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The TOronto ThromboProphylaxis Patient Safety Initiative (TOPPS): A cluster randomised trial

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ABSTRACT

Background: Although venous thromboembolism (VTE) is one of the most common and most preventable complications of hospital stay, review of the literature demonstrates large evidence-care gaps for VTE prevention.
Objectives: This study aimed to determine if a multi-component quality improvement (QI) strategy, including the support of hospital leadership, use of order sets, audit and feedback, and active pharmacy involvement, could increase the use of appropriate thromboprophylaxis in patients hospitalized for hip fracture surgery (HFS), major general surgery (MGS) and acute medical illness (MED).
Methods: TOPPS was a cluster randomized trial involving eight hospitals. After a baseline data collection phase, one of the three patient groups at each site was randomized to the targeted QI intervention while the other two groups served as controls. In the next phase, an additional patient group at each site was randomized to the intervention while the third group remained controls. Standardized chart audits were conducted to assess the rates of appropriate thromboprophylaxis use.
Results: At baseline, the rates of appropriate thromboprophylaxis were 79% in HFS, 43% in MGS and 31% in MED. By the end of phase 3, 89% of HFS, 65% of MGS and 70% of MED patients were receiving appropriate prophylaxis. Improvement was greater in the intervention groups compared to controls (85% vs. 76% in HFS; 67% vs. 54% in MGS; 64% vs. 62% in MED) and this difference reached significance in the MGS group ($p = 0.048$).
Conclusions: Use of a multi-component intervention can be effective in improving the appropriate use of thromboprophylaxis.

1. Introduction

Venous thromboembolism (VTE), which includes deep vein thrombosis (DVT) and pulmonary embolism (PE), is one of the most common and preventable complications of hospital stay.[1] It has been suggested that VTE is the second most common cause of excess length of hospital stay, and the third commonest cause of excess mortality and hospital charges.[1] Massive PE is the cause of approximately 10% of deaths in hospital making PE the most common preventable cause of hospital death.[2–4] Several hundred randomized trials of VTE prevention demonstrate that thromboprophylaxis reduces asymptomatic DVT, symptomatic VTE, fatal PE, and all-cause mortality, while, at the same time, reducing health

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care costs.[4] In addition, evidence-based consensus guidelines recommend the routine use of thromboprophylaxis in hospitalized patients at risk.[4–7] Among more than 75 safety interventions, thromboprophylaxis was ranked the number one patient safety strategy for hospitalized patients.[8] Despite the abundant evidence supporting the use of thromboprophylaxis, audits of patient care consistently find major gaps in the provision of this key patient safety intervention.[9–17] In many studies, fewer than 50% of patients at risk received thromboprophylaxis. Reviews of the literature on implementation strategies for VTE prophylaxis suggest that passive strategies, such as education alone or dissemination of guidelines, are relatively ineffective and that interventions should be multi-faceted, address local barriers and include a reminder mechanism or alert for physicians to prescribe appropriate thromboprophylaxis.[18–20] To date, studies designed to address implementation of evidence-based thromboprophylaxis have been either observational or before-after studies from single sites. A recent Cochrane review of interventions for implementation of thromboprophylaxis included only 8 RCTs and 47 non-randomized trials.[20] Furthermore, in most of these studies, the primary outcome was the use of *any* thromboprophylaxis rather than the use of *appropriate* thromboprophylaxis.

The TOronto ThromboProphylaxis Patient Safety Initiative (TOPPS) was a multi-centre, cluster randomized trial designed to assess the impact of a multi-component intervention on rates of appropriate thromboprophylaxis. The aim of the study was to assess if rates of appropriate thromboprophylaxis could be improved across 8 hospitals and in three patient groups: hip fracture surgery (HFS), major general surgery (MGS) and acute medical illness (MED).

2. Methods

2.1. Design

The chief executive officers (CEOs) at 8 Toronto area hospitals (seven community hospitals and one academic health sciences centre) were invited to participate in the study. Sites were chosen to represent a typical acute care hospital from various neighbourhoods in the Greater Toronto Area. When the CEO signed the participation agreement, a meeting was coordinated through the director of pharmacy which involved multidisciplinary stakeholders to confirm the commitment for a local VTE quality improvement (QI) team. TOPPS was designed as a cluster randomized trial with the unit of randomization being the specific patient groups in each of the hospitals rather than individual patients. Research ethics approval was obtained at each of the participating hospitals.

2.2. Participants

Three patient groups were selected to represent patients that would be commonly cared for at all general hospitals and that represent groups with known high (HFS), moderate (MGS) and lower (MED) risks of VTE without prophylaxis.[4] Inclusion criteria were: age at least 18 years, hospital admission for more than 48 h and at risk for VTE based on the American College of Chest Physicians (ACCP) thromboprophylaxis guidelines available at the time.[19] The only exclusion was the use of therapeutic anticoagulation. If patients at risk for VTE had a contraindication to anticoagulant prophylaxis, mechanical prophylaxis was considered appropriate.

2.3. Interventions

The study had three phases - baseline and two subsequent intervention periods. Appropriate thromboprophylaxis use at baseline was assessed by chart review of 50 consecutive eligible patients in each of the three groups at each centre (in some centres, patient volume required lowering the target number of patients). This convenience sample represented a feasible patient volume and time frame for the hospitals. All chart audits in each phase were completed by two expert abstractors (AD, TP) using formal definitions of eligibility and appropriate thromboprophylaxis based on ACCP guidelines.[21] Standardized patient selection and data abstraction was utilized to reduce variability in case selection and outcome assessment compared with using multiple local abstractors.

After baseline data collection (phase 1), local teams worked to implement the QI strategies in the patient group randomized to the active intervention (Fig. 1) while the other two patient groups at that centre continued with usual care (control) (Table 1). Randomization occurred at the level of the cluster. Each centre had one patient group assigned to the active intervention and two groups continued as controls (usual care) in phase 2. In phase 3, two groups at each centre received the active intervention (the active group in phase 2 plus a randomly selected second group) while the third group continued as controls. Randomization was computer-generated using a SAS Version 9.1 (SAS Institute, Cary, NC, USA). The randomization code was communicated to the PI and administered by the PI for each of the sites.

2.4. Outcomes

The primary outcome was the rate of prescribing appropriate thromboprophylaxis defined as: ordered within 24 h of admission to hospital or within 24 h after the end-of-surgery, guideline-recommended at the appropriate dose and continued for an appropriate duration (until discharge for MGS and MED and for at least 10 days after HFS).[21] For patients who did not receive appropriate thromboprophylaxis, the reasons for non-adherence were assessed. A secondary outcome was the impact of order sets on the prescribing of appropriate thromboprophylaxis. This was chosen to test the hypothesis that use of order sets was a key component of the intervention.

2.5. Sample size

Based on the rate of adherence of 55% in the 1175 patients from all three groups at baseline and an intraclass coefficient (ICC) of 0.24 (within clusters, based on our pilot data), it was calculated that a minimum sample size of 432 patients would be needed for the intervention phases of the study to detect an improvement of 20% in the rate of thromboprophylaxis (which would be an expected modest effect based on the literature)[22–25] with power of 80% at $\alpha = 0.05$. The sample size calculation, carried out using PASS Version 8.0.8, recommended clusters of 9 patients in each of the clusters in the post-intervention phases. In order to provide meaningful feedback to the teams, it was decided to increase the size of each cluster sampled to 15 patients. This resulted in cluster sizes of 15 patients in each of the 24 clusters in the post-intervention phases, leading to a total sample size of 720 patients (15 patients x 3 groups x 8 hospitals x 2 post-baseline sampling phases).

2.6. Timelines

Baseline data was collected in 2006 and represented a review of consecutive charts for eligible patients admitted that year. Each active phase of the study was approximately 1 year in length. The patient charts reviewed for each phase reflected patients admitted

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