Saudi Pharmaceutical Journal (2016) **24**, 29–34

King Saud University

Saudi Pharmaceutical Journal

www.ksu.edu.sa
www.sciencedirect.com

ORIGINAL ARTICLE

Patient adherence to warfarin therapy and its impact on anticoagulation control

Ahmed Y. Mayet *

Department of Clinical Pharmacy, College of Pharmacy, King Saud University, P.O. Box 2457, Riyadh 11451, Saudi Arabia

Received 6 January 2015; accepted 20 February 2015
Available online 28 February 2015

KEYWORDS

Oral anticoagulant;
Anticoagulation control;
Warfarin;
INR;
Medication adherence;
Saudi Arabia;
MMAS-8

Abstract Warfarin is a commonly prescribed oral anticoagulant in Saudi Arabia and yet patient adherence to warfarin therapy and its impact on anticoagulation control have not been well researched here. A cross-sectional survey was conducted over 6 weeks at the outpatient anticoagulant clinic on patients who were receiving warfarin. Adherence was assessed using the translated Arabic version of the Morisky Medication Adherence Scale (MMAS-8). Levels of adherence were classed as low (score $\leqslant 7$), or high (score $= 8$) based on the scores. Good anticoagulation control was defined as percent Time INR in Therapeutic Range (TTR) $\geqslant 75\%$ using the Rosendaal method. A total of 192 patients completed a questionnaire with a response rate of 68.1%. It was established that no association was found between adherence to warfarin therapy and INR control groups. Among the 89 (46.4%) patients who had high adherence, only 34 (38.2%) had an acceptable INR control. This was versus 103 (53.6%) patients who had low adherence but also 34 (33.0%) had good INR control. Multivariate logistic regression (MLR) analysis showed that when studying females and occupational status of unemployment, they were independently associated with poor INR control with an OR 2.31, 95% CI 1.10–4.92, and OR 2.71, 95% CI 1.12–6.61 respectively. MLR analysis also showed that age < 50 years alongside no formal education was independently associated with low adherence to warfarin therapy with an OR 2.67, 95% CI 1.29–5.52 and OR 2.63, 95% CI 1.01–6.93 respectively. The demographic background influences adherence and INR control, but no association was found between adherence and anticoagulation control.

1. Introduction

Poor adherence to medication use is one of the greatest challenges for the improvement of health outcomes (World Health Organization, 2003). Non-adherence to medications is ongoing as patients receive more medications to treat their chronic medical conditions. This is also apparent in the elderly population due to a decline in their mental and physical health (Gurwitz et al., 2003). The outcome of poor adherence to medications can be life threatening with certain drugs like warfarin

* Tel.: +966 507467280; fax: +966 14671985.
E-mail addresses: iymayet@gmail.com, iymayet@ksu.edu.sa
Peer review under responsibility of King Saud University.

Production and hosting by Elsevier

http://dx.doi.org/10.1016/j.jsps.2015.02.005

which has very narrow therapeutic index (Woodwell and Cherry, 2004). The drug is used as a long-term oral anticoagulation to prevent thromboembolic complications of various conditions including stroke; atrial fibrillation; venous thromboembolism; and valvular heart disease (Rose et al., 2009; Wysowski et al., 2007). Warfarin is effective when the therapeutic range is maintained, but when the levels are below or above the intended range, it is associated with increased risk of thrombosis and bleeding, respectively (Hylek et al., 1996).

Poor adherence to warfarin is common with one in five doses taken incorrectly even in the setting of a dedicated anticoagulation clinic (Platt et al., 2010). A study showed that up to 92% of the patients could not adhere to warfarin therapy and had under anticoagulation control. For each 10% increase in non-adherence to warfarin, there was a 14% increase in the risk of under-anticoagulation and caused significantly higher rates of morbidity and mortality (Kimmel et al., 2007). An older age, low level of education status and unemployment status were seen to be independent risk factors for nonadherence to warfarin therapy (Cruess et al., 2010).

Several studies have demonstrated that in patients on chronic warfarin therapy, adherence is one of the many factors that can affect anticoagulation control. Davis et al. concluded in their study that adequate adherence, as determined by the Morisky survey, was significantly associated with anticoagulation control (Davis et al., 2005).

An association between patients' adherence and anticoagulation control has not been well researched in Saudi Arabia. The study objective was to assess patient adherence to warfarin treatment using the MMAS-8 Arabic translated version, anticoagulation control, and the association between adherence and anticoagulation control. It will also help to identify factors associated with poor adherence and anticoagulation control. This study should help us to identify deficiencies and opportunities for strategic initiatives to improve medication adherence and INR control. It will be an imperative step toward optimizing the anticoagulation care at our clinic.

2. Materials and methods

This cross-sectional study was conducted in an outpatient anticoagulation clinic of King Khalid University hospital in Riyadh, Saudi Arabia. This was after receiving the institutional review board of approval. The hospital is a tertiary care hospital with a 1000-inpatient bed capacity. It provides medical services to Saudi citizens from all over the country. The anticoagulant clinic offers follow-up services to all of our discharged patients who are receiving anticoagulants. The study lasted for a period of 6 weeks. All patients with an age $\geqslant$16 years who were discharged from hospital on warfarin, and were taking the drug and attending the outpatient anticoagulant clinic at the King Khalid University Hospital for $\geqslant$6 months were asked to partake in the study during a regular clinic visit. The consent was taken from all participants prior to starting the questionnaire. Researchers administered the questionnaire face to face with the patients and recorded the answers.

To obtain an INR which reflected the warfarin dose and to obtain complete data, the following patients were excluded from the study; if the patients had a disruption in warfarin therapy for $\geqslant$5 days during the study period; if they were hospitalized for any reason during the study period; and if they did not have four consecutive INR readings or had an incomplete questionnaire.

Adherence was assessed using the Arabic version of the Morisky Medication Adherence Scale (MMAS-8). The MMAS-8 is a self-reported questionnaire that has been frequently used because of its low levels in both cost and time expenditure. Although earlier studies showed that the self-report method was underestimating non-adherence when compared with pill counts or biological assays, later studies suggest that the self-report method provides a reasonably accurate estimate of adherence. The MMAS-8 has been validated in many studies in patients with diabetes mellitus (Lee et al., 2013), hypertension (Korb-Savoldelli et al., 2012), and those taking warfarin (Wang et al., 2012). An 8-item self-report scale measured medication-taking behavior (Morisky et al., 2008, 1986). Items 1–7 were recorded as 'yes/no' dichotomous responses (scored 0/1) and item 8 was recorded using a 5-point Likert scale (never/rarely scored 1, other responses scored 0; Table 4). Thus, the total score of the 8-item scale ranges from 0 to 8′ and a total score of 8 was considered to represent high adherence and scores $\leqslant$7 were considered as low-adherence.

The translation to Arabic language for MMAS-8 was done by using "The Eight Steps Translation Process" that combined the recommendations of WHO (World Health Organization, 2007) and (Brislin, 1986) after placing "warfarin" in each item.

To assess the anticoagulation control, the most recent consecutive four INR readings, at an average of 4 weeks apart were obtained from the hospital central laboratory electronic data system for each patient. Anticoagulation control was defined as INR between 2 $\geqslant$ 3.0 for all indications except for mitral valve replacement (2.5–3.5): Good INR control was defined as percent Time INR in Therapeutic Range (TTR) $\geqslant$ 75% during study period using the Rosendaal method (Rosendaal et al., 1993). Previous studies had considered TTR $\geqslant$ 75% as good INR control (Davis et al., 2005; Wang et al., 2013).

Sensitivity and specificity of the MMAS-8 were calculated to determine the usefulness of the scale in identifying patients with poor anticoagulation control. Internal consistency of the MMAS-8 was measured using Cronbach's α with correlated item-total correlations.

The questionnaire was validated in a crossover pilot study conducted on 25 patients who were currently using warfarin from the same clinic. It was done on two separate occasions, and two weeks apart to avoid duplication of their first responses and the Cronbach's α was calculated. The value was 0.76 with moderate reliability.

Descriptive statistics (means, standard deviation, median, range, counts and percentages) were used to describe the quantitative and categorical study variables. Pearson's Chi-square tests and Fisher's exact test were used to detect if there were any associations between demographic characteristics, adherence and anticoagulation control. Univariate odds ratios were calculated between the categorical study and outcome variables were calculated to measure the strength of association. Multivariate binary logistic regression analysis was used to find out the independent associated variables among demographic background relating to adherence and anticoagulation control. A p-value of <0.05 and 95% confidence intervals were used to report the statistical significance and precision