Audit of anticoagulation after embolectomy for acute ischaemia

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ABSTRACT

INTRODUCTION Intravenous unfractionated heparin (UFH) is routinely used in patients after arterial embolectomy. Achieving and maintaining therapeutic levels requires a co-ordinated approach which may be difficult for busy junior doctors and laboratories. There is no current evidence regarding the use of subcutaneous low molecular weight heparin (LMWH) as an alternative.

PATIENTS AND METHODS The study retrospectively examined all patients who had undergone any form of embolectomy during 2006 and 2007 by review of their medical records, an electronic laboratory database, and the patients' drug charts.

RESULTS Overall, 45 patients were studied. A total of 389 activated partial thromboplastin time (APTT) tests were performed of which 146 (37.6%) were in the therapeutic range (50–90 s), 40.4% were < 50 s and 22.1% were > 90 s. Five patients (11.1%) had further surgical procedures. Significant bleeding occurred in two patients.

CONCLUSIONS The results indicate that many patients are not appropriately anticoagulated. Whilst a new UFH protocol is being developed by our hospital trust, the authors believe the use of LMWH could provide a more effective and user-friendly alternative to UFH.

KEYWORDS

Arterial embolus – Heparin – Anticoagulation

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Currently, the combination of heparin anticoagulation and surgical removal of emboli lodged in the larger arteries is effective and accepted practice in acute limb ischaemia due to peripheral embolisation.¹ Although there is no evidence showing any benefit to heparinisation, the aim is to maintain patency in the re-opened artery and to prevent further embolisation prior to long-term anticoagulation with a vitamin K antagonist. Whilst low molecular weight heparin (LMWH) has replaced unfractionated heparin (UFH) in many medical specialities for treatment of venous embolic disease, myocardial infarction, cerebrovascular accidents, as well as thromboprophylaxis,^{2–7} its use remains limited in vascular surgery.

Compared with UFH, LMWH preparations have a longer plasma half-life, less interindividual variability in anticoagulant response to fixed doses, and, in animal models, a more favourable antithrombotic to haemorrhagic ratio.^{8,9} As a result of their pharmacokinetic properties, a stable and sustained anticoagulant effect is achieved when LMWHs are administered subcutaneously, once or twice daily, without laboratory monitoring.¹⁰ The main precaution in using LMWH is that doses may have to be adjusted in patients

with renal failure (defined as creatinine clearance < 30 ml/min).⁹

In a surgical environment, the continued use of UFH is due to the need for rapid restoration of coagulation should a return to the operating theatre be necessary. The plasma half-life of UFH is around 45–60 min whilst that of LMWH is between 3–6 h post subcutaneous injection.^{11,12} In addition to this, LMWH can only partially be reversed by protamine.¹³

The aim of this retrospective study was to audit the use of UFH in patients undergoing arterial embolectomy in regards to: (i) accuracy of anticoagulation; (ii) complications secondary to treatment with heparin; and (iii) need for urgent return to theatre.

Patients and Methods

A departmental database was used to identify patients who had undergone any form of embolectomy between 1 January 2006 and 31 December 2007 at the John Radcliffe Hospital, Oxford, UK. This is a teaching hospital and regional referral centre for vascular surgery. The medical records of the patients, an electronic laboratory database, and the

Table 1 Vascular Unit Protocol for the use of intravenous unfractionated heparin

When starting the patient on heparin, a bolus of 5000 U is given and a rate of 2000 U/h started

APTT result (s)	Bolus	Rate change (units of intravenous heparin)
< 40	2500 U	Increase by 200 U/h
40–50	No	Increase by 200 U/h
50–70	No	Increase by 100 U/h
70–90	No	None
90–120	No	Decrease by 100 U/h
> 120	No	Turn off for 2 h and then decrease rate by 200 U/h

patients' drug charts were used to gather information on activated partial thromboplastin time (APTT) results as well as causes and complications of their embolectomies and return to theatre.

Management regarding the use of intravenous UFH was according to current departmental protocol (Table 1). This entails adjustment of dosage levels according to APTT results checked 4 h after the start of the infusion or after any change in rate, with a target APTT of 70–90. However, a broader range of target APTT of 50–90 was deemed acceptable anticoagulation with the current laboratory reagent (plateletin LS) and machine (MDA-180) for the purposes of this study. An APTT of 50–90 s corresponds to 0.35–0.7 anti-Xa U/ml which is the therapeutic range.¹⁰ Data were, therefore, collected into groups looking at whether the APTT time was less than 50 s, between 50–70 s, between 70–90 s, or over 90 s.

Results

Forty-eight patients underwent arterial embolectomy between January 2006 and December 2007. Three sets of notes could not be found, leaving 45 patients for analysis.

Management of intravenous unfractionated heparin

Thirty-six patients (80%) were placed on UFH with the median infusion time being 96 h (range, 21.5–401 h). There were 389 APTT results available for analysis with the median number of tests per patient being 10 (range, 2–48) and the average time between APTT tests for all the patients being 9.75 h. There was no clear documentation in the nine (20%) patients who were not placed on UFH as to why this decision had been taken.

Table 2 APTT results of the patients in the study

	APTT results (s)	Number of test results (percentage of total)
Therapeutic range	< 50	157 (40.4)
	50–70	89 (22.9)
	70–90	57 (14.7)
	> 90	86 (22.1)
Total		389

The majority of patients were not sufficiently anticoagulated for 40% of the time that they remained on heparin (Table 2). Overall, patients were only in therapeutic APTT ranges for 37.6% of the time according to the laboratory reagents (50–90 s) and 14.7% of the time for the vascular surgical protocol (70–90 s).

Time taken to achieve anticoagulation in the 36 patients on intravenous UFH was also analysed. The median time to achieve a therapeutic APTT (of at least 50 s) was 12.5 h (range, 1–79 h). Nevertheless, 16 patients (44.4%) had APTT results over 90 s as their first therapeutic APTT result – higher than the therapeutic range and indicating a rapid overshoot in anticoagulation. The total number of low (< 50 s) APTT results prior to either the first desired (APTT 50–90 s) or over anticoagulated (APTT > 90 s) was 72 (45.9% of all the APTT results < 50 s).

Re-interventions and complications of treatment

Five (9%) patients had surgical re-intervention, all of whom had been on UFH. One patient had an amputation of his limb, three patients had repeat embolectomies, and one patient had to return to control bleeding from the operation site. In none of these cases was the limb so acutely ischaemic, or bleeding so profusely, that return to theatre required reversal of the anticoagulant effects of heparin with protamine. The notes indicated that the interval between decision to operate (when heparin infusion was stopped) and return to theatre was between 8 h and 2 days.

Of the 36 patients who were placed on UFH postoperatively, six developed bleeding complications (four small haematomas, one returned to theatre with bleeding, and one upper gastrointestinal bleed), four had further emboli, and one had a cerebrovascular accident of uncertain aetiology and subsequently died. Of the bleeding patients there was no relationship between bleeding and high APTT results. Of those with further emboli, 52.5% of the APTT indicated inadequate anticoagulation (APTT < 50 s) whilst on UFH, compared to 42% APTT results in patients overall in the study. This difference was not statistically significant

($P = 0.20$ using a Student's t -test). Of the nine patients not started on UFH, one had to return to theatre for a repeat embolectomy and one patient subsequently had an amputation of their limb.

Thus, overall, there were two patients (4%) with significant bleeding problems and five (11%) with ischaemic problems in the postoperative period.

Discussion

This small study documenting vascular surgical practice in a regional vascular centre in the UK has raised several issues.

First, it shows that the management of anticoagulation with UFH is difficult. This is demonstrated by the variation of the APTT results in the study, the fact that therapeutic anticoagulation (APTT 50–90 s) was only present in 36.7% of samples and that 44.4% of patients had APTT results > 90 s quickly after starting UFH. In addition, in some patients there was a long delay in the APTT measurements becoming therapeutic (range, 1–79 h). Whilst the size of the study precludes a statistical analysis, this potentially leads to increased complications from both under- and over-anticoagulation.

Second, it is not clear why only 36 of the 45 patients were placed on UFH after their initial operation; there was no documentation as to whether there was a clear contra-indication for using UFH (for example, peptic ulceration). Current standards of practice recommend that all patients should be heparinised.¹ Of the nine patients not started on UFH, two suffered complications. We would recommend construction of guidelines regarding the management of patients with emboli that included the use of heparin.

It must be considered whether the protocol that the department is using is poorly designed and leading to poor control of APTT levels. The authors believe that it is the unpredictability of individual responses to UFH heparin that leads to the difficulty in controlling UFH infusions. At the time of writing, one of the authors (DK) has been involved in a new protocol that is in the process of being implemented across the trust involving more accurate dosing by weight and modifying the change in infusion rate depending on APTT results.

Lastly, the potential role for LMWH heparin in this group of patients must be considered. The operative re-intervention rate was low and the time-scale in which patients returned to the operating theatre would have allowed the anticoagulant effects of low molecular weight heparin to have reversed. It is clear that the use of LMWH would not have caused any patient a delay in their re-intervention in this study as there would have been sufficient time for the anticoagulant effect to wear off. Of more importance, however, is the fact that LMWH could ensure

more rapid and accurate anticoagulation for patients and potentially reduce the complication rate. It would also be beneficial to patients in reducing the large number of venesections they would endure during their hospital stay and to staff who have to manage the infusions during busy on call shifts.

Conclusions

Use of UFH in patients who have undergone arterial embolectomy is difficult to control, resource expensive, and ineffective in many patients. The use of LMWH should be considered as an alternative.

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