ARJOHUNTLEIGH

The importance of deep vein thrombosis prophylaxis in hospitalised cancer patients

Cancer is frequently associated with venous thromboembolism (VTE), a phenomenon first described by Trousseau in 1865 (Trousseau syndrome)[1]. VTE is a complex vascular disease with a multifactorial pathogenesis that results in two major clinical manifestations[2]. The first and more common is deep vein thrombosis (DVT), where one or more clots (thrombi) develop most commonly in the deep veins of the calf, thigh and pelvis. The second and more serious condition is pulmonary embolism (PE) that results if part of or all of the thrombus in the limb breaks off and enters the pulmonary arterial circulation occluding blood flow in the lungs. Thromboembolic events may be presenting symptoms of occult cancer and are also a marker of increased ongoing VTE risk in those with established malignancies[3]. Despite advances in VTE prophylaxis, fatal PE remains a leading cause of additional morbidity and premature death for those with cancer[4].

What is the magnitude of the problem?

A recent review[5] identified that patients with cancer have more than a 6 fold increased risk of VTE compared to those without cancer and 20% of new VTE events occurring in the community can be attributed to those with active malignancies. The risk of VTE varies according to the origin and stage of the tumour as well as the presence of additional risk factors. High VTE rates have been identified for adenocarcinoma of the lung, ovary, pancreas, colon, stomach, prostate and kidneys, malignant brain tumours and haematological cancers[5].

Those undergoing surgery for cancer have twice the risk of post-operative DVT and three times the risk of fatal PE compared to similar surgery undertaken for non-malignant conditions[5]. Studies have also demonstrated that cancer is an independent predictor of VTE prophylaxis failure whereby, despite usage of prophylaxis the patient still develops a VTE[5].

Although there is strong evidence to support routine thromboprophylaxis for hospitalised patients with cancer, it still remains underused. This was illustrated in a multi-national cross sectional survey[6] where chart audit of VTE prophylaxis occurred for more than 68,000 patients in 358 hospitals across 32 countries. The use of VTE prophylaxis was particularly poor for those medical patients with active malignancy where only 37% deemed to be at risk of VTE received a recommended form of prophylaxis[6].

Why is the cancer patient at risk of VTE?

Patients with cancer have a significantly increased risk of VTE due to tumour cells interacting with various haemostatic components, including the coagulation and fibrinolytic systems, the vascular endothelium, leukocytes, and platelets[7]. Tumour cells can directly activate the coagulation cascade by producing their own procoagulant factors, or they can stimulate the prothrombotic properties of other blood cell components[7,8]. Abnormalities of coagulation in terms of both clinical and laboratory findings, have been found to accompany up to 90% of all metastatic cancers[1]. The pro-coagulant state that accompanies cancer can result in a wide spectrum of manifestations ranging from an asymptomatic condition characterised by abnormal blood coagulation tests to a massive PE where the patient may die[8].

The most common clinical presentation of VTE is DVT of the lower limbs, however other manifestations may include DVT of upper limbs, PE, migratory superficial thrombophlebitis and disseminated intravascular coagulation[5]. Various cancer treatments including chemotherapy, radiotherapy, presence of central and peripheral venous catheters and surgery increase the thrombotic risk further[9]. Additionally this patient group is also often affected by reduced mobility due to effects of the disease or treatment increasing the likelihood of venous stasis.

Prophylaxis

Cancer related coagulopathy is thought to alter all 3 aspects of Virchow's triad[1] abnormal blood constituents, abnormal vessel wall and abnormal flow; this is particularly so for cancer patients undergoing surgery and as such aggressive thromboprophylaxis is recommended[5]. Prophylactic treatments aim to improve venous flow and/ or reduce blood coagulability[10].

Evidence based guidelines recommend that cancer patients undergoing surgical procedures receive routine prophylaxis that is appropriate for that type of surgery[5,9]. Similarly for those medical cancer patients, routine prophylaxis is recommended as for other high-risk medical patients. A recent Cochrane review[11], has highlighted that the combined modalities of intermittent pneumatic compression (IPC) and anticoagulant work synergistically and are more effective in reducing incidence of VTE than use of single methods alone in high risk patient groups. It is suggested that this is attributed to the fact that both modalities offer different mechanisms of action; IPC promotes active flow enhancement and increases levels of tissue factor pathway inhibitor. Unfractionated and low molecular weight heparin inhibit Factor X.

There are considerable numbers of patients who are not able to utilise anticoagulant therapies due to either active bleeding or high bleeding risk[5]. This figure equates to 10% of at risk medical patients and 9% of at risk surgical patient[6]. In such circumstances, guidelines and consensus papers recommend mechanical thromboprophylaxis as the optimal method[5,9].

MECHANICAL AND BIOCHEMICAL EFFECTS OF FLOWTRON® DVT PROPHYLAXIS SYSTEMS:

Prevention of venous stasis:

The *Flowtron* DVT Prophylaxis System prevents venous stasis by active augmentation of blood flow[12,13,14]. This reduces stasis, flushes valve pockets where thrombi originate, decreases venous hypertension and decreases interstitial oedema[15].

Increases fibrinolytic activity:

Use of *Flowtron* DVT Prophylaxis Systems results in an increase in the fibrinolytic activity of the blood[14] and suppression of procoagulant factors[16].

A recent comparative evaluation of 8 different types of IPC device from 4 different manufacturers[17] commonly used in the US identified the ArjoHuntleigh *Flowtron* Universal System as the best unit overall with excellent safety and ease of use features.

CONCLUSION

VTE is a common complication of patients with cancer in both medical and surgical specialities and is associated with increased morbidity and mortality, high recurrence rates and amplified costs. It is important to reduce the burden of VTE based disease in this patient group.

Evidence based guidelines strongly recommend the use of aggressive thromboprophylaxis with combination IPC and anticoagulant therapy for high risk patients. In those patients for whom anticoagulant prophylaxis is contraindicated or not tolerated, use of *Flowtron* DVT prophylaxis provides a safe and effective alternative method of VTE prophylaxis.

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