IJPSR (2024), Volume 15, Issue 7 **(Research Article)**

INTERNATIONAL JOURNAL OF PHARMACEUTICAL SCIENCES AND RESEARCH

Received on 30 January 2024; received in revised form, 18 March 2024; accepted, 16 April 2024; published 01 July 2024

VARIABILITY IN VENOUS THROMBOEMBOLISM PROPHYLAXIS FOR INPATIENT MEDICAL PATIENTS: A DESCRIPTION OF DIFFERENCES IN PRACTICE ACROSS THE PRAIRIE PROVINCES

Tammy J. Bungard [* 1], Darcy A. Lamb [2], William A. Semchuk [3], Jennifer Lowerison [4], Jennifer Bolt [5] and Peter Thomson [6]

Department of Medicine [1], University of Alberta, Edmonton, Alberta.
Pharmacy Services [2], Saskatchewan Health Authority, Saskatoon, Saskatchewan.
Pharmacy Services [3], Saskatchewan Health Authority, Regina, Saskatchewan.
Pharmacy Services [4], Alberta Health Services, Calgary, Alberta.
Pharmacy Services [5], Interior Health Authority, Kelowna, BC and Faculty of Pharmaceutical Sciences, University of British Columbia, Vancouver, Canada.
Pharmacy Services [6], Winnipeg Regional Health Authority, Winnipeg, Manitoba.

Keywords:

Deep vein thrombosis, Low molecular weight heparin, Prophylaxis, Pulmonary embolism, Venous thromboembolism

Correspondence to Author:
Mr. Monowar Hussain

BSP, Pharm D.,
Department of Medicine,
University of Alberta, Edmonton, AB.

E-mail: tammy.bungard@ualberta.ca

ABSTRACT: Background: Venous thromboembolism is the most common preventable cause of in-hospital mortality. Despite this, thromboprophylaxis practices vary related to order sets and special populations. **Aim:** To describe thromboprophylaxis strategies and awareness of institutional policies. **Methods:** Electronic survey of pharmacists having general medicine institutional practices within Alberta, Saskatchewan and Manitoba in 2017. **Results:** Amongst 88 (24.2%) respondents, the majority (60.2%) had practiced >5 years, and were working full time (81.8%) as staff pharmacists (94.3%). The majority (80.7%) used institutional order sets. In patients with normal weight and renal function, agents used were: dalteparin (36.4%), enoxaparin (31.1%), unfractionated heparin (UFH) (15.4%) and tinzaparin (11.3%), while for those with CrCl<30mL/min or hemodialysis, UFH (55.7% and 65.2%) and enoxaparin (23.5% and 26.3%) were used. Escalating doses for obesity were used by 86.7%, with upper weight extremes, defined in kilograms by 50.0% (median 100kg [range 100-150]), and BMI by 29.5% (median 40 [30-40]). Reduced doses were used for emaciation by 72.3%, with lower weight extremes defined in kilograms by 63.6% (median 40kg [30-50]). Prophylaxis was discontinued at discharge (58.0%) or once mobile (37.5%). However, 55.7% reported no standard mobility definition. When available, mobility was defined as home activity (46.2%) and bathroom use/walking distance (38.5%). **Conclusion:** Enoxaparin or dalteparin were most commonly used for thromboprophylaxis, while UFH was favored in those with severe renal dysfunction. Despite 80.7% having institutional order sets, mobility was not defined for the majority and some pharmacists identified not having weight cut off points for obese (29.5%) or emaciated (35.2%) patients.

INTRODUCTION: Venous thromboembolism (VTE) is the most common preventable cause of death in hospitals, mandating the implementation of VTE prophylaxis for institutional accreditation through Accreditation Canada [1-4]. While a strategy for VTE prophylaxis must be implemented at institutions, practices appear to differ in terms of definitions (e.g., mobility, extremes of weight) and use of pharmacotherapy. As such, we sought to describe practices for VTE prophylaxis amongst medical patients admitted to hospitals across Canadian prairie provinces.

QUICK RESPONSE CODE

DOI: 10.13040/IJPSR.0975-8232.15(7).2111-15

This article can be accessed online on www.ijpsr.com

DOI link: https://doi.org/10.13040/IJPSR.0975-8232.15(7).2111-15

MATERIALS and METHODS Pharmacists providing care to patients on general internal

medical units across Alberta (Calgary, Central, Edmonton and North Zones), Saskatchewan (Regina Qu'Appelle Health Region and Saskatoon Health Region) and Manitoba (Winnipeg Regional Health Authority) were electronically surveyed using Research Electronic Data Capture (REDCap) in November 2017. Sites were identified by the members of the prairie province pharmacist group, Collaborative Learning On Thrombosis (CLOT), that represented pharmacists serving as practice leaders for the jurisdictions surveyed. After the initial survey, 2 reminders were sent 2 weeks apart.

We sought to assess pharmacologic therapies used for VTE prophylaxis across various populations (average weight and renal function, extremes of weight, renal dysfunction [CrCl< 30 mL/min] and hemodialysis) and to determine definitions (if available) for mobility and the lower/upper extremes of weight. Medians were reported for prophylactic agent selection. Secondly, we assessed if institutional order sets were used and whether audits were performed. Lastly, using a Likert scale we assessed the frequency of pharmacist interventions related to VTE prophylaxis wherein 1 was defined as never, 3 was a few times per week and 5 was multiple times per day. Health Research Ethics Board approval was received through the University of Alberta (Pro00073294).

RESULTS: Approximately one-quarter (88 [24.2%]) of eligible pharmacists responded to the survey, with 36, 27 and 25 responses from Alberta, Manitoba and Saskatchewan, respectively. The majority of respondents were practicing for at least 2 years (53[60.2%]), and were working full time (72[81.8%]) as staff pharmacists (83 [94.3%]). For the average patient and across extremes of weight, dalteparin and enoxaparin were most commonly used; while for patients with renal dysfunction or undergoing hemodialysis, unfractionated heparin (UFH) and enoxaparin were most common **Table 1**. Most respondents altered dosing based on weight, with increased or decreased doses at the upper and lower extremes, respectively.

TABLE 1: VTE PROPHYLAXIS REGIMENS ACROSS POPULATIONS

Agent	Average weight, renal function	Obese	Emaciated	CrCl< 30mL/min	Hemodialysis
Enoxaparin	31.1%	30.1%	33.2%	23.5%	26.3%
Dosing*	84.3% 40 mg daily 11.8% 40 mg BID	70.2% 40 mg BID 14.9% 40 mg daily	93.3% 20-30 mg daily	95.2% 20-30 mg daily	92.3% 20-30 mg daily
Dalteparin	36.4%	36.7%	33.6%	9.9%	1.5%
Dosing*	98.5% 5000 U daily	96.7% 7500 U daily	81.7% 2500 U daily 16.7% 5000 U daily	55.6% 5000 U daily 42.2% 2500 U daily	66.7% 5000 U daily 33.3% 2500 U daily
Tinzaparin	11.3%	12.9%	13.1%	7.3%	0.7%
Dosing*	59.4% 4500 U daily 37.5% 75 U/kg daily	88.9% 75 U/kg daily	76% 75 U/kg daily 20% 3500 U daily	50.0% 4500 U daily 45.8% 75 U/kg daily	50.0% 4500 U daily 50.0% 75 U/kg daily
Unfractionated Heparin	15.4%	16.8%	16.6%	55.7%	65.2%
Dosing*	97.3% 5000U BID	88.5% 5000 U TID or 7500 U BID	41.5% 5000 U BID 40.0% 2500 U BID	96.4% 5000 U BID	93.2% 5000 U BID
Sequential Compression	3.6%	2.1%	2.7%	3.2%	3.6%
Other	2.0%	1.4%	0.8%	0.4%	2.8%

*reported frequencies of ≥ 10%, Kg=kilogram; BID=twice daily; U=units.

Variability in agent used was evident not only across provinces, but also within the 4 zones of Alberta and 2 health regions of Saskatchewan. For patients of average body weight with normal renal function across Alberta, the Calgary zone most commonly used either enoxaparin (30%) or dalteparin (30%), the Edmonton zone mostly used dalteparin (70%) and the Central and North zones predominantly used enoxaparin (70% and 77.5%, respectively). In Saskatchewan, the Saskatoon Health Region most commonly used tinzaparin (60%), whereas Regina Qu'Appelle Health Region predominantly used enoxaparin (90%).

For patients in Alberta with CrCl< 30 mL/min, UFH was the most commonly used agent in the Calgary zone (50%), central zone (60%) and Edmonton zone (50%), while in the North zone

enoxaparin predominated (80%). For those undergoing hemodialysis, the Central, Edmonton and North zones most commonly used UFH (>92.5%), as did the Calgary zone (72.5%). In Saskatchewan, those having a CrCl< 30 mL/min or undergoing hemodialysis in Saskatoon Health Region predominantly received UFH (90% and 95%, respectively) while in Regina Qu'Appelle Health Region enoxaparin was used (87.5% and 90%, respectively).

Twenty-six respondents (29.5%) reported that upper body weight cut off points were not defined at their institution (Alberta [18.6%], Saskatchewan [44%], Manitoba [24.1%]); when defined, 44(50.0%) used kilograms (median 100kg [range 100-150]) and 26 (29.5%) used BMI (median 40 [30-40]). For lower body weight, 31 (35.2%) lacked a definition (Alberta [50%], Saskatchewan [52%], Manitoba [22.2%]); when defined (56 [63.6%]) all used kilograms (median 40kg [30-50]).

Most indicated that prophylaxis was discontinued at discharge (51 [58.0%]) or once the patient was mobile (33 [37.5%]). A small portion (15.0%) noted continuing prophylaxis following discharge, largely amongst non-medicine patients with hip/knee replacements. The majority of pharmacists reported that no definition of mobility was evident at their institution (49 [55.7%]). When mobility was defined, the majority identified it to be activity as at home (18 [46.2%]) with most others defining this on the basis of walking (15 [38.5%]) with distances that ranged from going to and from the nursing desk to going around the unit 3 times a day. The majority (71 [80.7%]) used institutional-based order sets (75% Alberta, 80% Saskatchewan and 92.3% Manitoba), with 50 respondents (56.8%) aware of an institutional audit (36.1% Alberta, 96% Saskatchewan and 48% Manitoba). Pharmacists were more commonly responsible for performing the audits in Saskatchewan (100%) and Manitoba (71.4%) compared to Alberta (0%). In terms of pharmacist interventions related to VTE prophylaxis, pharmacists reported initiating VTE prophylaxis a few times per week **Table 2**. Changing prophylaxis was more commonly reported for renal dysfunction than extremes of weight or bleeding risk.

TABLE 2: FREQUENCY OF PHARMACIST INTERVENTIONS

Factor*	All Combined (median, IQR)	AB	SK	MN
To initiate VTE prophylaxis	3 (2, 3.25)	2.5	4	3
To risk stratify using a tool	2 (1, 3)	2	2	2
To change prophylaxis for obesity	2 (2, 3)	2	3	2
To change prophylaxis for emaciation	2 (2, 3)	2	3	2
To change prophylaxis for CrCl<30mL/min	3 (2, 3)	2.5	3	3
To change prophylaxis for hemodialysis	2 (1, 2)	1	2	2
To change for no indication	2 (2, 2)	2	2	2
To discontinue for bleed risk	2 (2, 2)	2	2	2

*used a 1-5 scale – MEDIANs (IQR) reported; 1=never; 3=few times per week; 5= multiple times per day

DISCUSSION: Across the three prairie provinces, thromboprophylaxis practices varied between provinces and across provincial zones/regions. However, within each site surveyed, similarities were reported for use of agents in the average patient, with consistent usage patterns for those at extremes of weight. LMWH's were most commonly used across all populations except renal dysfunction, wherein, UFH was predominantly used.

Formulary differences likely contributed to the different LMWH used for the average patient across provinces and provincial zones/health regions. Most Canadian product monographs (PMs) for the LMWHs used in the prairie provinces are clear on appropriate prophylactic dosing for the average medical patient [6-8]. Variability in the PMs, however, likely helps to explain the heterogeneity we observed from the survey responders, and differences within institutional order-sets. For example, tinzaparin does not have an official indication for VTE prophylaxis in medical patients, and dosing must be extrapolated from other indications/literature [7].

Other than cautions, there is a general lack of information and clear guidance in most LMWH PMs around what to do for patients at an extreme of weight. For severe renal insufficiency, the

enoxaparin PM provides definitive dosing recommendations, which is likely why use of this LMWH was observed in this population in one particular region (Reginal Qu'Appelle) wherein other LMWHs were not [8]. It is surprising that despite over a quarter century of use in millions of patients that more definitive evidence to direct prescribing in these common clinical scenarios is both lacking and somewhat inconsistent with wording. The majority of respondents reported no definition for mobilityin their institution and relied primarily on input from nursing colleagues to capture this. A systematic review of 21 studies of medical patients found the definition of immobility to be heterogeneous with some using objective criteria (duration, distance, time walked) and others being subjective (describing the nature of the immobility) [5]. This was reflected in our results as well with varying definitions put forward. The concept of immobility is broad, and encompasses the nature, level and duration of immobility. Having a simplified objective definition would allow front line clinicians to more consistently assess this.

The majority of respondents (80.7%) reported having institutional based order sets. Order sets have been shown to significantly improve the use of VTE prophylaxis and reduce VTE occurrence [9]. The low level of pharmacist intervention is likely attributable, in part, to the use of these standardized order sets. Not all order sets capture options for extremes of weight and for those that do, it may be that weight is not documented for a good portion of patients given the low level of pharmacist intervention for this and the reported lack of definition of weight extremes. Other barriers for pharmacist intervention could potentially have included limited patient information if working from the dispensary or reviewing orders for remote sites, and challenges accessing physicians at sites that do not have regular rounds.

Provinces having pharmacists conduct VTE prophylaxis audits (namely Saskatchewan and Manitoba) reported a greater awareness of policies and conduction of these audits.

Our study was limited as our response rate was 24.2%, lower than we had hoped. We did, however, have representation from 7 health zones dispersed over all three prairie provinces. Despite this low response rate, commonalities were reported within zones / health regions implying data collected reflected practices across jurisdictions.

CONCLUSION: In summary, most patients were prophylaxed with enoxaparin or dalteparinunless they had a CrCl<30mL/min or were undergoing hemodialysis wherein UFH was predominately used in institutions not using enoxaparin. Despite 80.7% having institutional order sets, mobility was not defined for the majority and some pharmacists identified not having weight cut off points for obese (29.5%) or emaciated (35.2%) patients. Further work to ensure standardization of order sets with integration of unique patient factors should be pursuedin these institutions to enhance consistency of clinical practice.

ACKNOWLEDGEMENT: None Funding was provided by an investigator initiated, unrestricted research grant from LEO Pharma.

CONFLICTS OF INTEREST: Nil

REFERENCES:

1. Mahlab-Guri K, Otman MS, Replianski N, Rosenberg-Bezalel S, Rabinovich I and Sthoeger Z: Venous thromboembolism prophylaxis in patients hopsitalzed in medical wards. Medicine 2020; 99(7): e19127. Doi: 10.1097/MD.0000000000019127
2. Accreditation Canada. Required organizational practices handbook 2020 [Internet; accessed 2024Mar 12]. Available from: https://store.accreditation.ca/products/required-organizational-practices-handbook-2017-version-2
3. Canadian Patient Safety Institute; Measures: Venous Thromboembolism (VTE). [Internet; accessed 2024 Mar 12]. Available from: https://www.patientsafetyinstitute.ca/en/toolsResources/psm/Pages/VTE-measurement.aspx
4. Thrombosis Canada. Thromboprophylaxis: hospitalized medical patients [Internet; accessed 2024 Mar 12]. Available from: https://thrombosiscanada.ca/hcp/practice/clinical_guides?language=en-ca&guideID=THROMBOPROPHYLAXISINHOSPITALIZ
5. Ye F, Bell LN, Mazza J, Lee A and Yale SH: Variation in definitions of immobility in pharmacological thromboprophylaxis clinical trials in medical inpatients: a systematic review. Clin Applied ThrombHemos 2018; 24(1): 13-21. DOI: 10.1177/1076029616677802
6. Fragmin product monograph. Kirkland (QC): Pfizer Canada; 2022 Dec 29.
7. Innohep product monograph. Thornhill (ON): LEO Pharma; 2017 May 26.
8. Lovenox product monograph. Laval (QC): Sanofi-aventis Canada; 2018 Sept 18.

9. Lovely JK, Hickman JA, Johnson MG, Naessens JM and Mogenthaler TI: Impact of a program to improve venous thromboembolism prophylaxis on incidence of thromboembolism and bleeding rates in hospitalized patients during implementation programs to improve venous thromboembolism prophylaxis. May Clin Proc Innov Qual Outcomes 2020; 4(2): 159-169.

How to cite this article:
Bungard TJ, Lamb DA, Semchuk WA, Lowerison J, Bolt J and Thomson P: Variability in venous thromboembolism prophylaxis for inpatient medical patients: a description of differences in practice across the prairie provinces. Int J Pharm Sci & Res 2024; 15(7): 2111-15. doi: 10.13040/IJPSR.0975-8232.15(7).2111-15.