Systemic anticoagulation related to heparin locking of non-tunnelled venous dialysis catheters in intensive care patients

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Summary

Heparin locking of venous dialysis catheters is routinely performed in intensive care to maintain catheter patency when the catheters are not being used. Leakage of heparin into the circulation can potentially cause systemic anticoagulation and may present a risk to intensive care patients. To assess the effect of 5000 units per millilitre heparin locking of non-tunnelled dialysis catheters on systemic anticoagulation, we performed a prospective observational study of ten intensive care patients receiving heparin locking of dialysis catheters in an adult tertiary intensive care unit between July and September 2015. Activated partial thromboplastin time (APTT) was measured prior to, and three minutes after, heparin locking of catheter lumens with the manufacturer's recommended locking volume to assess the effect on systemic anticoagulation. Heparin locking of venous dialysis catheters resulted in a significant rise in APTT (*P*=0.002). The median rise was by 56 seconds (interquartile range 30–166.5). Following heparin locking, 80% of patients had APTT values within or above the range associated with therapeutic anticoagulation. Heparin locking of non-tunnelled venous dialysis catheters can cause systemic anticoagulation in intensive care patients and therefore poses a potential risk to patient safety.

Key Words: renal replacement therapy, intensive care, renal medicine, heparin lock

The overall incidence of acute kidney injury (AKI) in the intensive care unit (ICU) is approximately 20% to 50%[1]. Approximately 5% of patients admitted to ICU with AKI will require renal replacement therapy (RRT), which is associated with a 60% mortality rate[2]. When RRT is stopped for prolonged periods (e.g. >2–3 hours) catheter locking by injection of concentrated heparin into each lumen of the dialysis catheter is commonly performed[3]. Heparin lock volumes are recommended by the catheter manufacturers, however the benefits of heparin locking catheters to maintain dialysis catheter patency have to be balanced against the risk of potential systemic heparinisation by inadvertent injection or leakage of drug. There is evidence in the nephrology literature to show that heparin locking of dialysis catheters is associated with systemic heparinisation[3, 4]. There are also case reports of clinically significant bleeding events in this setting and in one case report, major bleeding leading to transplant rejection and death[5, 6]. There are no studies published in the intensive care literature involving acute dialysis that assess the effect of heparin locking of dialysis catheters on systemic anticoagulation in ICU patients. Critically ill patients are at risk of adverse events from inadvertent systemic anticoagulation. We conducted a prospective observational study to assess our current practice, to inform decisions regarding catheter locking solutions.

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Methods

This prospective observational study was conducted in an adult tertiary ICU (Princess Alexandra Hospital, Brisbane, Queensland). The protocol was approved by the Metro South Research Ethics Committee (HREC reference number: HREC/15/QPAH/365). The study was performed over a period of three months from July to September 2015.

Patients with non-tunnelled venous dialysis catheters who were having heparin locking solution injected into the catheter as part of routine care were included. Exclusion criteria were patients receiving systemic anticoagulation within six hours prior to planned heparin lock, patients with known baseline coagulopathy (International Normalized Ratio [INR] >1.5, activated partial thromboplastin time [APTT] >47 seconds) and patients with prior inclusion in this study (i.e. one assessment per patient). The 13 cm or 20 cm ARROWg^{+}ard Blue® (Teleflex Medical Australia, Mascot, New South Wales) 12Fr dual lumen catheters were used for all patients.

Heparin locking of dialysis catheters is undertaken by intensive care nurses, and according to a unit protocol for RRT care. The protocol involves using a concentrated heparin solution of 5000 units per millilitre. Locking solution volume used is as per the catheter manufacturer's recommendations and this was, for 20 cm catheters: 1.7 ml in the red lumen and 1.8 ml in the blue lumen; and for 13 cm catheters: 1.4 ml in the red lumen and 1.5 ml in the blue lumen. The protocol requires that a second nurse check the appropriate volume of heparin is instilled into each lumen using a 3 ml syringe for each lumen.

Table 1
Baseline data

Patient number	Weight (kg)	Age (y)	Sex	Catheter length	Catheter position
1	120	39	Male	20 cm	Subclavian
2	113	59	Male	20 cm	Internal Jugular
3	120	71	Female	13 cm	Internal Jugular
4	80	28	Male	20 cm	Femoral
5	44	28	Male	20 cm	Internal Jugular
6	70	35	Female	20 cm	Femoral
7	50	19	Male	20 cm	Femoral
8	100	68	Male	20 cm	Femoral
9	90	56	Male	13 cm	Internal Jugular
10	90	65	Female	13 cm	Internal Jugular

Baseline APTT was determined immediately prior to administering heparin locking solution into the dialysis catheter. Three minutes after the heparin locking procedure, blood was collected again for repeat APTT testing. All blood samples were collected from existing arterial lines. Arterial line flush solutions did not contain heparin. Baseline characteristics of patients enrolled including age, sex, weight, type of dialysis catheter and site of dialysis catheter were collected. A convenience sample of ten patients was included. The primary outcome of interest was to assess whether there was a change in APTT following heparin locking of catheters.

Statistical analysis was performed using the GraphPad Prism version 4.00 for Windows (GraphPad Software, San Diego, CA, USA). The paired samples were compared using a two-tailed

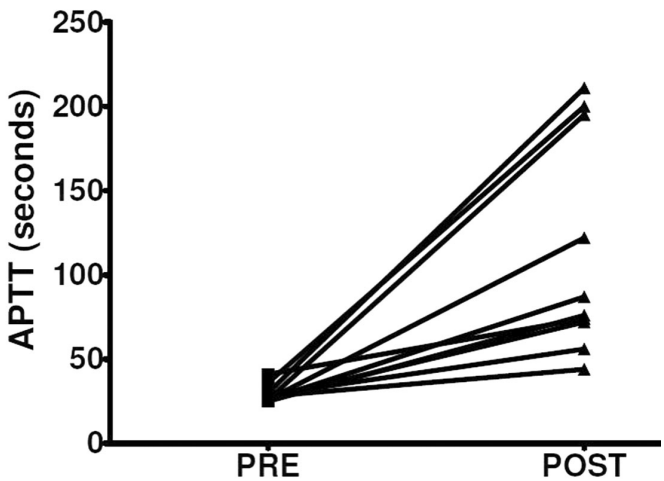

Figure 1: APTT prior to, and three minutes after, heparin locking dialysis catheter (delta APTT=56). APTT, activated partial thromboplastin time.

Table 2
APTT prior to, and three minutes after, heparin locking dialysis catheter

Patient number	Pre lock APTT (sec)	Post lock APTT (sec)	Change in APTT (sec)
1	29	56	+27
2	27	72	+45
3	25	76	+51
4	30	211	+181
5	26	122	+96
6	26	195	+169
7	26	87	+61
8	36	200	+164
9	28	44	+16
10	41	74	+33

APTT, activated partial thromboplastin time.

Wilcoxon Sign-Rank Test. A *P*-value of less than 0.05 was considered statistically significant.

Results

Ten patients were recruited over a period of three months and their baseline characteristics are presented in Table 1.

The pre and post heparin lock APTT is presented in Table 2 and Figure 1 along with the change in APTT. The normal range of APTT quoted for the assay used in our laboratory is 24 to 39 seconds. An APTT of 70 to 100 seconds is the target for therapeutic anticoagulation. The median increase of APTT post heparin lock was 56 (interquartile range, IQR 30–166.5). Two-tailed Wilcoxon Signed-Rank Test showed a statistically significant change in APTT post heparin lock, *P*-value of 0.002.

Eight out of ten patients revealed an APTT consistent with therapeutic anticoagulation and four of these patients were above the therapeutic range following heparin locking of their dialysis catheters.

Discussion

Our study showed that heparin locking of ARROWg^{+}ard Blue 12 Fr dual lumen catheters in ICU patients resulted in significantly increased APTT, representing systemic anticoagulation demonstrated three minutes after heparin lock, compared to baseline value.

An in vitro study by Sungur et al demonstrated that dual lumen short-term dialysis catheters had significant leakage of locking solution. They demonstrated leakage of 18% to 30% of injected volume (0.46 to 0.85 ml) in five different catheters tested, suggesting leakage occurs across a range of different catheter designs. In their study, the Arrow Blue FlexTip®, a catheter with design similar to the catheters tested in our

study, was associated with the lowest percentage of leakage and the second lowest volume of leakage[7]. In this study we demonstrated that despite being associated with the least amount of leakage in the Sungur et al study, heparin locking of the ARROWg+ard Blue catheters resulted in significant APTT rise and systemic anticoagulation.

Agharazii et al demonstrated in an in vitro study that leakage of catheter locking solutions was significantly greater at 30 minutes compared to at five minutes, suggesting that early leakage related to injection of locking solution may be followed by further diffusion of locking solution out of the dialysis catheters[8]. An in vivo study by Markota et al demonstrated an early leakage volume of 31.3% of the total volume of locking solution in non-tunnelled dialysis catheters and reported that both early leakage and late leakage were greater in non-tunnelled catheters when compared with long-term tunnelled catheters[9]. Our study did not investigate the effect of late leakage of heparin locking solution from dialysis catheters on systemic anticoagulation, but the results of these studies suggest that the degree of anticoagulation may be underestimated by early measurement of APTT at three minutes as performed in our study.

Arrow short-term percutaneous non-tunnelled dual lumen dialysis catheters were the most common choice of vascular access for patients requiring RRT in a recent review of practice in Australia and New Zealand ICUs[10]. Heparin locking of dialysis catheters is commonly performed in intensive care units. Inadvertent anticoagulation of critically ill patients poses a significant risk where a relative or absolute contraindication to heparinisation may exist.

The strength of this study is that this is the first prospective study to investigate the effect of heparin locking non-tunnelled venous dialysis catheters in the ICU patient population. The locking procedure was performed to a standard protocol with the volumes of solution recommended by the manufacturer. There are several limitations in this study. The sample size of the study is small and only one type of non-tunnelled venous dialysis catheter was investigated. APTT was measured early after heparin locking and we did not investigate the effect of late leakage of heparin solution.

Citrate, ethanol and less concentrated heparin solutions can be considered as alternative locking solutions to 5000 units per millilitre heparin solution. Citrate-based solutions are increasingly being used as locking solutions in the nephrology patient population. A recent meta-analysis reported a lower rate of catheter-related bloodstream infections and equal effectiveness in maintaining catheter patency when citrate was compared to heparin as a locking agent[11].

Conclusions

We have demonstrated that locking ARROWg+ard Blue 12Fr dual lumen catheters with a solution containing 5000 units per millilitre of heparin led to a significant rise in APTT in ICU patients when measured after three minutes. In patients with a contraindication to systemic anticoagulation, 5000 units per millilitre heparin locking of catheters similar to those in this study is not recommended.

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