Locking Solutions for Hemodialysis Catheters; Heparin and Citrate—A Position Paper by ASDIN

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ABSTRACT

There is wide variation in the use of solutions to "lock" or fill tunneled central venous catheters for dialysis. Some centers use undiluted heparin concentrations ranging from 1000 to 10,000 U/ml and other centers place from 1000 to 10,000 U per lumen. Based on available evidence, it appears that heparin 1000 U/ml, or 4% sodium citrate are suitable choices for lock solution to maintain patency of tunneled central venous catheters for dialysis. Risks from systemic anticoagulation are lower with heparin 1000 U/ml and 4% sodium citrate, compared with higher concentrations of heparin (5000 and 10,000 U/ml). The need for use of tissue plasminogen activator for maintaining catheter patency is increased by using heparin lock at 1000 U/ml, vs. higher concentrations. Higher concentrations of heparin lock should be reserved for patients who have evidence of catheter occlusion or thrombosis when heparin is used at 1000 U/ml. Similar choices for lock solution are sensible for acute hemodialysis catheters. When heparin is used for catheter lock, the injected volume should not exceed the internal volume of the catheter.

Instillation of heparin at high concentration in the lumens of tunneled central venous catheters (catheter lock) at the end of hemodialysis (HD) sessions is the currently adopted practice among dialysis centers and nephrologists. Studies examining the optimal catheter lock heparin concentration are limited. Furthermore, none of the solutions commonly used to lock HD catheters are currently approved by the FDA for this purpose, resulting in a lack of manufacturer's recommendations for catheter locking. There is also a wide variation in lock solution concentrations with some centers using undiluted heparin concentrations ranging from 1000 to 10,000 U/ml and other centers placing 1000–10,000 U per lumen. Lock solutions are usually instilled to the listed volume of each catheter port lumen, though some centers purposefully instill up to 20% more than catheter volume. Hence, our attempt is to review the available data on the lock solutions and formulate the most reasonable recommendation on this matter.

Heparin Lock Solution

The use of heparin as a routine locking solution is associated with several risks:

- Systemic heparin administration occurs even when the catheter lock volume is limited to the volume of the catheter lumen or recommended fill volume. Systemic anticoagulation is greater when heparin concentrations of 5000 or 10,000 U/ml are used as a lock solution. In a study in which the catheter fill volume was calculated and a volume of 10,000 U/ml heparin was used, the average patient aPTT 10 minutes after instillation was 2.42 ± 0.73 times normal, with one patient > 3.75 times normal (1). A recent study documented high activated partial thromboplastin time (aPTT) levels post-HD in six of 10 patients 1 hour after receiving a catheter lock of 5000 U/ml (2). In vitro studies demonstrate that even in laboratory condition where the fill volume is precisely the catheter volume, there is 15–20% leakage of lock solution from the catheter, due to parabolic flow patterns in the catheter. Spillage increases to 25–40% of the lock solution with a 20% overfill of the catheter and greater leakage is observed in catheters with distal side-holes (3,4).
- Heparin-induced antibodies (HIA) are a significant problem in HD patients. In a study in which 207 unselected patients were screened by ELISA, HIA were found in 37 (17.9%) (5).
- Heparin does not prevent biofilm formation and in fact, induces biofilm formation in the presence of *Staphylococcus aureus*. Higher concentrations of heparin increase biofilm faster than lower concentrations (6,7).

Studies indicate that heparin catheter locks of 1000 U/ml are effective in maintaining catheter patency. In one prospective study the routine concentration of

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heparin lock was decreased from 10,000 to 1000 U/ml. There was no change in the incidence of catheter malfunction but there was a significant increase in the frequency of use of recombinant tissue plasminogen activator (tPA) (26.6 uses per 1000 HD sessions vs. 8.2, $p < 0.001$) (8). In a retrospective study, catheter patency was similar between two HD units in which one used 1000 U/ml heparin and the other used 10,000 U/ml. Use of tPA was significantly higher in the unit using 1000 U/ml, being administered to 12 of 14 patients vs. 14 of 45 patients using 10,000 U/ml heparin lock ($p = 0.0009$) (9).

Reduced heparin concentrations are associated with a lower risk of bleeding from systemic anticoagulation. In a prospective study among HD patients with tunneled catheters, the heparin lock concentration was changed from 5000 to 1000 U/ml for the "initial" lock because of postinsertion bleeding (10). A retrospective study evaluating the effect of changing the catheter lock from heparin 5000 U/ml to either heparin 1000 U/ml or sodium citrate demonstrated that the risk of immediate postinsertion bleeding was 11.9 times higher in the high-dose heparin group (11). In another study, locking catheters with 60% of the listed catheter fill volume resulted in no increase in catheter loss over a 2-week period, and diminished systemic anticoagulation (1).

Sodium Citrate Lock Solution

Sodium citrate is also an effective anticoagulant catheter lock; and at 4% concentration the lock volume has not been demonstrated to induce systemic anticoagulation or hypocalcemia. Two recent retrospective studies from Toronto compared 4% sodium citrate vs. heparin for catheter lock. These studies evaluated the effect of changing from heparin 10,000 U/ml (12) or approximately 2500 U/ml (13) to 4% sodium citrate. In the first study, there was no difference in the rate of flow-related catheter exchange (4.1 vs. 3.2 per 1000 days, $p = 0.07$), and the rate of tPA usage was lower among the citrate patients. In the second study, catheter exchange was less frequent with citrate (2.98 vs. 1.65/1000 days) as was tPA usage (5.49 vs. 3.3/1000 days). Another randomized study demonstrated comparable catheter dysfunction episodes and rates of catheter-related bloodstream infection (CRBSI) using 4% sodium citrate or heparin (14). These studies suggest that 4% sodium citrate is as effective as high concentrations of heparin as a catheter lock solution. In the United States, 4% sodium citrate is available only in 250 or 500 ml bags, designed primarily for plasmapheresis procedures; however, one bag can serve as a source for filling multiple syringes for catheter locks.

Antibacterial Catheter Locks

In an attempt to salvage HD catheters in patients with bacteremia or sepsis, catheter locks with antibiotics or antiseptic components are beneficial (15–17). Two meta-analyses of prophylactic antimicrobial locking solution have demonstrated a 50–90% reduction in the incidence of CRBSI using a number of such locks (18,19). An accompanying editorial confirms the benefits of antimicrobial lock solutions, but also discusses problems of using antibiotics as prophylaxis for catheter infections (20). Antimicrobial locks may be created by adding antibiotics to heparin or citrate solutions, but compatibility problems are greater with heparin and very small concentrations of antibiotic must be used in combination with heparin. Sodium citrate at higher concentrations, such as 30%, also appears to be effective in preventing CRBSI (21), but it is unlikely that this product will be made available in the United States. Randomized clinical trials are now evaluating products with modest concentrations of citrate and antiseptic compounds to determine the effects on CRBSI rates and patency of HD catheters.

Recommendation

Based on available evidence, it appears that the following solutions are suitable choices for lock solution to maintain patency of tunneled central venous catheters for dialysis:

- Heparin 1000 U/ml or
- 4% Sodium citrate

Risks from systemic anticoagulation are lower with heparin 1000 U/ml and 4% sodium citrate, compared with higher concentrations of heparin (5000 and 10,000 U/ml). The need for use of tPA for maintaining catheter patency is increased by using heparin lock at 1000 U/ml, vs. higher concentrations. Higher concentrations of heparin lock should be reserved for patients who have evidence of catheter occlusion or thrombosis when heparin is used at 1000 U/ml. Similar choices for lock solution are sensible for acute HD catheters. When heparin is used for catheter lock, the injected volume should not exceed the internal volume of the catheter.

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