Venous Thromboembolism Prophylaxis following Lower Extremity Orthopedic Surgery: A Review of the Biomedical Research Literature and Evidence-Based Policy in the United States.

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Introduction

The risk of events related to Venous Thromboembolism (VTE) such as Deep Vein Thrombosis (DVT) and Pulmonary Embolism (PE) following hip and knee arthroplasty is a ongoing concern among orthopedic surgeons. Surgical orthopedic interventions to the lower limb is characterized by venous stasis, increased coagulation, and vessel wall trauma. Consequently, in the absence of prophylaxis, the risk of VTE events following total hip arthroplasty (THA) is estimated at 42-57% (Fisher, 2011). Furthermore, VTE represents the most common reason for a return to the hospital after undergoing major orthopedic procedures to the lower limb (Pellegrini et al, 2008). It has been estimated that DVT can occur in as many as 25% patients within the first six weeks after discharge (Trowbridge et al, 1994).

There are two distinct methods of VTE prophylaxis that have traditionally been incorporated in the hospital setting. Anticoagulant pharmacotherapy and Pneumatic Compression Devices (PCDs). Despite their well-established efficacy, there are significant shortcomings with both methods of VTE prophylaxis. Anticoagulants have long been recognized as the standard of care for VTE prophylaxis. However, there is an increased the risk of major bleeds. Accordingly, pharmacotherapy prophylaxis represents a contraindication for those patients with an increased bleeding risk. Specifically, Low Molecular Weight Herapin (LMWH) is associated with increased blood loss, an increased need for transfusions, decreased wound healing and delayed rehabilitation

(Colwell et al, 2010). Conversely, PCDs prevent the formation of blood clots by increasing venous flow rates and stimulating the release of relaxing factors and urokinase (Vanhoutte et al, 1995). However, PCDs are also associated with low rates of compliance due to patient intolerance resulting from the unpleasant sensation of rapid inflation. Additionally, hospital-based PCDs are often complex devices that render the patient immobile. Accordingly, there has been ongoing research identifying VTE prophylaxis that provides the most optimal outcomes combined with increased levels of compliance while mitigating the risk of major bleeding. Furthermore, a solution is required for VTE prophylaxis in an outpatient setting. Policy-makers have utilized the existing research literature to establish best-practice protocols for VTE prophylaxis and cost analyses to determine the best allocation of healthcare funding in these circumstances. Recently, researchers have identified portable PCDs, alternatively known as Mobile Compression Devices (MCDs) as an effective means of DVT prophylaxis following discharge from the hospital. As outlined in the following review, national policy-makers in the US have supported portable PCDs/MCDs for VTE prophylaxis in various clinical settings as an alternative to pharmacotherapy.

Research

In a study conducted by Sobieraj-Teague et al (2012) in Hamilton Canada, the efficacy of a portable, battery-powered compression device called the Venowave was assessed in relation to VTE prophylaxis. The Venowave is a 250 gram wave-form generating compression device powered by a single AA battery that can provide up to eight hours of continuous operation. It has been determined that the Venowave can generate up to 130 mm Hg which compares favourably with hospital-based PCDs. A randomized clinical trial involving 150 high-risk neurosurgical patients was performed to determine if the Venowave could prevent VTE events in this high risk population. All patients were randomized into a Venowave group or the control group. As part of the neurosurgical protocol, all participants were prescribed graduated compression stockings as well as early mobilization. Patients could also be prescribed pharmacologic anticoagulants at the discretion of their treating surgeon. The outcome measures consisted of asymptomatic DVTs as detected by venography or compression ultrasound, symptomatic DVT confirmed by compression ultrasound, and symptomatic PE confirmed by computed tomography pulmonary angiography. Additionally, patient satisfaction was also assessed at study completion. The rate of VTE events in the Venowave group was 4.0% versus a VTE rate of 18.7% in the control group. The difference between groups was deemed statistically significant and represents a reduced risk of VTE by 79%. It was also reported that there was a high rate of tolerance to the device for patients assigned to the Venowave group. Only 9% of patients described adverse events with use of the Venowave device. This translated to higher compliance rates relative to hospital-based PCDs.

Colwell et at (2010) compared a Mobile Compression Device (MCD) to Low Molecular Weight Herapin (LMWH) for VTE prophylaxis in a prospective randomized clinical trial. Four hundred and ten patients undergoing total hip arthroplasty were randomized to either a group using a portable, battery-powered compression device or to a group receiving daily dosages of LMWH (enoxaparin

sodium). This study utilized the Continuous Enhanced Circulation Therapy plus Synchronized Flow Technology compression device. The device weighs 740 grams and provides up to six hours of battery power through an external battery pack. It can produce a maximum pressure during inflation of 50 mm Hg. Duplex ultrasonography was used to detect the existence of deep venous thromboembolism. It was determined that there were 11 major bleeding events in the 395 cases investigated. All 11 events occurred in the herapin group. The differences in cases of major bleeding was statistically significant between the two groups. There were no significant differences in the rates of VTE events between the MCD group and the LMWH group. The authors concluded that mobile compression devices are associated with significantly less bleeding than with low-molecular-weight herapin in patients undergoing total hip arthroplasty.

In a subsequent larger scale study conducted by Colwell et al (2014), researchers investigated the effectiveness of the ActiveCare + SFT mobile compression devices with or without aspirin to pharmacological prophylaxis against VTE in patients undergoing hip or knee arthroplasty. It was found that the incidence of VTE with pharmacological prophylaxis was quite low. As such, the authors hypothesized that the mobile compression device would offer the same level of efficacy. This was termed a noninferiority study in which a 1.0% margin in VTE rates between both methods of prophylaxis would not represent a clinically meaningful difference. There were 3060 patients who partook in this investigation and included those that underwent either unilateral hip arthroplasty or unilateral knee arthroplasty. All participants used the MCD for a minimum period of 10 days. It was found that 28 (0.92%) of the patients experienced symptomatic VTE. Specifically, the rates of VTE was 0.5% (eight of 1509 patients) for the hip arthroplasty group and 1.3% (18 of 1551) for the knee arthroplasty group. In relation to traditional pharmacological prophylaxis, the authors reported that the rates for symptomatic VTE has been reported as 2.2% for warfarin, 1.1% for enoxaparin, 0.64% for rivaroxaban and 1.2% for dabigatran. Accordingly, the MCD was deemed noninferior at a margin of 1.0% compared to the reported rates for pharmacological prophylaxis with the exception rivaroxaban in the knee arthroplasty group.

Policy and Evidence-Based Clinical Practice Guidelines

The American College of Chest Physicians developed The Antithrombotic Therapy and Prevention of Thrombosis, 9th edition in 2012. The authors acknowledged that the current 9th edition of the clinical practice Guidelines differs from previous editions. Dr. Jack Hirsh, an expert in the field of thrombosis, was recognized as the leader in this important project in terms of creating a platform that made the latest edition of the Guidelines possible and also as a pioneer in advancing antithrombotic therapy. Notably, Dr. Hirsh was also a co-developer of the Venowave mobile compression device which was granted FDA approval through the 510k process in October of 2007. Based on a comprehensive review of the existing literature, for patients undergoing total hip arthroplasty or total knee arthroplasty, the panel recommended pharmacological prophylaxis or intermittent pneumatic compression devices for 10-14 days following the procedure. For patients undergoing major

orthopedic surgery with an increased risk of bleeding, the panel suggested pneumatic compression device rather than pharmacological treatment. The recommendations were based on research where it has been repeatedly demonstrated that reduced rates of bleeding occurs with pneumatic compression devices versus traditional pharmacological prophylaxis. More specifically, the panel recommended the use of only portable, battery-powered compression devices such as MCDs for periods of 18 hours daily in both inpatient and outpatient settings.

The Centres for Medicare and Medicaid Services (CMS) conducted a cost analysis of a mobile compression device for VTE prophylaxis following total hip arthroplasty. A decision tree model was designed where the primary focus was cost incurred within 30 days of hospital admission in 2010 US dollars. The cost total in the model considered the probability and cost of VTE events such as DVT, PE, and minor and major bleeding. The model demonstrated that VTE prophylaxis with MCD generated cost savings of $369.50 per patient. The authors concluded that the cost discrepancy between MCD and pharmacotherapy was primarily the result of reduced major bleeding events with the former. Major bleeding is associated with prolonged hospital stays, increased levels of care from health care professionals, additional laboratory expenses and blood transfusions. In their analysis, the cost associated with a major bleeding event was determined to be $5,363.13. As there are approximately 234,000 patients undergoing total hip arthroplasty each year in the US, use of MCDs for VTE prophylaxis would amount to $86 million dollars in annual health care savings.

The CMS also created a National Medical Policy for PCDs Post Surgery in September of 2013. In the current policy statement, PCDs were considered medically necessary in three clinical situations: i) following hip, knee, neurosurgery or major surgical procedure where the patient has contraindications to anticoagulation, a known bleeding disorder, or is unable to ambulate; ii) as an adjunct prophylaxis for patients undergoing hip or knee arthroplasty with a medical history of VTE; and iii) as an alternative to LMW herapin following hip surgery due reduced probability of bleeding complications. The CMS identified ActiveCare and Venowave as the two manufacturers of mobile compression devices that have obtained 510k FDA approval. In this Policy, a number of position statements were cited as supporting the use of MCDs in VTE prophylaxis including: The American Academy of Orthopaedic Surgeons, The American College of Chest Physicians, The Australia and New Zealand Working Party, The French Society for Anaesthesiology and Intensive Care, The International Consensus Statement, and the National Institute for Health Care and Excellence. A number of studies supporting compression devices for VTE prophylaxis were also presented in this Policy included those mentioned in this review. It was concluded that compression devices are superior than no prophylaxis and graduated compression stockings and may offer additional clinical benefit to patients concurrently being managed with LMW herapin.

The BlueCross BlueShield Association investigated outpatient use of PCDs for VTE prophylaxis. Once again, only MCDs such as the Venowave, the ActiveCare as well as the Restep System were identified as the portable compression devices that have been cleared by the FDA. In this policy, it was reported that outpatient use of portable PCDs for VTE prophylaxis following

major orthopedic surgery may be considered medically necessary in patients with a contraindication to pharmacotherapy prophylaxis such as those with a high risk for major bleeding events. Additionally, outpatient use of portable PCDs for VTE prophylaxis following major non-orthopedic surgery may also be considered medically necessary in patients with a moderate or high risk for VTE and a contraindication for pharmacotherapy prophylaxis. Major orthopedic surgery was defined as total hip arthroplasty, total knee arthroplasty, and hip fracture surgery. Based on the American College of Chest Physicians (ACCP) guidelines, the following were considered as general risk factors for bleeding events: i) previous major bleeding, ii) severe renal failure, iii) simultaneous antiplatelet agent, and iv) various surgical factors. With respect to major non-orthopedic surgery, as identified by the ACCP, the highest risk for VTE was for those patients undergoing abdominal and pelvic surgery for cancer. In summary, the use of portable PCDs for VTE prophylaxis may be considered medically necessary when prophylaxis is clinically indicated in the presence of contraindications to anticoagulation pharmacotherapy.

Conclusion

The formalized research investigations of pneumatic compression therapy provides compelling evidence of this particular health technology's clinical and economic efficacy with VTE prophylaxis following elective major orthopedic surgery to the lower extremity. Furthermore, provided the prevalence and cost associated with major bleeding events, these devices represent a medically necessary alternative for VTE prophylaxis in populations where there is an increased bleeding risk or where anticoagulant pharmacotherapy is contraindicated. However, despite the documented success of PCDs for VTE prophylaxis, issues remain regarding mobility, compliance and complexity in outpatient settings. Portable battery-operated Mobile Compression Devices mitigate these compliance issues and are endorsed by policy-makers such as the ACCP and have obtained FDA approval for VTE prophylaxis. Furthermore, MCD units allow patients to remain ambulatory while receiving therapy. Measured peak pressures and resultant peak venous flow rates with battery-operated units such as the Venowave were found to be equivalent to those of hospital-based PCDs. As indicated in this review, the cost of MCDs relative to pharmacotherapy allows for a more efficient allocation of national insurer spending. Moreover, the improved quality of life and expedited return to pre-surgical functional states experienced by this patient population will lead to greater and sustained benefits for the country at-large.

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