



Thromboprophylaxis in cancer patients in palliative care setting

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Background: The prevalence of venous thromboembolism (VTE) is high in oncologic patients and can lead to a lower quality of life or result in a fatal event. There are no guidelines for the use of thromboprophylaxis in these patients under palliative care and its use is controversial. In one side there is the prevention of symptoms and death, and in the other side iatrogeny, discomfort and prolongation of life.

Methods: Retrospective, unicenter, descriptive study, based on medical records of hospitalizations during 6 months at the Palliative Care Unit of Instituto Português de Oncologia do Porto.

Results: Five hundred and six hospitalizations were enrolled in the study. The mean age of patients was 67.2 years (SD \pm 12.7) and 48% were women. More than a third of patients (37%) were admitted at the Palliative Care Unit in the terminal phase of their disease. Previously, 13.8% of the patients were on thromboprophylaxis. At the Palliative Care Unit 6.7% of the patients received prophylactic anticoagulation. Considering the population of terminal patients, 15% received anticoagulation: 9% in therapeutic dosage and 6% in prophylactic dosage. Half of them suspended anticoagulation. The anticoagulant most frequently used was low molecular weight heparin. The incidence of VTE was 1% (0.6% with imaging confirmation) and in 0.2% of the cases VTE was associated with inpatient mortality.

Conclusions: Thromboprophylaxis is not routinely used in this Palliative Care Unit. Still, some terminal patients received prophylactic anticoagulation. The incidence of VTE in this population was quite low and it doesn't seem to have an important impact on inpatient mortality. Given the absence of guidelines about the use of thromboprophylaxis in the palliative care setting, it should be a shared decision with the patient and his family. The establishment of evidence-based guidelines for thromboprophylaxis in oncologic patients under palliative care is imperative.

Keywords: Anticoagulation; oncology; palliative care; thromboprophylaxis; venous thromboembolism (VTE)

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Introduction

The prevalence of venous thromboembolism (VTE) is high in oncologic patients and can lead to a lower quality of life or result in a fatal event. This population presents an imbalance between coagulation and the fibrinolytic system developing a procoagulation state (1). It is estimated that the frequency of thromboembolic events in cancer patients is between 4–20%, though it could be underestimated. A series of autopsies showed a prevalence of 50% (2). VTE in cancer patients is associated with an increased mortality (3).

This population presents several risk factors for VTE: history of previous VTE, immobility, inflammation and cancer, that constitute indications for prophylaxis outside

the palliative care setting (4).

There is an increased risk for VTE in hospitalized patients with more advanced cancer stages (5). However, cancer patients have a 2.2-fold risk of major bleeding (6).

Meta-analyses suggest that even in patients without VTE low-molecular-weight heparine (LMWH) can reduce the risk of death in 8% of cancer patients (7). A prospective randomised study enrolled in a Palliative Care Unit with 20 patients didn't show a clear benefit for the administration of prophylactic LMWH (8). The discontinuation of thromboprophylaxis in the end-of-life care wasn't associated with a significant increase in the incidence of symptomatic VTE (9).

Besides, the occurrence of thrombosis may justify a hospitalization or prolong the length of stay, increasing the costs (1).

There are no guidelines for the use of thromboprophylaxis in these patients under palliative care and its use is controversial. Yet, palliative care teams have started to pay more attention to this issue and are more inclined to offer prophylaxis (4).

The ethical principle of non-maleficence seems to be the base for the absence of thromboprophylaxis with heparine in palliative care since some doctors believe that they are affecting negatively the quality of life of their patients (10). Thromboprophylaxis is also seen as a mean for prolongation of life, instead of a mean for the prevention of adverse events. Deaths from pulmonary embolism are in general symptomatic and not sudden and symptom control is difficult because of cardiovascular collapse and diminished perfusion (11). In studies enrolled in Palliative Care Units the subcutaneous administration of LMWH caused minimal distress or inconvenience (2,12).

This issue is an ethical dilemma: on the one hand there are prevention of symptoms and death, and on the other hand there are iatrogeny, discomfort and prolongation of life.

Methods

A retrospective, unicenter, descriptive study was performed, based on medical records of hospitalizations during 6 months (from September 2015 to February 2016) at the Palliative Care Unit of Instituto Português de Oncologia do Porto. This study pretends to describe the clinical use of thromboprophylaxis in oncologic patients in a Portuguese Palliative Care Unit; to determine the prevalence of VTE in this Palliative Care Unit and its impact on inpatient mortality.

The protocol for the research project was approved by the Ethics Committee of Instituto Português de Oncologia do Porto. Patient's personal data were secured.

Patient's hospital medical records without information about diagnosis and treatment during hospitalization were excluded.

Results

Five hundred and six hospitalizations were enrolled in the study. The mean age of patients was 67.2 years (SD \pm 12.7)

and 48% were women.

A great percentage of patients had stage IV (91.7%) solid tumors (96.8%). Almost 16% of patients received no antineoplastic treatment. Almost two thirds of patients were totally dependent and more than a third of patients (37%) were admitted at the Palliative Care Unit in the terminal phase of their disease.

Previously, 29% used anticoagulants and 13.8% of the patients were on thromboprophylaxis. The reasons for anticoagulation were: previous pulmonary embolism (3.6%), deep venous thrombosis (8.1%), pulmonary embolism and deep venous thrombosis (0.4%), cardiovascular disease (2.8%), superficial venous thrombosis (0.4%).

The anticoagulant most frequently used in Palliative Care Unit was LMWH.

At the Palliative Care Unit, 6.7% of the patients received prophylactic anticoagulation and 10.7% were on therapeutic dosage. Half of them suspended anticoagulation during hospitalization mainly because of clinical worsening (4.5%). The incidence of hemorrhage and thrombocytopenia was 1.8% and 0.2% respectively. No major bleeding was recorded.

Considering the patients admitted in terminal stage, anticoagulation was provided in 15%: 9% in therapeutic dosage and 6% in prophylactic dosage.

The incidence of VTE was 1%: 0.2% of pulmonary embolism and 0.8% of deep venous thrombosis. None of them was under anticoagulation. Signs and symptoms associated with VTE were: pain (0.6%), edema (0.4%) and dyspnoea (0.2%). Only 0.6% had imaging confirmation. In 0.2% of the cases VTE was associated with inpatient mortality.

In general, almost 8% of patients that died received anticoagulation until the time of death.

Discussion

Literature review shows a growing interest concerning the prophylaxis of thromboembolic events mainly in the advanced stages of disease where opinions diverge.

Thromboprophylaxis is not routinely used in this Palliative Care Unit (only 6.7%). Although this is the largest unit in Portugal, it may not be representative of the national clinical practice. The great majority of patients (82.6%) didn't receive any anticoagulant during hospitalization. Note that almost 14% of patients admitted in this PCU were under prophylactic anticoagulation, showing the practice of

some medical departments in this area.

Anticoagulation was considered safe since no major events were recorded. Clinical worsening was the reason for the suspension of anticoagulation in more than a half of the patients, showing that for some doctors this measure is considered futile in the last days of life. In the other hand, some terminal patients received prophylactic anticoagulation. This fact exalts the ambivalence between health professionals concerning thromboprophylaxis.

The incidence of VTE in this population was quite low and it doesn't seem to have an important impact on inpatient mortality. Still, we consider that the incidence of VTE was underestimated. In palliative care setting imaging exams for diagnosis are not commonly requested (0.6% in this study) and some signs and symptoms presented at the time of death might be due to a thromboembolic event.

We consider that in the terminal phase, it is more important the symptoms control than the prevention of events.

This study has limitations since it is a retrospective study based on medical records. Taking into account that the dosage of anticoagulation is dependent of renal function and in the majority of patients it was not accessed, some may have been under therapeutic/supratherapeutic dosage.

Given the absence of guidelines about the use of thromboprophylaxis in the palliative care setting, it should be a shared decision with the patient and his family. All the risks and benefits should be communicated and explained and an informed and free consent should be obtained.

Palliative care patients are a peculiar population and the extrapolation of data from other areas sometimes is not consistent with the philosophy of Palliative Medicine. The establishment of evidence-based guidelines for thromboprophylaxis in oncologic patients under palliative care is imperative.

A pharmaco-economic analysis of the cost implications is also needed (13). The author considers that the indiscriminate use of thromboprophylaxis would not be cost-effective.

Nevertheless, the initiation of thromboprophylaxis in palliative care setting does not preclude its suspension, since it is part of a therapeutic plan in constant revision.

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Footnote

Conflicts of Interest: The author has no conflicts of interest to declare.

Ethical Statement: The study was approved by the Ethics Committee of Instituto Português de Oncologia do Porto.

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