Pharmacological and Non-Pharmacological Management Methods of DVT and Pulmonary Embolism

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Abstract

Thromboembolic disease that includes deep vein thrombosis (DVT) and Pulmonary Embolism (PE) has become one of the most important challenges that face physicians and remain a significant concern of most general and orthopedic surgeons. In this study, we review all the available treatment methods that are used in prophylaxis and management of DVT. Secondly, we compare between pharmacological such as anticoagulation therapy, and non-pharmacological treatment methods such as Intermittent Pneumatic Compression (IPC) devices. Finally, we investigate the differences, if any, between some of the IPC devices that are used in management and prophylaxis of DVT.

Background

The cause of thrombosis is usually unknown but is universally attributed to Virchow’s triad: stasis, hypercoagulability, and intimal injury.

Patients with malignancy, cranio-cerebral and/or spinal injuries and patients after childbirth or after any major surgical, gynecological and orthopedic procedures are at high risk for developing DVT and eventually might develop the fatal PE.

Other risk factors for thromboembolic disease include pregnancy, immobilization, congestive heart failure, cigarette smoking, and the use of oral contraceptive. In the UK, pulmonary thromboembolism is the leading cause of maternal death. [1]

There are strong and unequivocal evidences that without prophylaxis of venous thromboembolism, the risk of DVT after orthopedic surgeries exceeds 50%. Some studies show that DVT can occur in 40 to 60 % of postoperative patients, despite primary prophylaxis. [2-7] Consequently, Pulmonary Embolism occurs in more than 600,000 patients a year in the United States and results in death in approximately one sixth of them. Other studies show that each year, approximately 5 million patients have an episode of DVT. Acute pulmonary embolism develops in 500,000 of these patients and is fatal in 50,000. [8] The magnitude of this potentially preventable problem has resulted in the development of new diagnostic methods and treatment strategies for thromboembolic disease. [9] It is estimated that PE is the third most common overall cause of death and the most common cause of preventable hospital death in the United States. [8 & 9]

The current approach to pulmonary embolism (PE) is to consider it not as a separate disease entity but rather as a complication of deep vein thrombosis (DVT). Consequently, current management strategies for pulmonary embolism have revolved around the prevention of DVT and early and accurate diagnosis once it occurs.

Diagnosis

The diagnosis of venous thromboembolic diseases, that include both DVT and PE, remain problematic. These diagnostic tests include Ventilation-Perfusion lung scans, Compression Ultrasound of the proximal leg veins, Pulmonary Arteriogram, Computed Tomography (CT scan) and Magnetic Resonance Imaging (MRI). Unfortunately, the results from most of these high tech diagnostic tests are usually inconclusive. The most important factor in establishing the diagnosis is the patients’ symptoms.

Prevention

Physicians should be encouraged to strongly consider highly aggressive prophylactic measures if the best available diagnostic tests are inconclusive, because treatment is usually safe and successful. The use of prophylactic measures in high-risk patients is not controversial, but rather an indispensable measure. Nonetheless, it is not universally practiced, even in patients without contraindications. The optimal type and duration of prophylaxis is controversial, and whether to use the pharmacological such as Heparin and Warfarin therapy, or the non-pharmacological treatment methods such as Intermittent Pneumatic
Compression (IPC) devices. The use of compression devices as early prophylaxis is warranted in patients undergoing major pelvic surgery who although at high risk for thrombosis, may [10] or may not [11] be prone to develop lymphoceles while receiving anticoagulants.

**Pharmacological Methods**

There are many clinical studies that provide various ways of pharmacological methods for prophylaxis and/or management of DVT. The challenges facing physicians is not only to identify patient at risk for thromboembolism, but also to chose the appropriate method and regimen of treatment.

Although these well-conducted studies provide strong and unequivocal evidence that pharmacological agents reduce the frequency of symptomatic venous thromboembolism, the tag price for such treatments is continuously increasing.

There are various pharmacological products in the market, but there are still a lot of questions that need to be raised and need answers.

Physicians are uncertain which is the best way to treat and/or prevent the DVT. Many doctors chose to treat DVT with anticoagulants that thin the blood and prevent clots from forming, such as Heparin. Others prefer the combination of Heparin and Streptokinase. Streptokinase is a thrombolytic enzyme that can dissolve existing blood clots, but carries a small risk of an immediately fatal intracranial hemorrhage.

Furthermore, the optimum duration of anticoagulation therapy for DVT and PE is not clear and never been adequately determined. The standard anticoagulation scheme Heparin is given for five-seven days and Warfarin therapy started on day 33. [12] Initial therapy with intravenous Heparin is usually followed by a period of oral anticoagulation with Warfarin. [13 & 14] For calf-vein thrombosis, three months anticoagulation is effective in preventing recurrence. [14] For more extensive deep-vein thrombosis (DVT) and for patients with pulmonary embolism (PE), the recommended duration of treatment varies from one to six months. [15-18]

Review of data on DVT recurrence and hemorrhage showed that four weeks’ Warfarin therapy had the best ratio of risk to benefit in treating a first episode of DVT, PE, or both. [19] If venous thromboembolism arises after surgery, four weeks of anticoagulation should be adequate. In other settings, patients with new DVT, PE, or both, who do not have a persisting underlying cause or risk factor should receive anticoagulants for three months. [20]

Treatment costs per patient for pharmacological DVT prophylaxis and complications (according to W.E. Wade, PharmD et al):

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Cost</th>
</tr>
</thead>
<tbody>
<tr>
<td>UFH</td>
<td>$24.84</td>
</tr>
<tr>
<td>LMWH</td>
<td>$132.65</td>
</tr>
<tr>
<td>Warfarin</td>
<td>$2.10</td>
</tr>
</tbody>
</table>
| Proximal vein DVT                | $2,075.00| [b]  
| Pulmonary embolism               | $6,994.35| [c]  
| Major bleed                      | $2,973.42|

[a] Seven days of therapy
[b] Includes five additional days of hospitalization, physician services, Heparin, Warfarin, diagnostic radiography, and laboratory monitoring.
[c] Includes fifteen additional days of hospitalization, physician services, Heparin, Warfarin, diagnostic radiography, and laboratory monitoring.

The expense, discomfort, limited availability, risk of reactions to most pharmacological agents, and the contraindications associated with these agents have made them less-than-ideal treating regimen for DVT and have resulted in the development of the non-pharmacological treating techniques. In addition to these factors, HMOs were looking for less expensive methods to manage the prophylaxis and treatment of DVT.

**Non-Pharmacological Methods**

To reduce the side effects of pharmacological agents and to increase the effectiveness of prophylaxis and treatment of DVT and PE, non-invasive method was introduced. The goal of this method is to achieve an augmentation of venous blood flow in lower limbs via external mechanical devices. These devices are called External Pneumatic Compression (EPC) or Intermittent Pneumatic Compression (IPC) devices. Our meta-analysis from a review of the medical literature that examined the clinical effectiveness of IPC devices clearly reveals that these devices are effective in reducing the incidence of DVT.

There are two types of IPC: Pneumatic Compression Devices (PCD) such as VasoPress® and Sequential Compression Devices (SCD) such as Kendall SCD. Both systems use an intermittent regimen
that delivers a sustained pressure in distal to proximal manner. The only difference between the two devices is that the compartments in PCD devices are uniformly inflated to the same pressure rather than in a graded-sequential fashion as in SCD devices.

The first medical article on IPC devices was published in 1971. [21] In 1989, the Department of Surgery at St. Elizabeth Health Center made recommendations regarding the venous thromboembolism prophylaxis. They recommended that one of the prophylactic treatments that should be available was the Sequential Compression Device (SCD). Clinical studies that evaluated different intermittent pneumatic compression (IPC) devices showed that there is no convincing evidence that the SCD were more effective than the PCD. [21, 22] Furthermore, these studies showed that both nurses and patients seemed to prefer the PCD over the SCD devices because of their convenience. On the other hand, physicians prefer PCDs over SCDs because of their results and cost-effectiveness. In 1994, due to these results and in an attempt to minimize hospitals’ costs, most hospitals made the conversion to the PCDs. In 1996, in another effort to further reduce hospitals’ costs, the idea of converting from the thigh-high to the exclusive use of knee-high (calf) sleeves was suggested.

**Physiological effects of IPC devices**

IPC devices consist of a lightweight pump and garments (sleeves) that are manufactured from a combination of foam/fabric or plastic with non-woven liners or a combination thereof. These garments are designed to be wrapped around and easily conform to the lower extremity and secured with Velcro®. Depending upon the style chosen, a garment can be a calf or thigh length. The garment(s) are then connected to a pump that intermittently inflates and deflates bladders contained within the garment. Cycle times vary from manufacturer to manufacturer. Typically, the inflation (compression) cycle is 10-15 seconds with a 45-50 second relaxation (rest) before the subsequent inflation occurs. The pumps run continuously and some inflate both lower extremities simultaneously, while others alternate between the left and right lower limbs. By using a timing sequence of compression and relaxation on lower limbs, venous blood flow is augmented. This augmentation of the venous blood flow is regarded as an important therapy for the prevention of DVT.


In addition to the local effects via augmenting venous blood flow that decreases venous stasis, IPC devices also have general (systemic) effects via increasing the systemic fibrinolysis and via the release of endothelium-derived Nitric Oxide (NO) that plays important role in vascular homeostasis. Usually, trauma or any surgical procedure decreases fibrinolysis and cause vasoconstriction, and eventually will make patients more susceptible to venous thromboembolism. Several studies showed that venous compression secondary to IPC results in the release of plasminogen (natural anticoagulant) and Nitric Oxide (vasodilator) into the blood stream from the endothelial layer of the vein wall that increase the fibrinolysis and reduce the stasis, which may account for the systemic effects seen with IPC.

**Conclusions**

This study has significant clinical ramifications for any practicing physician who treats patients susceptible to DVT.

Thromboembolic disease results in significant morbidity and mortality and appropriate patient risk assessment and proper use of prophylactic measures is crucial. DVT cases are on the rise but they can be significantly reduced by the use of appropriate prophylactic measures. It is very important to understand that post traumatic and/or post surgical DVT and PE remain a significant concern of most physicians regardless of their specialties.

There are various approaches in prophylaxis and management of DVT and PE that includes both pharmacological and non-pharmacological methods. Subcutaneous heparin (unfractionated or fractionated) may be the most effective means of prophylaxis. However, neurological injuries and major bleeding often preclude its use due to the increased risk of hemorrhagic complications. [22] IPC devices are excellent alternative methods for DVT and PE prophylaxis in such cases. IPC devices can be compared favorably with the other prophylactic and treatment methods and are equivalent or in some cases better than pharmacological agents. A comparison study as well as our own case study had unequivocally proven that PCDs such as VasoPress® device are better in performance and more cost-efficient than SCD in DVT and PE prophylaxis.
References


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