Paul Jansson | R in Emergency Medicine at BWH/MGH, PGY 2

Title: Clinical Fellow in Emergency Medicine

PI Information: Paul Jansson, Clinical Fellow in Emergency Medicine -- pjansson@partners.org

Faculty Sponsor: Chris Kabhrel, Associate Professor of Emergency Medicine -- ckebrhel@partners.org

Additional Investigators: None

RESEARCH NARRATIVE

Problem to be addressed: Venous thromboembolism (VTE) is a common yet life-threatening diagnosis that is regularly encountered in clinical care and represents a continuum of disease between deep venous thrombosis (DVT) and pulmonary embolism (PE). The mainstay of VTE treatment is pharmacologic anticoagulation to prevent growth and propagation of the blood clot. Despite the recent emergence of novel anticoagulant medications, intravenous dosing of unfractionated heparin (UFH) remains the most common method of treating VTE in the in-hospital setting. This is especially true for patients with severe PE for whom thrombolysis or other intervention may be considered. Traditional administration of UFH uses weight-based dosing and requires frequent blood testing (typically using partial thromboplastin time [PTT]) and dose adjustment to maintain a therapeutic level of anticoagulation. Although a standard dosing strategy for UFH has been established in the literature, there is little research on the efficacy of this strategy in terms of consequent time spent within the therapeutic range and time to achieve therapeutic range of anticoagulation for these patients. Because of the life-threatening nature of this disease process, Massachusetts General Hospital (MGH) has established a Pulmonary Embolism Response Team (PERT) comprised of clinicians from various medical specialties, including emergency medicine, vascular medicine, surgery, and radiology to provide expert interdisciplinary care for patients diagnosed with PE at MGH. While the primary goal of PERT activation is to provide exceptional medical care, a secondary goal remains to advance scientific knowledge of VTE through clinical research. As such, clinical data are gathered prospectively on patients for whom PERT is activated and provides a unique opportunity for study. The PERT database now has more than 600 variables collected on over 400 patients, information that is shared with a pulmonary embolism research consortium. At a recent meeting of PERT members, frustration with the traditional dosing and monitoring of UFH were raised as issues of clinical significance. Many members of the team reported anecdotal experiences where patients spent significant time outside the therapeutic range, exposing them to the risks of sub- and supratherapeutic anticoagulation. Frequently, patients experienced serious delays in achieving their first therapeutic level. This represents a considerable patient safety issue, as sub-therapeutic anticoagulation can result in growth of the clot or progression of DVT to PE, while supra-therapeutic dosing can expose the patient to the risk of life-threatening hemorrhage. Furthermore, the frequent lab draws and dose adjustments represent multiple further potential for medical error. Despite the major risks associated with treatment using UFH, little research exists to support the currently accepted dosing regimen. The goal of this research project is to perform a cohort analysis of patients enrolled in the PERT database to assess the efficacy of the traditional treatment regimen of UFH by measuring the time spent within the therapeutic range of anticoagulation, as measured by the PTT values at traditional six hour windows within the first 24 hours of anticoagulation. The outcomes of this research may have both local and national significance in the treatment of PE and will influence future trials of the optimal anticoagulation dosing in the hospital setting. We plan to implement results from this study to improve quality and safety both within and outside MGH. Data from this analysis will help guide improvements in hospital dosing and monitoring protocols, including PERT guidelines, which will be disseminated throughout the PERT consortium, a national platform.
**Literature Review:** Venous Thromboembolism (VTE) is a spectrum of disease that encompasses both deep venous thrombosis (DVT) and pulmonary embolism (PE). DVT represents a blood clot lodged in the deep veins of the extremities while PE occurs when a clot breaks off and becomes lodged in the pulmonary arterial vasculature. (1) Similarly, the clinical presentation of VTE can range from asymptomatic incidental findings to massive circulatory shock and sudden death. The incidence of VTE is between 100 and 200 per 100,000 patients, resulting in approximately 548,000 hospitalizations for VTE each year in the United States. (2) The mainstay of treatment for VTE is anticoagulation. (3) While newer “novel” anticoagulants are beginning to enter the treatment algorithm for VTE, the acute management of VTE typically involves administration of heparin, whether in its low molecular weight form (“Lovenox”) or unfractionated as a continuous intravenous drip. Unfractionated heparin has traditionally been dosed for VTE with a dose of 80 units per kilogram administered as a bolus, followed by a dose of 18 units per kilogram per hour, a dosing regimen which was created over two decades ago. (4) The degree of anticoagulation is traditionally followed by the prothrombin time (PTT), which measures the effectiveness of the intrinsic coagulation pathway, which is disproportionately affected by the administration of UFH. (5) According to the MGH policy, PTT times should be checked every six hours with dose adjustments performed as needed to keep the values within the reference range. Thus, administration of heparin therapy is a resource-intensive treatment, with lab testing required four or more times a day with changes in dosing between each check requiring communication between nursing, physician staff, and pharmacy, potentially exposing the patient to significant errors in medication administration. (6) References: 1. Di Nisio M, van Es N, Büller HR. Deep vein thrombosis and pulmonary embolism. Lancet (London, England) [Internet]. 2016 Jun 30;6736(16):171–219. 2. Heit JA, Spencer FA, White RH. The epidemiology of venous thromboembolism. J Thromb Thrombolysis. 2016;41(1):3–14. 3. Kearon C, Akl EA, Ornelas J, Blaiwas A, Jimenez D, Bounaumeaux H, et al. Antithrombotic Therapy for VTE Disease: CHEST Guideline and Expert Panel Report. Chest [Internet]. 2016 Feb;149(2):315–52. 4. Raschke RA, Reilly BM, Guidry JR, Fontana JR, Srinivas S. The weight-based heparin dosing nomogram compared with a “standard care” nomogram. A randomized controlled trial. Ann Intern Med [Internet]. 1993 Nov 1;119(9):874–81. 5. Ng VL. Prothrombin Time and Partial Thromboplastin Time Assay Considerations. Clin Lab Med. 2009;29(2):253–63. 6. Grissinger MC, Hicks RW, Keroack MA, Marella WM, Vaida AJ. Harmful medication errors involving unfractionated and low-molecular-weight heparin in three patient safety reporting programs. Jt Comm J Qual Patient Saf. 2010;36(5):195–202.

**Study Hypothesis:**

1. More than 50% of patients treated with UFH will have at least one PTT value outside of the reference range within the first 24 hours of the initiation of anticoagulation.
2. More than 25% of patients treated with UFH will have at least one PTT value above and below the reference range within the first 24 hours of the initiation of anticoagulation.
3. Patients receiving the drip only (no bolus) method will have fewer supratherapeutic PTT values but more subtherapeutic values than patients in the traditional dosing cohort.

**Population:** Patients within the PERT database started and maintained on unfractionated heparin with PTT data for at least 24 hours after heparin start time.

**Description of intervention or study design:** Retrospective analysis of prospective cohort data. A trained research assistant will extract dosing information from the medication administration record (MAR) and PTT values from the lab worksheet. Descriptive and analytic statistics will then be calculated from the extracted data.

**Description of comparison group (if relevant):** The reference group includes all patients treated with the traditional bolus/drip dosing of UFH. Comparison groups include patients treated without a bolus (“drip only”) and patients treated with non-standard dosing.
Outcome variable to be used to determine efficacy of the intervention (if relevant): PTT values within the reference range for therapeutic anticoagulation within the first 24 hours of treatment with UFH. Secondary analysis will examine short- and long-term mortality, bleeding rates, and changes in anticoagulation regimen.

Power analysis to determine feasibility (when relevant): As of the time of application, there are 655 patients in the PERT registry of whom approximately 400 received UFH therapy. Given our comparison of three values within the reference range versus less than three, and an estimated standard deviation of one value, a sample size of only 22 would have 90% power to distinguish between the groups, assuming a two tailed distribution.

Timeline:
- September 2016- December 2016: Data collection
- December 2016 – January 2017: Analysis
- January 2017 – February 2017: Write Manuscript

IRB Status of Project: The protocol has been approved (Protocol Number 2016P000701)

BUDGET

Line item budget and budget narrative:
- Research Assistant for Chart Review – 400 Charts x 15 minutes per chart x $25 per hour = $2500
- Statistician – 5 hours x $100 per hour = $500
- Total Budget: $3000

Disclosure of other funding sources: This grant would be sole source of funding.

LETTERS OF SUPPORTS

PD Name: Eric Nadel Letter of Support Received? yes
Mentor Name: Chris Kabhrel Letter of Support Received? yes

OTHER

COE Involvement: I have attended multiple COE dinner sessions.

Previous COE Funding: I received a COE Quality and Safety research grant in Fall 2015.
Jessica Cintolo-Gonzalez | F in Complex Surgical Oncology at BWH/MGH, PGY 9

Title: Associate Professor of Surgery

PI Information: Chandrajit Raut, MD, Associate Professor of Surgery -- CRAUT@PARTNERS.ORG

Faculty Sponsor: Chandrajit Raut, MD, Associate Professor of Surgery -- CRAUT@PARTNERS.ORG

Additional Investigators: None

RESEARCH NARRATIVE

Problem to be addressed: We believe that we can do a better job educating our cancer patients about the surgical process and preparing them for both surgery and recovery. This belief is based on assessment of patient calls with questions before surgery, uncertainties that are expressed in the preoperative holding area prior to procedures, and the questions our practitioners receive following discharge. The objective of this study is to implement and assess our quality improvement initiative, which consists of providing patients of the Division of Surgical Oncology with structured educational materials focusing on each phase of care along their surgical course (preoperative preparation, day of surgery flow, inpatient recovery, discharge process, and recovery at home/aftercare). These sheets encourage patients to ask appropriate questions and also prompt providers to address essential patient-specific information (for example which medications to stop and when, dietary restrictions, and preoperative medications including bowel regimen). We would like to assess the impact of these educational materials on patient knowledge; their perception of being informed both regarding the surgical process and their consent, and patient satisfaction. We also hope to identify ongoing areas that would benefit from improved patient education.


Study Hypothesis: We hypothesize that implementation of our educational materials will help patients to be better informed about their preoperative preparation, the flow of their surgical day, postoperative recovery, discharge process and instructions, and recovery at home. We also hypothesize that this improvement in patient understanding will lead to an overall increase in satisfaction with their care.