Embolic Complications From Central Venous Hemodialysis Catheters Used With Hypertonic Citrate Locking Solution
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Many hemodialysis patients continue to dialyze using central venous access catheters in clinical practice. Catheters are associated with a number of recognized complications, including infection, catheter-associated fibrin sheath and thrombus leading to malfunction, central venous stenosis, and right atrial thrombus. However, symptomatic catheter embolus rarely is reported. We report our experience of catheter-associated emboli in patients dialyzing with a twin catheter designed with multiple small side holes in combination with a hypertonic citrate locking solution. 8 patients developed symptomatic emboli from catheter-associated thrombus, typically resulting in sudden hypotension and chest pain shortly after starting hemodialysis, with documented pulmonary and cerebral emboli in 3 cases. Catheters with multiple side holes are susceptible to seepage of the catheter locking solution through the side holes and therefore may be at greater risk of catheter thrombus formation. This may be exacerbated by the use of a hypertonic citrate lock given to just fill the internal catheter lumen because hyperosmolar locks are more likely to leave the catheter tip, resulting in increased risk of catheter associated thrombus.


INDEX WORDS: Hemodialysis; catheter; embolus; pulmonary emboli; embolic stroke.

A lthough arteriovenous fistulas are recommended as the preferred choice of vascular access for hemodialysis patients, many patients dialyze using central venous catheters (CVCs). During the past 30 years, these catheters have changed from relatively simple single-lumen to large-bore dual-lumen catheters designed to achieve high blood flows.1 The increased size of catheters has led to a number of mechanical complications, including venous thrombosis and thrombus around the catheter tip, including right atrial thrombus. In addition, CVCs can lead to venous medial hypertrophy, with narrowing resulting in venous stenosis, and fibrosis at the site of insertion into the vein, leading to difficulties on removal.3

To prevent catheter clotting, heparin typically is placed into the catheter at the end of dialysis as a catheter lock. The concentration of heparin used varies markedly from 1,000 to 10,000 IU/mL.4 The risk of clot formation is greater using 1,000 IU/mL; however, high-dose heparin locks potentially can lead to leakage of heparin systemically, with the consequent risk of hemorrhage, and also the risk of heparin-induced thrombocytopenia.5 As a result, other locking solutions have been introduced in an attempt to reduce catheter-associated thrombus6 and prevent catheter dysfunction.

We have recently observed a number of cases of symptomatic emboli from hemodialysis CVCs in patients in whom hypertonic citrate was used as the locking solution, causing pulmonary and cerebral emboli and symptomatic hypotension during hemodialysis.

CASE REPORTS

All patients described dialyzed using an Ash Split Cath (Medcomp, New Orleans, USA) for vascular access, which then was locked using 43% trisodium citrate (Dura Lock; Medcomp) after dialysis, with 1.6 and 1.7 mL instilled into the arterio and venous lumens, respectively. Patients underwent systemic anticoagulation using a single bolus dose of low-molecular-weight heparin, tinzaparin, except for 2 patients, 1 prescribed daily subcutaneous prophylactic tinzaparin, and the other, warfarin (Table 1).

Before the acute presentation, all patients were noted to have developed catheter malfunction, with increased arterial and/or venous pressures during dialysis, or required reversal of blood flow because of poor flows.
Case 1

The patient had been receiving dialysis treatment for 5 years after a scleroderma renal crisis and was attended for routine outpatient dialysis. Flows through the CVC were noted to be decreased, with high arterial and venous access pressures and online recirculation > 10%. The following day, she developed sudden weakness of the right arm and leg and was admitted to the local hospital with a diagnosis of acute cerebrovascular event. This started to recover within 24 hours, and she made a full recovery. She was normotensive. A computed tomographic brain scan suggested an ischemic infarct. Additional investigation with a standard transthoracic echocardiogram excluded atrial thrombus or valvular heart disease, and Doppler studies showed normal carotid and femoral vessels. A nuclear medicine isotope brain scan suggested an embolic stroke (Fig 1), and a second echocardiogram using a bubble test showed a patent foramen ovale.

Case 2

The patient, who had been established on dialysis therapy for 4 months, suddenly lost consciousness shortly after starting an outpatient session, with a precipitous decrease in blood pressure. A recent transthoracic echocardiogram had shown a CVC-associated clot, and computed tomographic scanning after collapse showed that the CVC thrombus had disappeared, but he had experienced a left upper lobe pulmonary embolus (Fig 2).

Case 3

An elderly man had been stable on dialysis therapy for 18 months when the nurses had difficulty aspirating the catheter lock. After multiple attempts at aspiration and then forced flushing, he was started on dialysis, but suddenly felt unwell and became markedly hypotensive, reporting nausea and severe left-sided loin and thoracic back pain. He was resuscitated and his symptoms settled after 30-40 minutes. An acute cardiac event was excluded and he declined further immediate investigations. On the dialysis treatment before this event, catheter malfunction with poor blood flows had been recorded. A subsequent isotope ventilation perfusion scan was reported as compatible with a left lower lobe pulmonary embolus.

<table>
<thead>
<tr>
<th>Patient No.</th>
<th>Age (y)</th>
<th>Sex</th>
<th>Catheter Position</th>
<th>Duration (mo)</th>
<th>Anticoagulant</th>
<th>Hypotension</th>
<th>Embolus</th>
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<tr>
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<td>Tinzaparin 4,500 IU</td>
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<td>Pulmonary embolus</td>
</tr>
</tbody>
</table>

Note: Duration refers to the time since the central venous catheter was inserted; hypotension refers to hypotension shortly after starting dialysis; and type of embolus is categorized as pertaining to brain (cerebrovascular accident) or lung (pulmonary embolus).
Case 4

This patient had started dialysis therapy 2 months earlier because of underlying myeloma for which he was administered thalidomide and therefore had been prescribed warfarin, although international normalized ratio (INR) was ≤ 1.4. He attended outpatient dialysis, and the nurses had difficulty aspirating the catheter lock and obtaining good blood flows. Shortly after starting dialysis, he reported sudden-onset right-sided pleuritic chest pain associated with marked hypotension and tachycardia. He was resuscitated, and after 30-40 minutes, his symptoms resolved. An acute cardiac event was excluded. A computed tomographic scan a few weeks later showed a new peripheral wedge-shaped area of atelectasis that developed post embolus, then subsequently resolved (Fig 3).

Cases 5-8

Four additional patients (Table 1) who were found to have thrombus attached to the tip of their dialysis CVC with poor blood flows were investigated for sudden hypotensive episodes, typically occurring during the first hour of hemodialysis, associated with acute onset of severe pleuritic chest pain and dyspnea, with either sinus tachycardia or palpitations. Although clinical presentations were highly suggestive of acute pulmonary emboli, specific imaging was not obtained.

DISCUSSION

All cases reported used the same type of CVC, which ends with 2 separate twin catheters, each with a “D”-shaped terminal hole, and multiple side holes in all directions. Catheters differ in their performance, and similarly, design also affects leakage of the catheter lock between dialysis sessions. The size of the catheter, in particular, catheter diameter, also determines the frequency of catheter-associated thrombus, particularly in pediatric practice. The Ash Split Cath has been designed to provide good blood flows and also to create a high shear jet effect around the tips to disrupt catheter-associated thrombus. However, it also creates areas of stagnation, thus allowing blood to clot and form a thrombus. One of our patients also had pacing wires, and the thrombus formed between the CVC and the pacing wires. Thus, other mechanical devices may increase the risk of thrombus formation and subsequent potential embolization.

Although multiple side holes provide good blood flow, they also may allow the catheter lock to seep out, thus increasing the risk of clotting. Seepage of the catheter locking solution increases the risk of clotting and thrombus formation between the last of the side holes and the catheter tip.

Catheter-associated bacteremias have been the predominant complication of dialysis CVCs, and as such, many dialysis centers have turned from traditional heparinized catheter locks to antisepsics, including various concentrations of citrate and/or antibiotics in heparin solutions, because both types of lock have been shown to reduce the risk of catheter-associated bacteremia. In our center, the introduction of citrate reduced Staphylococcus aureus CVC-associated bacteremias from 39 to 17 per year. Although citrate locks have been noted to reduce infection rates compared with heparin, they have not been universally reported to reduce catheter malfunction caused by thrombus formation.

Concentrations...
of citrate used for catheter locks vary from isosmolar citrate solutions, typically in combination with an additional antiseptic, such as methylene blue and parabens, to hypertonic solutions ranging in strength from 23%-46.7%.12-15 We used a very hyperosmolar solution (4,160 compared with 154 mOsmol/kg for unfractionated heparin, 5,000 IU/mL), and some authors have suggested that hypertonic solutions are more likely to be lost by seepage from CVCs. This may explain in part the superior results reported with 4% trisodium citrate.14

Shortly after citrate initially was introduced as a catheter locking solution, concerns were expressed about overfilling the catheter and introducing hypertonic citrate directly into the heart.16 Because of these concerns, only the exact amount required to fill the catheter lumen was instilled, and this may have led to possible underfilling. In addition, our nursing staff only tried to aspirate the catheter lock, then when the locking solution had been removed, the catheter was flushed. This may have led to less mechanical flushing of the catheter compared with when heparin locks were used.

Most, if not all, catheters develop fibrin sheaths,17 and this may be associated with thrombus in 25%-42% of cases, although clinical sequelae from emboli are uncommon,18 with very few clinical reports. We report 8 cases, with an estimated prevalence of 4%, probably caused by a combination of events: using a small volume of very hypertonic catheter lock designed to just fill the internal lumen; a catheter with multiple side holes, both of which increased the risk of seepage, coupled with a probable decrease in manual catheter flushing; and anticoagulation with bolus low-molecular-weight heparin.

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REFERENCES