RESEARCH

UK practice in the prevention of central venous catheter-associated thrombosis in adults on home parenteral nutrition

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ABSTRACT

Background Maintaining central access is imperative for the delivery of home parenteral nutrition (HPN) in those with intestinal failure. Methods to reduce central venous catheter infection are well recognised; however, the prevention of line thrombosis is less well studied.

Methods This paper reviews the current evidence and reports a survey of current practice within the UK. Using an electronic survey, respondents were asked to detail their use of anticoagulation in different patient groups and the type of anticoagulation used.

Results 41 replies were received from 31 centres. Only one responder used low-dose warfarin routinely; 80% however anticoagulated those with a previous line thrombosis and 65% anticoagulated those that had any deep vein thrombosis or pulmonary embolus. The most commonly used anticoagulant was dose-adjusted warfarin aiming for an international normalised ratio of 2–3.

Conclusions The evidence from the current literature in both HPN and the wider field is that there is no clear evidence that anticoagulation is either beneficial or harmful in the prevention of line thrombosis. This survey suggested that practice is varied across the UK likely reflecting the lack of evidence within the current literature.

INTRODUCTION

Intestinal failure is characterised as the inability to maintain protein energy, fluid, electrolyte or micronutrient balance and can have multiple causes, including extensive resection, dysmotility, obstruction or malabsorption.[1] Intestinal failure is a spectrum and can span from a temporary condition to an irreversible state. It has been classified into three types. Type I failure is acute, short term and usually self-limiting; type II failure is used to describe those that normally have had an acute insult but continue to have intestinal failure for over 28 days. This can last weeks to months but eventually resolves, whereas type III is a chronic condition in which patients require intravenous supplementation, delivered at home, for months to years, this can be a reversible or irreversible condition.[2] Those with irreversible intestinal failure are destined to remain on home parenteral nutrition (HPN) lifelong or be referred for intestinal transplantation.[3] For the majority of these patients, HPN therefore remains the mainstay of treatment. To deliver HPN, patients require central venous access as peripheral access can limit the delivery of feed. Maintaining central access is imperative to deliver HPN. Access can be complicated by line infections, occlusion of the catheter or line thrombosis. Infection rates have already been shown to improve with dedicated nutrition support teams[4] and patient education.[5] This article concentrates on possible strategies to reduce line thrombosis events.

RATES OF CENTRAL VENOUS CATHETER-ASSOCIATED THROMBOSIS

Central venous catheter (CVC)-associated thrombosis is defined as mural thrombosis extending from the catheter into the lumen of the vessel and leading to partial or total catheter occlusion with or without clinical symptoms.[6] If patients have an episode of line-associated

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thrombosis, this may lead to interruption in the delivery of their HPN and may require an inpatient hospital stay. Recurrent line thrombosis can become a major barrier to delivering HPN. Loss of vascular access is one of the prime indicators for consideration of small bowel transplantation.[7] Rates of CVC-associated thrombosis vary and can be symptomatic or asymptomatic with rates of symptomatic thrombosis reported at 0%–28% and asymptomatic at 12%–66%.[6] A Spanish study[8] found in a retrospective review of 46 patients that thrombotic events were low at $0.115/10^3$ HPN days. They do however comment that 22% of patients were on anticoagulation due to previous pulmonary embolus or thrombosis and so this may be an underestimate.

RISK FACTORS FOR CVC-ASSOCIATED THROMBOSIS

It is accepted that mechanical factors associated with the catheter itself can reduce the risk of thrombosis. The position of the catheter tip should be between the lower third of the vena cava and the upper third of the right atrium due to reduced turbulence.[9] There is also evidence that lines sited in the femoral region are prone to increased infection rates and increased thrombosis risk.[9]

The use of anticoagulation agents to reduce CVC-associated thrombosis is, however, a more contentious issue. ESPEN Guidelines on Parenteral Nutrition: Central Venous Catheters[9] state 'the decision to start prophylaxis against venous thromboembolic events in patients with CVCs…remains unsupported by evidence even in those with underlying malignancy'. They do however go on to state that prophylaxis with low-molecular-weight heparin (LMWH) in certain groups may be reasonable but do not specify which patient groups.

USE OF ANTICOAGULATION IN HPN

Studies of the use of anticoagulant drugs to prevent CVC-associated thrombosis in patients on HPN are either small or observational. Veerabagu *et al*[10] studied the effect of low-dose warfarin (1–2 mg/day) compared with therapeutic warfarin in a retrospective review. They found no significant difference between the two groups. However, when patients who had thrombotic events were converted to therapeutic warfarin, there was a significant decrease in thrombotic events. However, non-fatal haemorrhagic complications occurred in those on therapeutic warfarin (four episodes in 619 patient-months) compared with no haemorrhagic incidents in those on low-dose warfarin.

USE OF ANTICOAGULATION IN PATIENTS WITH CANCER

The use of anticoagulants to reduce the risk of CVC-associated thrombosis has been studied to a greater extent in patients with cancer. Guidelines from 2008 published by a working group from the French National Federation of Cancer Centres[6] reviewed the results of studies that consider the use of warfarin and LMWH. They reviewed both meta-analyses and randomised controlled studies. In terms of warfarin study, results varied, a single study had reported the benefit of low-dose warfarin (1 mg/kg) but this was not replicated on other studies reviewed. There was some evidence that if an international normalised ratio (INR) was maintained between 1.5 and 2, there was a lower risk of thrombosis. They reported that studies of the benefit of prophylactic LMWH had very mixed results with two reporting a benefit compared with no treatment; however, three larger placebo-controlled studies showed no benefit. The group concludes that the use of anticoagulant drugs in primary prevention of CVC-associated thrombosis in patients with cancer is not recommended.

In 2014, an updated Cochrane review[11] was performed; this assessed the risk of CVC-associated thrombosis in patients with cancer. They concluded that the use of prophylactic LMWH did appear to reduce asymptomatic DVT but had no effect on mortality. Comparing warfarin with LMWH, there was increased asymptomatic DVT with LMWH, but no beneficial or detrimental effect of warfarin over LMWH when considering symptomatic DVT or mortality. They conclude however that although the level of evidence on which to draw conclusions in patients with cancer is low, there may be some benefit of anticoagulation.

HAEMATOLOGY GUIDELINES

The British Care Standards for Haematology (BCSH) produced guidelines for the insertion and management of central venous access devices in 2007[5] in all patient groups. There is no documented evidence that heparin flushes are of any benefit over saline flushes. The efficacy of heparin flushes remains uncertain and carries a risk of heparin-induced thrombocytopaenia and risk of bleeding due to inadvertent heparinisation secondary to multiple heparin flushes. The guidelines do however state that many manufacturers recommend heparin flushes for their devices.

In the use of anticoagulation, BCSH state that low-dose warfarin is contraindicated as it carries no benefit for the reduction of symptomatic catheter thrombosis. Dose-adjusted warfarin may be of benefit but needs to be balanced with increased bleeding risk. In documented cases of line thrombus, the BCSH suggest using warfarin, if patient factors allow, aiming for INR of 2–3 for 3 months duration. This should only be continued if there is clinical or radiological evidence of persistent thrombus.

More recently, the BCSH have produced guidelines on all aspects of thrombosis in patients with cancer.[12] With regard to catheter-associated thrombosis, they

conclude that there is no evidence to support the routine use of either prophylactic or therapeutic dose anticoagulants for the prevention of catheter-associated thrombus.

CURRENT UK PRACTICE IN PATIENTS ON LONG-TERM HPN

To determine current UK practice in adult patients receiving HPN, we conducted a survey of UK centres regarding line thrombosis prevention techniques.

METHODS

A questionnaire survey was administered via SurveyMonkey. An email detailing the study and containing a link to the survey was sent to all those on the British Intestinal Failure Association mailing list. After 3 weeks, a reminder email was sent to the same email list. The survey remained open for 6 weeks in total commencing on April 2013. Hospital and number of patients on HPN were recorded, along with the use of routine anticoagulation. If not used routinely, respondents were asked whether they would use it in a list of specific patient groups. Type of anticoagulation was recorded, whether any products were given through the line to try and prevent thrombus formation and whether centres had a written protocol.

RESULTS

Forty-one replies were received over the 6-week period. These included respondents from 31 centres. As we wanted to ascertain practice in adults, we excluded replies from paediatric centres. On initial review of the data, respondents from the same centre did not necessarily respond identically. Given this discrepancy, we opted to analyse data by respondent rather than by centre, 34 replies were therefore analysed. These centres collectively looked after adult patients receiving HPN. Only one respondent recommended routine anticoagulation, this was given as low-dose warfarin at 1–2 mg/day. Only 38% of respondents stated that their unit had a written protocol.

Use of anticoagulation in specific patient groups is recorded in table 1. The group most likely to be given anticoagulation was that which had a previous line thrombosis; 80% in this group stated that they would routinely use anticoagulation. Sixty-five per cent would anticoagulate those that had any previous deep vein thrombosis or pulmonary embolism. The type of anticoagulation used varied and several participants stated that this might vary even in patients with the same risks factors depending on concerns regarding malabsorption of oral products. The most common choice of anticoagulant was dose-adjusted warfarin aiming for an INR in a therapeutic range. Five respondents used low-dose warfarin and two used only LMWH. Thirteen (37%) respondents used a line agent, 12 used low-dose heparin with saline and 1 urokinase. In those with a previous mesenteric infarct as a cause for HPN, respondents were split evenly as to whether anticoagulation was recommended.

Table 1 Use of anticoagulation in adult patients on home parenteral nutrition

Patient group	Anticoagulation used (%)	Anticoagulation not used (%)
Previous DVT/PE	22 (65)	12 (35)
Previous line thrombosis	24 (80)	10 (20)
Family history VTE	2 (6)	32 (94)
Crohn's disease	2 (6)	32 (94)
Malignancy	2 (6)	32 (94)
Smoker	0	34 (100)
Mesenteric infarct	17 (50)	17 (50)

CONCLUSION

Current literature in both HPN and the wider field suggests that there is no clear evidence that anticoagulation is either beneficial or harmful in the prevention of line thrombosis. However, studies specific to the HPN population are limited. A Cochrane review of CVCs in patients with cancer[11] found that there may be a reduction in thrombosis; however, patients with malignancy have a four to sixfold increase in thrombosis due to the nature of malignancy. More recent guidelines from the British Haematology Advisory group do not recommend anticoagulation in this patient group.[12] In all fields, it is accepted that tip position reduces the risk of thrombotic events and good line care is imperative to reduce rates of line sepsis which can be associated with or complicated by thrombotic events.

A survey of those looking after HPN patients in the UK has shown a variable approach to CVC-associated thrombosis prevention. In keeping with ESPEN guidelines, the vast majority of respondents did not use low-dose warfarin as prophylaxis, although one respondent still adopted this practice. Many respondents however opted for anticoagulation in certain patient groups. Eighty per cent of respondents stated that they would use anticoagulation for those who had previous CVC-associated thrombotic events. The BCSH 2007 guidelines[5] state that symptomatic CVC-associated thrombus should be treated for 3 months either with dose-adjusted warfarin or with therapeutic LMWH. It is unclear, however, whether this takes into account the long-term nature of the need for CVC in HPN patients and whether advice would alter given this context. Differences in opinion as to whether to anticoagulate those who had a mesenteric infarct may relate to the lack of clarity in the question and whether treating the possible cause of the infarct as opposed to reduction in risk of line thrombosis.

In this survey, not only did practice differ from unit to unit but also responses differed between

respondents from the same unit. This reflects that this is clearly an area of uncertainty, most units did not have written protocols. Further research is required to define which patients groups, if any, would benefit from anticoagulation and the optimal regimen to be used, including in those who are unable to absorb oral medications. In the meantime, our unit opts to anticoagulate those that have had a previous line thrombosis and continue to require a CVC. Warfarin is used in the first instance but switched to LMWH in those in which a stable INR cannot be achieved.

Significant of this study

What is already known on this topic?

- Central access is essential for the delivery of home parenteral nutrition; recurrent line thrombosis can become a barrier to its delivery.
- The position of the central venous catheter can reduce the risk of thrombosis but the use of anticoagulants is unclear.

What this study adds?

- This paper reports a survey of UK practice which demonstrates that the use of anticoagulants to try and prevent line thrombosis is variable although is being used in some centres if there is a perceived risk factor, such as a previous thrombotic event.

How might it impact on clinical practice in the foreseeable future?

- There is a need for further research in this area, particularly whether patients in high-risk groups may benefit from anticoagulation.

Contributors NPT conceived the idea for the study with input from all authors. All authors contributed to the literature review. LM collected and analysed the data and wrote the initial draft; all authors then extensively reviewed and revised this draft.

Competing interests None declared.

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