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Full Length Article

Self-reported adherence to anticoagulation and its determinants using the Morisky medication adherence scale

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ABSTRACT

Background: Direct oral anticoagulants (DOACs) are used for treatment of venous thromboembolism (VTE) and stroke prevention in atrial fibrillation (AF). Given the shorter half-life and lack of laboratory monitoring compared to vitamin-K antagonists (VKAs), adequate adherence to DOACs is important. Reported anticoagulation adherence is unclear in clinical practice.
Objectives: To assess self-reported anticoagulation adherence in a tertiary center anticoagulation clinic.
Patients/Methods: Cross-sectional study of patients on oral anticoagulants (VKAs, rivaroxaban, dabigatran and apixaban). Anticoagulation adherence was assessed using the 4-item Morisky score. Baseline characteristics were evaluated for association with adherence.
Results: Five hundred patients completed the survey; 74% were on VKAs and 26% on DOACs: rivaroxaban 102 (79%); dabigatran 26 (19%); apixaban 2 (2%). Main indications for anticoagulation were VTE (72%) and AF (18%). Self-reported anticoagulation adherence using the 4-item Morisky scale was 56.2% for patients on VKAs and 57.1% for patients on DOACs. Predictors of anticoagulation adherence were age (OR = 1.02; 95% CI:1.01-1.03), female gender (OR = 1.58; 95% CI:1.10-2.27), use of additional oral medications (OR = 2.78; 95% CI:1.67-4.63), and retired employment status (OR = 2.31; 95% CI:1.51-3.55). In backward selection multivariate analyses age, female gender and use of other oral medications remained significantly associated with anticoagulation adherence.
Conclusions: Self-reported anticoagulation adherence was similar between VKAs and DOACs. Until laboratory assays are universally available to evaluate DOAC adherence, physicians should emphasize the importance of anticoagulation adherence at each patient encounter. The Morisky scale provides simple assessment of anticoagulation adherence; however it has not yet been validation for this purpose.

1. Introduction

Oral anticoagulation therapy is employed for a variety of prophylactic and therapeutic indications. Warfarin, an oral vitamin-K antagonist (VKA), has been used extensively for decades for prevention and treatment of arterial and venous thromboembolic disease. Warfarin therapy can be complicated by a number of factors, such as a narrow therapeutic window requiring regular laboratory monitoring, numerous drug-drug interactions, dietary restrictions, as well as a slow onset and offset of action [1,2]. In recent years, the use of Direct Oral Anticoagulants (DOACs) has been able to circumvent some of the inconveniences of warfarin therapy.

The DOACs include the direct Xa inhibitors rivaroxaban, edoxaban, and apixaban, and the direct thrombin inhibitor dabigatran [1]. These agents provide reliable anticoagulation, predictable pharmacokinetic parameters, shorter onset and offset due to a relatively short half-life, consistent dosing regimens, fewer drug-drug and drug-food interactions, and they obviate the need for routine laboratory monitoring of anticoagulant effect [3]. Several phase III studies have evaluated the use of rivaroxaban, apixaban, and dabigatran for stroke prevention in the setting of non-valvular atrial fibrillation [4–7], as well as the treatment of

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1.	Do you ever forget to take your medicine?	Yes/No
2.	Are you careless at times about taking your medicine?	Yes/No
3.	When you feel better, do you sometimes stop taking your medicine?	Yes/No
4.	Sometimes if you feel worse when you take the medicine, do you stop taking it?	Yes/No

*Adequate adherence defined as answering "no" to all four questions

Fig. 1. 4-item Morisky Medication Adherence Scale*[23]. *Adequate adherence defined as answering "no" to all four questions.

acute deep vein thrombosis and pulmonary embolism [8–11]. These medications demonstrated non-inferiority compared to warfarin and are approved for use in North America and Europe [12–14].

Despite addressing a number of the shortcomings regarding warfarin use, many concerns persist around the use of DOACs including medication adherence and lack of therapeutic monitoring as an indication of adherence [15–19]. Monitoring time in therapeutic range is a marker of quality of warfarin anticoagulation and can be used as a surrogate to predict anticoagulation complications [20]. In contrast, laboratory tests for monitoring DOACs are not yet readily available and their associated therapeutic serum concentration unclear. Therefore, physicians often have to depend on patient self-reporting to ensure DOAC adherence. Due to the differences of relatively short half-life of the DOACs compared to warfarin, missed doses of DOACs might expose patients to greater risk of arterial or venous thrombosis. Few trials have reported medication adherence to DOACs and the estimates relied on pill counts, which is susceptible to overestimating adherence rates [15]. The investigators of EINSTEIN PE and AMPLIFY reported 94% and 96% of patients, respectively, had high adherence to rivaroxaban and apixaban, defined as >80% adherence [9,11]. The RE-COVER trial reported 98% adherence to dabigatran, which was comparable to warfarin adherence at 97.5% [10] and the RE-LY trial reported >95% adherence with dabigatran [20,21]. These adherence rates in clinical trials are often artificially inflated due to patient selection, intensive patient follow-up and pill counts that may influence patient behaviour [22]. Furthermore, these adherence rates do not include drop-out patients. Real-world data on adherence to DOACs is also sparsely reported in the literature. We performed a cross-sectional cohort study assessing the self-reported adherence of patients receiving anticoagulation therapy in a tertiary care hospital practice. We also evaluated patient characteristics for association with self-reported anticoagulation adherence.

2. Methods

2.1. Patient Population and Study Design

This cross-sectional survey was performed on consecutive outpatients attending the anticoagulation clinic at The Ottawa Hospital, Ottawa, Canada between September 1st 2012 and September 30th 2013. Patients attending clinic and who were anticoagulated with warfarin, rivaroxaban, apixaban or dabigatran for arterial or venous thrombotic diseases were eligible to participate, regardless of anticoagulation duration.

Data were collected by self-administered questionnaires. The survey was anonymous, consisted of 22 questions and was available in both English and French. The study was approved by local ethics review board. Data was collected on the following parameters: [1] patient demographic characteristics: age, gender, ethnicity, level of education, current employment status; [2] oral anticoagulation therapy: type of anticoagulant used, duration of therapy, indication for anticoagulation; [3] Number of additional medications used daily; [4] self-reported adherence to anticoagulation.

2.2. Adherence

Adherence was assessed using the 4-item Morisky Scale (Fig. 1) [23]. The 4-item scale was first validated in outpatients on antihypertensive therapy [23] and was found to have concurrent and predictive validity [23]. This Morisky 4-item scale has not been validated for anticoagulation adherence; however it has demonstrated significant association between warfarin adherence and good anticoagulation control [24]. In the current study, adequate adherence is defined as a response of "no" to all 4 questions and inadequate adherence as a "yes" response to any one of four questions. The advantages to using this 4-item scale over other methods of evaluating adherence are its ease of use, quick administration, and low-cost in a busy clinic setting.

2.3. Statistical Analysis

The primary outcome measure was adequate anticoagulation adherence as determined by the four-item Morisky scale [23]. Patient characteristics are reported with descriptive statistics. Odds ratios were used to analyze the effect of specific characteristics on the adherence of patients. Variables associated with adequate adherence in univariate analysis (p-value < 0.2) were included in the multivariate model. Forward and backward selection to identify independent predictors of adherence were also performed. Data analysis was performed using SAS, version 9.2 (SAS Institute).

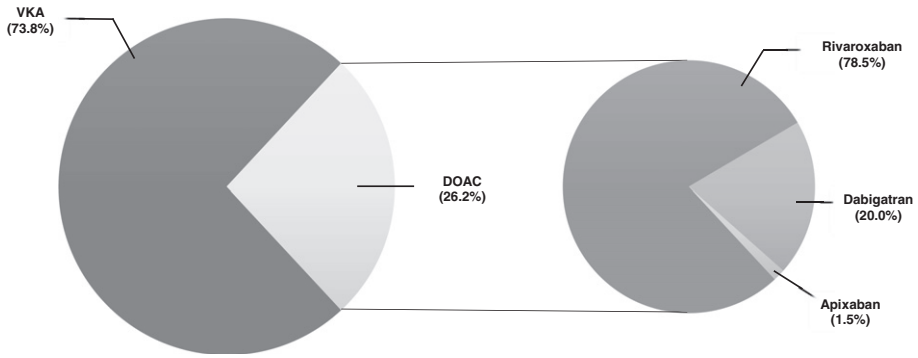

Fig. 2. Proportion of patients on Vitamin-K Antagonists (VKA) and Direct Oral Anticoagulants (DOAC).