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Full Length Article

Exploring the impact of route of administration on medication acceptance in hospitalized patients: Implications for venous thromboembolism prevention

Victor O. Popoola[a,b,1], Farrah Tavakoli[c,1], Brandyn D. Lau[a,d,e,f], Matthew Lankiewicz[g], Patricia Ross[c,h], Peggy Kraus[h], Dauryne Shaffer[a,i], Deborah B. Hobson[a,f,i], Jonathan K. Aboagye[a], Norma A. Farrow[a], Elliott R. Haut[a,e,f,j,k,2], Michael B. Streiff[f,l,*,2]

[a] Division of Acute Care Surgery, Department of Surgery, The Johns Hopkins University School of Medicine, Baltimore, MD, United States
[b] Department of Epidemiology, The Johns Hopkins Bloomberg School of Public Health, Baltimore, MD, United States
[c] School of Pharmacy, The University of Maryland Baltimore, Baltimore, MD, United States
[d] Division of Health Sciences Informatics, The Johns Hopkins University School of Medicine, Baltimore, MD, United States
[e] Department of Health Policy and Management, The Johns Hopkins Bloomberg School of Public Health, Baltimore, MD, United States
[f] The Armstrong Institute for Patient Safety and Quality, Johns Hopkins Medicine, Baltimore, MD, United States
[g] Krieger School of Arts and Sciences, Johns Hopkins University, Baltimore, MD, United States
[h] Department of Pharmacy, The Johns Hopkins Hospital, Baltimore, MD, United States
[i] Department of Nursing, The Johns Hopkins Hospital, Baltimore, MD, United States
[j] Department of Anesthesiology and Critical Care Medicine, The Johns Hopkins University School of Medicine, Baltimore, MD, United States
[k] Department of Emergency Medicine, The Johns Hopkins University School of Medicine, Baltimore, MD, United States
[l] Division of Hematology, Departments of Medicine and Pathology, The Johns Hopkins University School of Medicine, Baltimore, MD, United States

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ABSTRACT

Background: Non-administration of venous thromboembolism (VTE) prophylaxis contributes to preventable patient harm. We hypothesized that non-administration would be more common for parenteral VTE prophylaxis than oral infectious disease or cardiac prophylaxis or for treatment medications. The primary study goal was to determine if non-administration of parenteral VTE prophylaxis is more frequent than other prophylactic or treatment medications.

Methods: In this retrospective cohort study of consecutive admissions we used descriptive statistics and risk ratios (RR) to compare the number of non-administered doses of VTE prophylaxis, oral infectious disease and cardiovascular prophylaxis and treatment medications. To quantify the influence of demographic and clinical characteristics on non-administration, we estimated incidence rate ratios from Poisson regression models.

Results: 645 patients were admitted from July 1, 2014 through March 31, 2015. Median age was 52 years (Interquartile range 43–57) and 365 (56.6%) were male. Subcutaneous VTE prophylaxis doses were not administered nearly 4-fold more frequently than oral infectious disease and cardiovascular prophylaxis (RR = 3.93; 95% CI 3.36–4.59) and 3-fold more frequently than treatment medications (RR = 3.06; 95% CI 2.91–3.22). Ninety percent of non-administered doses of VTE prophylaxis were refused. Risk factors for non-administration included younger age (age 18–35 years), male sex, uninsured status, HIV-positivity and high VTE risk status.

Conclusions: Subcutaneous VTE prophylaxis is not administered more frequently than oral infectious diseases or cardiac prophylaxis and treatment medications. These data suggest that availability of an oral medication could improve the effectiveness of VTE prophylaxis in real world settings.

* Corresponding author at: Division of Hematology, Department of Medicine, The Johns Hopkins University School of Medicine, The Armstrong Institute for Patient Safety and Quality, Johns Hopkins Medicine, 1830 East Monument Street, Suite 7300, Baltimore, MD 21205, United States.
E-mail addresses: vpopool1@jhmi.edu (V.O. Popoola), ftavakoli@umaryland.edu (F. Tavakoli), blau2@jhmi.edu (B.D. Lau), mlankie2@jhu.edu (M. Lankiewicz), pross5@jhmi.edu (P. Ross), pkraus2@jhmi.edu (P. Kraus), dshaffe1@jhmi.edu (D. Shaffer), dhobson1@jhmi.edu (D.B. Hobson), jaboagy1@jhmi.edu (J.K. Aboagye), nfarrow1@jhmi.edu (N.A. Farrow), ehaut1@jhmi.edu (E.R. Haut), mstreif@jhmi.edu (M.B. Streiff).
[1] Dr. Popoola and Ms. Farrah Tavakoli should be credited as co-first author.
[2] Drs. Streiff and Haut should be credited as co-senior author.

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1. Introduction

Venous thromboembolism (VTE) is an important cause of preventable harm that is estimated to affect > 600,000 Americans annually and result in as many as 100,000 deaths [1]. Recognition of the importance of VTE has led patient safety, health care quality and accrediting organizations and federal agencies to make VTE prevention a top priority [2–4]. Development and implementation of electronic alerts and computer decision support tools have been demonstrated to significantly increase the prescription of risk-appropriate thromboprophylaxis and reduce VTE [5–8]. Prescription of thromboprophylaxis, however, does not ensure its administration. Our group and others have highlighted the importance of non-administered doses of thromboprophylaxis in hospitalized patients as an important patient care deficit [9–11]. A retrospective study of general surgery and trauma patients noted that non-administration of thromboprophylaxis was associated with an increased risk of VTE [12].

Numerous studies have reported on medication non-adherence among patients in ambulatory settings; however, there are limited data on this major public health issue among inpatients. Patient refusal has been reported to be a major cause of VTE prophylaxis medication non-administration in hospitalized patients [9–11]. Patient surveys suggest that route of administration plays an important role in patient acceptance of VTE prophylaxis [13–15]. In a national survey of patients and their family members, we found that 78% of patients preferred an oral route of administration for VTE prophylaxis if oral and parenteral medications were equally effective [14]. We noted similar findings in a prospective study of 227 hospitalized patients at our institution [16].

Therefore, we hypothesized that non-administration of subcutaneous VTE prophylaxis will be greater than commonly used prophylaxis for infectious and cardiac diseases or medications for treatment of acute illnesses. The purpose of this retrospective study was to examine patient adherence, comparing subcutaneous VTE prophylaxis to oral cardiovascular and ID prophylaxis and therapeutic medications.

2. Methods

In this retrospective cohort study, we reviewed the electronic records of consecutive patients hospitalized on the Johns Hopkins Hospital infectious disease floor from July 1, 2014 through March 31, 2015. We selected this particular floor because it admits a high percentage of patients who take medications for prevention of infectious diseases and thus offers a unique opportunity to study the impact of route of administration on adherence to prophylactic medications.

Demographic and clinical data were retrieved from administrative databases and electronic health records, respectively. At the time of this study, our electronic health record had a mandatory VTE prophylaxis module that required providers to assess patients' risks for VTE and bleeding on admission and upon transfer to a different level of care within the hospital. Therefore, all patients except those on systemic therapeutic dose anticoagulation received some form of VTE prophylaxis. Patients considered to be at high risk for VTE had one or more of the following risk factors: a history of previous VTE, active cancer, decompensated New York Heart Association Class III or IV heart failure, respiratory failure requiring mechanical ventilation, sepsis, acute stroke, age > 60 years, or thrombophilia. Patients without any of these risk factors were considered at moderate VTE risk. High risk patients were recommended to receive unfractionated heparin 5000 units every 8 h. Moderate risk patients were recommended to receive unfractionated heparin 5000 units every 12 h. Patients with platelets < 50,000/μL, a PT/INR > 1.5 or an aPTT ratio > 1.3 or evidence of active bleeding were considered to be at increased risk of bleeding and mechanical prophylaxis with intermittent pneumatic compression devices or graduated compression stockings was recommended. Further details on the VTE order set and the VTE and bleeding risk stratification are available in our previous publication [7].

The numbers of prescribed and administered doses of medications and reasons for non-administration were confirmed by retrospective, manual chart review. We classified medications as prophylactic or therapeutic, depending on dosage and the indication for their prescription. For example, to fulfill criteria as chemoprophylaxis for *Pneumocystis jiroveci* pneumonia (PJP), the doses of trimethoprim-sulfamethoxazole (TMP/SMX) had to correspond to prophylactic rather than treatment doses of this medication. Subcutaneous heparin injections were categorized as prophylactic when the prescribed dose was within the prophylactic dose range for the particular patient. Aspirin was considered primary cardiovascular/stroke prophylaxis if the patient did not have a personal history of cardiovascular disease or stroke. Patients were categorized by age into younger (18–35 years), middle-aged (36–65 years) and older (> 65 years) age groups.

Our primary outcome measure was the proportion of prescribed medication doses not administered. Our secondary outcome measure was the proportion of non-administered medication doses due to patient or family member refusal as documented in the electronic health record. Employing descriptive statistics and risk ratios (RRs), we compared these dose-level measures by medication category (prophylactic versus therapeutic) and by route of administration (subcutaneous vs. oral). Median proportions of non-administered doses were compared using the Wilcoxon rank sum test. To quantify the influence of demographic and clinical characteristics (age, gender, race, length of hospital stay, insurance status, HIV status, VTE risk category) on incidence rates of non-administered doses of VTE prophylaxis, we estimated incidence rate ratios (IRRs) from Poisson regression models. For these models, the unit of analysis was a patient and the exposure variable was specified as the number of VTE prophylaxis doses ordered. All statistical analyses were carried out using Stata version 13 (Stata Corp, College Station, TX). This study was approved by the Johns Hopkins Medicine Institutional Review Board.

3. Results

From July 1, 2014 through February 1, 2015, 645 patients were admitted to the infectious disease floor at the Johns Hopkins Hospital. These patients were prescribed 60,815 doses of routine medications including 52,631 (86.5%) doses of therapeutic medications, 5855 (9.6%) doses of VTE prophylaxis, 2092 (3.4%) doses of infectious disease prophylaxis and 237 (0.4%) doses of cardiovascular prophylaxis (aspirin). The median age of study participants was 52 years (interquartile range [IQR] 43–57) and 365 (56.6%) were male. The median length of stay was 4 days (IQR 2–7). Other characteristics of the study participants are described in Table 1. Pharmacologic VTE prophylaxis was ordered for 540 (83.7%) subjects. Mechanical prophylaxis was prescribed to 47 (7.3%) patients. Forty-six patients (7.1%) were on systemic therapeutic dose anticoagulation. The medications prescribed for VTE, infectious disease, and cardiac prophylaxis are displayed in Table 2.

Overall, 6381 (10.5%) ordered doses were not administered. Of 5855 doses of subcutaneous VTE prophylaxis prescribed, 1579 (27.0%) doses were not administered. In comparison, only 160 (6.9%) doses of oral infectious disease and cardiovascular prophylaxis and 4642 (8.8%) doses of treatment medications were not administered (Fig. 1). Subcutaneous VTE prophylaxis was not administered nearly 4-fold more frequently than oral infectious disease and cardiovascular prophylaxis (RR = 3.93; 95% CI 3.36–4.59, p < 0.0001) and over 3-fold more frequently than therapeutic medications (RR = 3.06; 95% CI 2.91–3.22, p < 0.0001). Among non-administered doses of VTE prophylaxis, 1424 of 1579 (90.2%) doses were documented as refused by patients or family members. Other reasons for non-administration documented by nurses at the time of administration included patient condition not appropriate (83 of 1579 doses, 5.3%), patient off the floor/unavailable (40 of 1579 doses, 2.5%) and other/miscellaneous (32 of 1579, 2.0%). In contrast, 63 of 160 (39.4%) doses of non-