Thrombosis Research 131 (2013) 210–217

Contents lists available at SciVerse ScienceDirect

Thrombosis Research

journal homepage: www.elsevier.com/locate/thromres

Regular Article

Anticoagulant use in patients with cancer associated venous thromboembolism: A retrospective cohort study

Elham Rahme [a,*], Guillaume Feugère [b], Caroline Sirois [a], Sean Weicker [b], Elodie Ramos [c]

[a] McGill University Health Centre, Division of Clinical Epidemiology, 687 Pine Avenue West, V Building, Montreal, Quebec, Canada H3A 1A1
[b] Pfizer Canada, 17300 Trans-Canada Highway, Kirkland, Quebec, Canada H9J 2 M5
[c] Pfizer World Headquarters, 235 East 42nd Street, New York, NY 10017, USA

ARTICLE INFO

Article history:
Received 24 September 2012
Received in revised form 16 November 2012
Accepted 7 December 2012
Available online 3 January 2013

Keywords:
Low Molecular Weight Heparin
Cancer
Venous Thromboembolism
Administrative Data Base
Drug Use

ABSTRACT

Introduction: Long term anticoagulant therapy is recommended for treatment and secondary prevention of venous thromboembolism in cancer patients. We assessed outpatient anticoagulants [warfarin, low molecular weight heparins (LMWHs), fondaparinux and unfractionated heparin (UFH)] use in adult, cancer patients, 20 years of age or older, who incurred a venous thromboembolism (primary or secondary in-hospital diagnosis) in Quebec, Canada between 2007 and 2009.

Materials and methods: Data were obtained from the Quebec Health Insurance Agency. Patients with an in-hospital cancer diagnosis between April 2007 and June 2009 and an in-hospital venous thromboembolism diagnosis either concurrently or consequently were eligible at the date of discharge (index date). Those patients registered with the provincial drug plan and discharged to the community were included in the study and followed for 6 months.

Results: Among 2,070 study patients, 72.4% received anticoagulant therapy at index date, 60% of whom were persistent with therapy and received it for ≥80% of follow-up days. Outpatient anticoagulant use was more likely in those with primary versus secondary diagnosis of venous thromboembolism and less likely in patients with cerebrovascular disease, peptic ulcer disease or previous anticoagulant use. The small number of patients who used either UFH (n = 11) or fondaparinux (n = 5) at index date were included in the LMWH group. Warfarin use was less likely than LMWH use in corticosteroid users, previous anticoagulant users, patients with metastatic cancer and those with catheter or chemotherapy in the previous three months. Warfarin use was more likely than LMWH use in: older patients, those residing in rural areas, those with lower income and those suffering from ischemic heart disease, atrial fibrillation or chronic kidney disease. Patients with ischemic heart disease were more likely to have used a non-dalteparin LMWH versus dalteparin (currently, the only LMWH approved by health Canada for chronic treatment of VTE), while those residing in rural areas and those with catheter/chemotherapy were less likely to have used them. A primary (versus secondary) discharge diagnosis of venous thromboembolism [Odds Ratio 1.42; 95% confidence interval (1.14, 1.76)], and metastatic cancer 1.27 (1.00, 1.60) were associated with persistence on anticoagulant treatment.

Conclusion: Guideline recommended outpatient use of anticoagulant in cancer patients hospitalized with venous thromboembolism was influenced by cancer status, old age and low income. Risk factors for bleeding prevented outpatient anticoagulant use in some patients.

© 2012 Elsevier Ltd. All rights reserved.

Introduction

The risk of venous thromboembolism (VTE) is two to six fold higher in cancer patients than in the general population [1–3]. VTE, including deep vein thrombosis (DVT) and pulmonary embolism (PE), increases the burden of disease in these patients and is associated with a high risk of VTE recurrence and mortality, particularly during the first few months following cancer diagnosis [4,5]. The aetiology underlying the increased risk of VTE in cancer patients is complex and not well understood. Many cancer patients are in a malignancy-induced hypercoagulable state [6,7], which likely contributes to this increased

Abbreviations: ACCP, American College of Chest Physicians; ASCO, American Society of Clinical Oncology; BMI, body mass index; CI, confidence intervals; DVT, deep vein thrombosis; ED, emergency department; FRSQ, Fonds de Recherche en Santé du Québec; GIS, Guaranteed Income Supplement; ICD, International Classification of Disease; INR, international normalized ratio; LMWH, low molecular weight heparin; NSAIDs, non steroidal anti-inflammatory drugs; OR, odds ratios; PE, pulmonary embolism; RAMQ, Régie de l'Assurance Maladie du Québec; SD, standard deviation; SSRI, serotonin reuptake inhibitors; UFH, unfractionated heparin; VTE, venous thromboembolism.

* Corresponding author. Tel.: +1 514 934 1934x44724; fax: +1 514 934 8293.
E-mail address: elham.rahme@mcgill.ca (E. Rahme).

0049-3848/$ – see front matter © 2012 Elsevier Ltd. All rights reserved.
http://dx.doi.org/10.1016/j.thromres.2012.12.004

risk of VTE. In addition, this hypercoagulable state can be worsened by the pro-coagulant effects of cancer treatment (chemotherapy and radiotherapy), surgery, infection, immobilization [5,8–10], and central venous catheter placement [11,12]. The risk of VTE in cancer patients increases with age, comorbidity and tumour stage [13–17]. It is higher in women than in men, varies by tumour site and is higher in cancers associated with short life-expectancies, such as pancreatic cancer [3,5,10,18,19].

Anticoagulant treatment is required in these patients to prevent VTE recurrence and potentially mortality, although response to treatment varies between agents [20,21]. The American College of Chest Physicians (ACCP) and the American Society of Clinical Oncology (ASCO) guidelines recommend low molecular weight heparins (LMWHs) for 3 to 6 months for the treatment of VTE in cancer patients [22,23]. Among the LMWHs, dalteparin is the only one approved by Health Canada for chronic treatment of VTE [24,15,25]. LMWHs are superior to unfractionated heparin (UFH) in decreasing the risk of mortality in the initial phase of VTE treatment [11]. LMWHs have also been shown to be superior to the vitamin-K-antagonist, warfarin; it reduces the risk of VTE recurrence by half in the maintenance phase [6,13,26,27]. The use of warfarin is further disadvantaged in this patient population because of its slow onset of action (72–96 hours), lengthy clearance from the body (2–5 days) [1] and the requirement to closely monitor patients with frequent blood tests while they achieve the target therapeutic international normalized ratio (INR) [1]. In addition, INR target achievement is complicated by the interference of commonly used medications [e.g., aspirin, birth control pills, antibiotics and non steroidal anti-inflammatory drugs (NSAIDs)], and food high in vitamin K (e.g., broccoli, lettuce and spinach) [28]. However, in spite of these disadvantages, warfarin is oftentimes preferred to LMWHs because of the convenience of outpatient oral use and its lower cost. LMWHs are therefore frequently co-prescribed with warfarin during the initial phase until the therapeutic INR (between 2 and 3) is reached, at which point treatment with warfarin alone is maintained for at least 3 months [1,29].

Among Quebec cancer patients, 20 years of age or older, who experienced a VTE in-hospital and were discharged alive between April 1, 2007 and June 30, 2009, we aimed to describe the profile of those who received anticoagulant therapy for treatment and/or prevention of VTE recurrence in the following 6 months.

Materials and methods

Study design and data sources

We conducted a retrospective cohort study using demographic, physician billing, prescription drug and hospital discharge abstract records obtained from the Quebec public drug insurance program administered by the Régie de l'Assurance Maladie du Québec (RAMQ) for the period of April 2005–December 2009. In Quebec, all residents are covered by the RAMQ for outpatient and inpatient physician services. Available data from the RAMQ physician services database include details of the service provided, specialty of the physician, location of the service [e.g. hospital, emergency department (ED) or outpatient clinic], and diagnostic (International Classification of Disease (ICD)-9th revision) and procedure codes pertinent to the service. In addition, drug insurance coverage is mandatory in Quebec for all residents. Therefore, citizens eligible for coverage by the RAMQ drug plan include: those aged 65 years or older (1,091,618 individuals; 92% of that population), individuals younger than 65 years of age who receive social assistance (493,673 individuals; 100% of that population), and all residents younger than 65 years of age who do not have a collective private drug insurance (e.g., those self-employed) (1,763,277 individuals; 32% of that population) [30]. The RAMQ prescription claims database provides information on all dispensed prescriptions including drug name, dispensation date, dosage, drug form, duration and quantity of the drug dispensed. Drugs dispensed to patients in hospitals or nursing homes and over the counter medications are not included in this database. All other medication dispensations have been demonstrated to be accurately and reliably recorded in the RAMQ prescription claims database [31]. The Québec hospital discharge abstract database provides information on all hospital admissions for the entire province including primary and secondary discharge diagnoses (ICD-9 codes until April 2006 and ICD-10 codes thereafter), comorbid conditions, and admission/discharge dates and destination. Permissions from the Government of Quebec Ethics Committee, the Commission d'Accès à l'Information, were obtained to link the data and conduct this study.

Study patients

Adult patients who had a principal or secondary diagnosis (ICD-10) code for cancer between April 2007 and June 2009 were identified as cancer patients at the date of their first cancer diagnosis in that period. Cancer patients who had an in-hospital diagnosis (principal or secondary) for VTE concurrently or any time following their cancer diagnosis were identified at the time of VTE hospital discharge (index date). VTE codes included: I26 (PE), I80.1–I80.9, I82.8 and I82.9 (DVT). Among those patients with a VTE code, patients discharged alive and registered with the RAMQ drug plan from one year prior to 6 months after the index date were included. Women who were pregnant or became pregnant at anytime during the study period and patients discharged to an institution at index date were excluded. Study patients were followed for 6 months or until death, whichever occurred first.

Exposure to study drugs

The anticoagulants available in Quebec during the study period included warfarin, UFH, LMWHs and the selective factor Xa inhibitor, fondaparinux (rivaroxaban, an oral selective factor Xa inhibitor that was approved for reimbursement by RAMQ in June 2009 in patients with knee replacement, and dabigatran, an oral selective factor II A inhibitor that was approved for reimbursement by RAMQ in April 2011 for patients with atrial fibrillation were not included in our database during the study period) [32,33] patients were said to have used an anticoagulant at index date if they filled a prescription for that anticoagulant within the first two days following index date. Anticoagulant treatment was assessed during the 6-month follow-up in terms of agents received at index date and switch to another anticoagulant agent (any dispensed and total duration of anticoagulant use until the switch). A switch was deemed to occur when a patient was dispensed a different anticoagulant during the days supplied or within the 7 days following the last supplied day on another anticoagulant. Patients who were dispensed a LMWH and warfarin at index date and then stopped using the LMWH and continued warfarin did not constitute a switch as this is considered usual clinical practice. Medication possession ratio (MPR) was also calculated, and was defined as the ratio of the total number of supplied days of any anticoagulant until the first interruption (at least 7 days without anticoagulant supply) over the duration of follow-up. The 6 patients who used UFH and the 11 patients who used fondaprinux at index date were included in the LMWH group, as described below.

Patient baseline characteristics

Patient characteristics assessed at index date included: age, sex, type of insurance plan [based on patient eligibility for premium subsidies; low income patients receiving premium subsidies Guaranteed Income Supplement (GIS), those receiving partial premium subsidies (partial-GIS), and those not receiving premium subsidies (no-GIS). GIS and partial GIS were grouped in one category and labelled 'low income'], region of residence (urban or rural), specialty of the physician who prescribed

Download English Version:

https://daneshyari.com/en/article/6002688

Download Persian Version:

https://daneshyari.com/article/6002688

Daneshyari.com