U.S. census, residents of the Greater Cincinnati 5-county area are representative of the U.S. population with regard to median age, percentage of blacks, median household income, educational level, and percentage of population below the poverty level. The survey respondents were quota-matched by demographics: age, sex, and race groups that are at high risk for ischemic stroke. A quota was filled for each of these groups to make our respondents representative of the population of stroke patients in this region based on our longstanding stroke epidemiology studies. ^{13,15}

In addition to demographic and medical history questions, we asked respondents if they were prescribed antithrombotic medication and, if so, if they had stopped the antithrombotic medication by request of their physician for scheduled surgery or other medical procedure during the past 60 days. ^{15,16} The respondents were asked which medication they stopped, and for which medical procedure they had stopped the medication. The respondents were not asked if they had stopped medications for reasons of noncompliance. Chi-square and Cochran–Armitage trend tests were used, as appropriate, for comparing the proportions. SAS version 9.3 (SAS Institute, Cary, NC) was used for analysis. A *P* value less than .05 was considered statistically significant.

Results

Between June 15 and September 7, 2011, 36,951 households (with 1 person identified per household) were called. Of the total number of households, 3210 people were identified as demographically eligible to participate in the survey. Of these, 1154 (36.0%) did not complete the interview due to language barriers, illness, or unavailability despite multiple callbacks during the study period, and 20 (.6%) others refused to complete the survey. The remaining 2036 (66.8%) respondents completed telephone interviews. Demographics of the nonresponders are not known due to the nature of the survey. Of the 2036 households who completed the telephone interview, 1959 selfidentified as either black (544) or white (1415) race. The mean (±standard deviation) age of the 1959 was 66.3 years ± 14.7, with 61% being female. Of the 1959 respondents, 1207 (62%) were on antithrombotic medication; overall, 63 (3%) were taking only an anticoagulant agent, 1073 (55%) were taking only an antiplatelet agent, and 71 (4%) reported being on both anticoagulant and antiplatelet agents. Antithrombotic usage increased with age (P < .0001) and was more common in whites than in blacks (64% and 55%, respectively; P < .001).

The distribution of antithrombotic medication users in the Greater Cincinnati area by age group, sex, and race is shown in Table 1. Antithrombotic usage did not differ significantly between males and females. Of the 1207 respondents who had been taking an antithrombotic medication, 120 (10%) reported that they had stopped

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