



ORIGINAL ARTICLE

Factors influencing warfarin response in hospitalized patients



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Abstract The objective of this study was to investigate the influence of simultaneous factors that potentially keep patients far from achieving target INR range at discharge in hospitalized patients. Prospective cross-sectional observational study conducted at the Cardiology Department and Intensive Care Unit (ICU) of the Assiut University Hospitals. One-hundred and twenty patients were enrolled in the study from July 2013 to January 2014. Outcome measures were discharge INRs, bleeding and thromboembolic episodes. Bivariate analysis and multinomial logistic regression were conducted to determine independent risk factors that can keep patients outside target INR range.

Patients who were newly initiated warfarin on hospital admission were given low initiation dose (2.8 mg ± 0.9). They were more likely to have INR values below 1.5 during hospital stay, 13 (27.7%) patients compared with 9 (12.3%) previously treated patients, respectively ($p = .034$). We found that the best predictors of achieving below target INR range relative to within target INR range were; shorter hospital stay periods (OR, 0.82 for every day increase [95% CI, 0.72–0.94]), being a male patient (OR, 2.86 [95% CI, 1.05–7.69]), concurrent infection (OR, 0.21 [95% CI, 0.07–0.59]) and new initiation of warfarin therapy on hospital admission (OR, 3.73 [95% CI, 1.28–10.9]).

Gender, new initiation of warfarin therapy on hospital admission, shorter hospital stay periods and concurrent infection can have a significant effect on discharge INRs. Initiation of warfarin without giving loading doses increases the risk of having INRs below 1.5 during hospital stay

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and increases the likelihood of a patient to be discharged with INR below target range. Following warfarin dosing nomograms and careful monitoring of the effect of various factors on warfarin response should be greatly considered.

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1. Introduction

Warfarin has been utilized as an anticoagulant drug for about 60 years but still causing a variety of adverse effects. Routinely, warfarin is monitored by measuring the International Normalized Ratio (INR). The target INR range for most indications of warfarin therapy is 2–3 or 2.5–3.5 (Keeling et al., 2011; Holbrook et al., 2012). Keeping patients within target INR range is a challenge. A number of worldwide studies have been conducted to examine the response to warfarin therapy in both ambulatory and hospital settings (Doecke et al., 1991; Brigden et al., 1998; Fang et al., 2006; Clark et al., 2014). Response to warfarin therapy is patient specific; however, various factors have been reported to alter warfarin response and target INR such as older age, disease states, warfarin dose and influence of other medications (Doecke et al., 1991; Brigden et al., 1998; Demirkan et al., 2000; Hylek et al., 2001; Froom et al., 2003; Torn et al., 2005; Fang et al., 2006; Clark et al., 2014). Conflicting results have been reported for some of these factors such as age, gender and concurrent disease states (Fihn et al., 1996; Demirkan et al., 2000; Sivrikaya et al., 2013). The presence of these factors can keep patients away from achieving target INR range and may cause unnecessary complications. Consequently, monitoring and watching for these influential factors is essential. The objective of this study was to report on the degree to which various factors can hinder achieving target INR range in a sample of adult Egyptian patients on their discharge from hospital care setting.

2. Methods

2.1. Study design and settings

This prospective cross-sectional observational study was conducted at Cardiology Department and Intensive Care Unit (ICU) of Assiut University Hospitals. The study was approved by the Research Ethics Committee at the Faculty of Medicine of Assiut University.

2.2. Study participants

All patients admitted to the Cardiology Department and ICU of Assiut University Hospitals and received warfarin anticoagulation therapy, from July 2013 till January 2014, were included in the study.

2.3. Data collection

Patients' data regarding warfarin anticoagulation therapy were collected by reviewing patients' medical records, laboratory measurements of INR and when necessary by interviewing

health care professionals as well as patients when some data were missing. Actual warfarin usage and INR measuring laboratories were monitored for one month before designing and formulating data collection sheets.

2.4. Data analysis

All statistical analyses were performed using IBM SPSS v. 22.

Data are presented as mean (standard deviation), median (interquartile range) or proportions as appropriate. A *p*-value of less than 0.05 was considered significant for all comparisons and all tests were two-tailed.

Independent sample *t*-test with bootstrap was used to compare mean difference between two unrelated groups. Non-parametric tests; Mann–Whitney U test and Kruskal Wallis H test were used to find difference in discharge INRs within the different groups.

Pearson and spearman's rank correlations with bootstrap were used to examine associations between groups.

Multinomial logistic regression was used to examine the influence of different factors on the state of discharge INRs (below, above and within target range groups).

3. Results

3.1. Baseline characteristics

Table 1 shows baseline patients' characteristics. A total of 120 patients were admitted to the Cardiology Department and the ICU. Their mean age was 48.35 years. Seventy-one (59.2%) patients were females. The majority of patients 83 (69.2%) were non-educated, and only 9 (7.5%) patients finished university education. One hundred patients (83.3%) were admitted to the Cardiology Department. Warfarin was most commonly prescribed for atrial fibrillation, 66 (55%) patients.

3.2. Warfarin management metrics

Table 2 shows warfarin management metrics for the patients. Seventy-three patients were previously treated with warfarin before hospital admission and 47 (39.2%) patients were newly initiated warfarin on hospital admission. Prescribed dose, admission and discharge INRs were significantly higher for patients previously treated with warfarin.

3.3. Warfarin prescribed dose in different patient groups

Table 3 shows difference in prescribed warfarin doses in different patient groups. Elderly patients (≥ 60 years) and patients with congestive heart failure were given lower mean prescribed doses than other patients. Patients with mechanical valve replacement were given higher mean prescribed dose than

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