Does the Heparin Lock Concentration Affect Hemodialysis Catheter Patency?

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Background and objectives: Concentrated heparin solutions are instilled into the catheter lumens after each hemodialysis session to prevent catheter thrombosis. The heparin lock concentration at many centers has been decreased recently to reduce the risk of systemic bleeding and contain costs. However, the effect of this change on catheter patency is unknown. We compared catheter patency between two heparin lock solutions: 1000 versus 5000 units/ml.

Design, setting, participants, & measurements: With use of a prospective, computerized, vascular access database, 105 patients with newly placed tunneled hemodialysis catheters, including 58 patients receiving a 5000 units/ml heparin lock and 47 patients receiving a 1000 units/ml heparin lock, were retrospectively identified. The primary endpoint was cumulative catheter patency and the secondary endpoint was frequency of thrombolytic instillation.

Results: Cumulative catheter survival was similar in the two groups, being 71% versus 73% at 120 days in the low- and high-concentration heparin lock groups (hazard ratio of catheter failure, 0.97; 95% confidence interval, 0.45 to 2.09; \( P = 0.95 \)). The frequency of tissue plasminogen activator instillation was significantly greater in the low-concentration heparin group (hazard ratio, 2.18; 95% CI, 1.26 to 3.86; \( P = 0.005 \)). No major bleeding complications were observed in either treatment group. The overall drug cost for maintaining catheter patency was 23% lower with the low-concentration heparin lock ($1418 versus $1917) to maintain catheter patency for 1000 days.

Conclusions: Low-concentration heparin lock solutions do not decrease cumulative dialysis catheter patency, but require a twofold increase in thrombolytic instillation to maintain long-term patency.


Thrombosis is a common complication of tunneled hemodialysis catheters. Anticoagulant solutions are instilled into both catheter lumens after each dialysis session in an effort to prevent interdialytic catheter thrombosis (1). Heparin is the predominant anticoagulant lock solution used in U.S. hemodialysis units. The optimal heparin lock concentration is unknown and has ranged between 1000 and 10,000 units/ml. The Kidney Disease Outcomes Quality Initiative (KDOQI) guidelines for vascular access do not recommend an optimal heparin lock concentration (2). An aliquot of the catheter solution invariably leaks into the systemic circulation (3,4). As a result, higher heparin lock concentrations have the potential to cause systemic bleeding caused by inadvertent systemic anticoagulation (5,6). A recent study reported a higher frequency of hemorrhagic complications after placement of a new dialysis catheter in patients receiving a high-concentration heparin lock (7). Higher heparin concentrations have also been implicated in promoting the formation of Staphylococcus aureus biofilm (8,9). On the basis of these observations, a recent position paper recommended that a 1000 units/ml heparin solution be adopted as the standard concentration for locking hemodialysis catheters (10). Finally, recent contamination problems associated with the manufacturing process have substantially increased the cost of heparin (11).

As a result of all these considerations, our dialysis provider decided to switch the standard heparin lock for hemodialysis catheters from 5000 to 1000 units/ml, effective July 1, 2008. It is not clear, however, whether using a lower dose of heparin lock might adversely affect catheter patency or increase the frequency of thrombolytic instillation. We decided to use this opportunity to compare the patency of newly placed hemodialysis catheters using 5000 and 1000 units/ml heparin locks.

Materials and Methods

Study Population

The University of Alabama at Birmingham (UAB) provides medical care for approximately 500 hemodialysis patients, under the supervision of 10 full-time clinical nephrologists. The patients dialyze at five in-center hemodialysis units in metropolitan Birmingham, which are owned by a large dialysis organization. The medical directors of these units, who are on the faculty of UAB, agree upon a set of uniform treatment protocols. About 25% of our hemodialysis population is catheter-dependent at any given time. An interventional nephrologist or radiologist at UAB places the tunneled dialysis catheters. The vast majority of catheters placed have a split-tip catheter design.

Management of Catheter Malfunction and Infection

Before July 2008, all catheters were instilled with 5000 units/ml of heparin in each lumen at the end of each dialysis session. The intralu-
ables. The frequency of tPA instillation was calculated by dividing the
concentrations.

maintain catheter patency was compared between the two heparin lock
protocol. The low-concentration heparin lock concentration group
was estimated (Table 3). The

Statistical Analysis

Baseline patient characteristics were compared between both groups
using t tests for continuous variables and \( \chi^2 \) tests for categorical vari-
ables. The frequency of tPA instillation was calculated by dividing the
total number of instillations by the total number of days of follow-up,
and compared between groups using the exact test for homogeneity of
Poisson rates. Survival curves were generated using Kaplan-Meier
methodology, and the differences between groups were analyzed by
the log rank test. Univariate Cox proportional hazard models were
performed. Hazard ratios and their 95% confidence intervals (CI) were
computed. \( P < 0.05 \) was considered statistically significant.

Results

The two study groups (5000 and 1000 units/ml heparin lock) were similar in terms of age, gender, race, diabetes, hypertension, coronary artery disease, peripheral vascular disease, and congestive heart failure (Table 1). Approximately 70% of cath-
ters in both groups was placed in the right internal jugular vein. The patients in the low-concentration heparin group were more likely to have a Decathlon catheter and less likely to have an Ash-split catheter. Both catheter types have a similar split-
tip design, but the Decathlon catheter is heparin-coated and the
Ash-split catheter is not coated. A higher proportion of patients in
the low-concentration heparin group had a history of a
previous dialysis catheter.

The catheter outcomes in the two groups are summarized in
Table 2. The mean duration of catheter use was about 3 months
in both patient groups. The proportion of unscheduled catheter
removal or replacement was similar in both groups (26% versus
25%), although dysfunction tended to be more common in the
low-concentration heparin group, whereas infection tended to
be more common in the high-concentration heparin group. Similarly, about three fourths of catheters in both groups were
removed electively because of a mature vascular access or remained patent. Mean dialysis blood flows did not differ
between the two groups.

Cumulative catheter survival was similar in the high- and
low-concentration heparin groups (81% versus 80% at 60 days
and 73% versus 71% at 120 days). The hazard ratio of catheter
failure was 0.97 (95% CI, 0.45 to 2.09; \( P = 0.95 \)) (Figure 1). The
frequency of tissue plasminogen activator (tPA) instillation was
8.4 in the low-concentration heparin group versus 3.8 per 1000
catheter days in the high-concentration heparin group. The
likelihood of tPA instillation was significantly greater in the
low-concentration heparin group (hazard ratio, 2.18; 95% CI,
1.26 to 3.86; \( P = 0.005 \)). None of the patients in either group had
a hospitalization or emergency room visit related to a hemor-
rhagic complication.

The relative cost of maintaining catheter patency using the
two heparin lock concentrations was estimated (Table 3). The
cost of the drugs for our dialysis organization was $0.16 per
1000 units of heparin and $72 per 2-mg vial of tPA. We assumed
that each catheter lumen was 2 ml, requiring 4000 units of
heparin to lock the catheter after each dialysis session. We also
assumed that 2 mg of tPA was instilled into each lumen to treat
catheter dysfunction. All costs were calculated to maintain
patency during 1000 catheter days, or 428 hemodialysis treat-
ments (3 hemodialysis sessions per week). The total cost of
drugs (heparin and tPA) to maintain catheter patency for 1000
days was $1484 in patients treated with 1000 units/ml heparin
locks, as compared with $1917 for patients treated with 5000

Data Analysis

Two full-time access coordinators scheduled all access procedures
and maintained a prospective, computerized database of all vascular
access procedures and complications (14). Permission was obtained
from the UAB Institutional Review Board to retrospectively review
each patient’s medical records for research purposes. We queried the
prospective, computerized vascular access database to identify all new
permanent hemodialysis catheters placed. We excluded from our anal-
ysis femoral dialysis catheters, as they have worse patency than do
catheters placed in the internal jugular vein (15). The high-concen-
tration heparin lock concentration (5000 units/ml) group was composed
of all patients receiving a new tunneled dialysis catheter during the
3-month period from January 1, 2008, to March 31, 2008. These patients
were analyzed through June 30, 2008.

On July 1, 2008, our dialysis provider switched to a low-concentra-
tion (1000 units/ml) heparin lock. We allowed for a one-month transi-
tion period to ensure consistent implementation of the new heparin
lock protocol. The low-concentration heparin lock concentration group
consisted of patients receiving new tunneled dialysis catheters during the
3-month period from August 1, 2008, to October 31, 2008. This
group of patients was analyzed through January 31, 2009. If a patient
received more than one dialysis catheter during the study period, only
the first catheter was included in our analysis.

Baseline demographic and clinical information was extracted from
the electronic medical records of the study patients. Catheter outcomes,
including dialysis blood flows, tPA instillation, and catheter removals
or exchanges as a result of infection or loss of patency was derived from
electronic hospital and dialysis records. Dialysis blood flows obtained
during the first three dialysis sessions of each month were averaged for
each patient. Finally, the electronic records were used to identify any
hospitalizations or emergency room visits associated with bleeding
complications. Survival analysis techniques were used to calculate cu-
mulative catheter survival. Patient follow-up was censored for death,

Catheter-related bacteremia was suspected when a patient had fever
or chills without evidence of an alternate source of infection. Empiric
antibiotics were initiated after blood cultures were obtained. Patients
received a 3-week course of systemic antibiotics, in conjunction with an
antibiotic-heparin lock instilled into the catheter lumen (12,13).
The dialysis catheter was replaced in patients with persistent symptoms
despite appropriate antibiotics or in patients with recurrent bacteremia.

In other words, using the lower (1000 units/ml) concentration of heparin locks was associated with a 23% reduction in cost of maintaining the catheter patency.

**Discussion**

The recent decision by our large dialysis organization to switch to a lower heparin concentration for catheter locks was driven by two major considerations. First, the use of a lower heparin concentration may mitigate the potential risk of serious hemorrhagic complications arising from heparin leaking into the systemic circulation. Second, the recent problems with heparin contamination have substantially increased the cost of heparin, which is not separately reimbursable as a dialysis injectable drug. Notwithstanding these important considerations...

**Table 1. Clinical and catheter features of the study population**

<table>
<thead>
<tr>
<th></th>
<th>High-Concentration Heparin (5000 units/ml)</th>
<th>Low-Concentration Heparin (1000 units/ml)</th>
<th><strong>p</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>N</strong></td>
<td>58</td>
<td>47</td>
<td></td>
</tr>
<tr>
<td>Age, years</td>
<td>53 ± 15</td>
<td>55 ± 14</td>
<td>0.39</td>
</tr>
<tr>
<td>Gender, N (%) female</td>
<td>21 (36%)</td>
<td>20 (42%)</td>
<td>0.55</td>
</tr>
<tr>
<td>Race, N (%) black</td>
<td>48 (83%)</td>
<td>35 (74%)</td>
<td>0.34</td>
</tr>
<tr>
<td>Diabetes</td>
<td>30 (52%)</td>
<td>19 (40%)</td>
<td>0.32</td>
</tr>
<tr>
<td>Hypertension</td>
<td>55 (95%)</td>
<td>42 (89%)</td>
<td>0.24</td>
</tr>
<tr>
<td>Coronary artery disease</td>
<td>12 (21%)</td>
<td>8 (17%)</td>
<td>0.80</td>
</tr>
<tr>
<td>Peripheral vascular disease</td>
<td>19 (33%)</td>
<td>11 (23%)</td>
<td>0.38</td>
</tr>
<tr>
<td>Congestive heart failure</td>
<td>17 (29%)</td>
<td>15 (32%)</td>
<td>0.83</td>
</tr>
<tr>
<td>Catheter type</td>
<td></td>
<td></td>
<td>0.02</td>
</tr>
<tr>
<td>Decathlon</td>
<td>43 (74%)</td>
<td>43 (91%)</td>
<td></td>
</tr>
<tr>
<td>Ash-split</td>
<td>15 (26%)</td>
<td>1 (2%)</td>
<td></td>
</tr>
<tr>
<td>Duraflow</td>
<td>2 (4%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Palindrome</td>
<td>1 (2%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Catheter location</td>
<td></td>
<td></td>
<td>0.54</td>
</tr>
<tr>
<td>right IJ</td>
<td>40 (69%)</td>
<td>35 (74%)</td>
<td></td>
</tr>
<tr>
<td>left IJ</td>
<td>18 (31%)</td>
<td>12 (26%)</td>
<td></td>
</tr>
<tr>
<td>Previous catheter</td>
<td>11 (19%)</td>
<td>19 (40%)</td>
<td>0.02</td>
</tr>
</tbody>
</table>

IJ, internal jugular.

**Table 2. Clinical outcomes using different heparin lock concentrations**

<table>
<thead>
<tr>
<th></th>
<th>High-Concentration Heparin (5000 units/ml)</th>
<th>Low-Concentration Heparin (1000 units/ml)</th>
<th><strong>p</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>N</strong></td>
<td>58</td>
<td>47</td>
<td></td>
</tr>
<tr>
<td>Catheter duration, days</td>
<td>90 ± 49</td>
<td>84 ± 48</td>
<td>0.53</td>
</tr>
<tr>
<td>Catheter dysfunction</td>
<td>6 (10%)</td>
<td>9 (19%)</td>
<td>0.26</td>
</tr>
<tr>
<td>Catheter infection</td>
<td>8 (14%)</td>
<td>3 (6%)</td>
<td>0.33</td>
</tr>
<tr>
<td>Deep vein thrombosis</td>
<td>1 (2%)</td>
<td>0 (0%)</td>
<td>0.99</td>
</tr>
<tr>
<td>Elective removal</td>
<td>23 (40%)</td>
<td>15 (32%)</td>
<td>0.54</td>
</tr>
<tr>
<td>Remaining patent</td>
<td>20 (34%)</td>
<td>20 (42%)</td>
<td>0.42</td>
</tr>
<tr>
<td>Dialysis blood flow</td>
<td>418 ± 44</td>
<td>403 ± 49</td>
<td>0.14</td>
</tr>
<tr>
<td>tPA instillations (per 1000 catheter days)</td>
<td>3.8 (2.3 to 5.9)</td>
<td>8.4 (5.8 to 11.7)</td>
<td>0.005</td>
</tr>
<tr>
<td>Major hemorrhagea</td>
<td>0</td>
<td>0</td>
<td></td>
</tr>
</tbody>
</table>

aHemorrhage requiring hospitalization or emergency room visit.

units/ml heparin locks. In other words, using the lower (1000 units/ml) concentration of heparin locks was associated with a 23% reduction in cost of maintaining the catheter patency.
Conclusions

A low-concentration (1000 units/ml) heparin lock solution is associated with similar cumulative catheter patency as that from the catheter into the circulation. In this study, we did not observe any episodes of hospitalization or emergency room visits as a result of hemorrhage during 5220 catheter days in the high-concentration heparin group and 3948 catheter days in the low-concentration heparin group (Table 2). We cannot exclude, however, the possibility of a reduction in minor hemorrhages occurring in the outpatient dialysis unit after switching to the low-concentration heparin lock. In a previous study, the frequency of hospitalization for bleeding was equally low (approximately 0.75 events per 1000 hemodialysis sessions, or approximately 0.3 events per 1000 catheter days) in both heparin groups (16). In contrast, a preliminary report observed a significantly lower frequency of bleeding episodes after switching the heparin lock concentration from 5000 to 1000 units/ml (18).

Our calculations suggest that the cost of maintaining catheter patency (heparin plus tPA) was 23% lower when the low-concentration heparin locks were used, as compared with that of the high-concentration heparin locks. The relative cost would change if the cost of these drugs changed. We did not observe any major bleeding complications in either treatment group in this study. If the frequency of bleeding were lower in the low-concentration heparin group, the relative cost savings would be even greater.

Our study has some limitations. First, it was a retrospective study. However, it would be difficult to design a randomized study to compare high- and low-concentration heparin locks because current practice has already changed to the use of a low-concentration heparin lock. Second, our study represents a relatively small patient sample derived from a single institution, and the results may vary at other dialysis centers. Third, the proportion of patients with heparin-coated catheters (Decathalon) was greater in the low-concentration heparin group than in the high-concentration heparin patient group. Theoretically, heparin coating may improve catheter patency and reduce the need for thrombolytic therapy, thereby affecting the results. However, two recent studies found no difference in cumulative catheter patency or requirement for thrombolitics between patients with heparin-coated dialysis catheters and those with noncoated catheters (19,20).

Table 3. Comparison of costs of maintaining catheter patency using a high or low heparin lock concentration

<table>
<thead>
<tr>
<th></th>
<th>High-Concentration Heparin (5000 units/ml)</th>
<th>Low-Concentration Heparin (1000 units/ml)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Heparin cost per HD session</td>
<td>$3.20</td>
<td>$0.64</td>
</tr>
<tr>
<td>Heparin cost per 1000 catheter days</td>
<td>$1370</td>
<td>$274</td>
</tr>
<tr>
<td>tPA cost per instillation</td>
<td>$144</td>
<td>$144</td>
</tr>
<tr>
<td>tPA instillations per 1000 catheter days</td>
<td>3.8</td>
<td>8.4</td>
</tr>
<tr>
<td>tPA cost per 1000 catheter days</td>
<td>$547</td>
<td>$1210</td>
</tr>
<tr>
<td>Cost of heparin + tPA per 1000 catheter days</td>
<td>$1917</td>
<td>$1484</td>
</tr>
</tbody>
</table>

Assumptions: (1) Catheter lumen is 2 ml (2 lumens per HD session); (2) instillation of 2 mg of tPA per lumen; (3) three hemodialysis sessions per week (or 428 sessions per 1000 catheter days). HD, hemodialysis.

Table 2. Comparison of costs of maintaining catheter patency using a high or low heparin lock concentration

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<tr>
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<td>$547</td>
<td>$1210</td>
</tr>
<tr>
<td>Total cost per HD session</td>
<td>$1917</td>
<td>$1484</td>
</tr>
</tbody>
</table>

Assumptions: (1) Catheter lumen is 2 ml (2 lumens per HD session); (2) instillation of 2 mg of tPA per lumen; (3) three hemodialysis sessions per week (or 428 sessions per 1000 catheter days). HD, hemodialysis.
obtained with a high-concentration (5000 units/ml) heparin lock. However, maintaining long-term catheter patency requires a twofold increase in thrombolytic requirements. Despite the increased use of tPA, the low-concentration heparin lock is associated with a substantial cost savings. Thus, we believe that a 1000 units/ml heparin lock concentration should be used routinely in tunneled hemodialysis catheters.

Disclosures
None.

References
18. Degapudi B, Gupta M, Ahmed Z: Effect of different concentrations of heparin solution as catheter locks in haemodialysis patients on bleeding and catheter dysfunction. Abstract SA-PO2497. Presented at the American Society of Nephrology meeting in San Diego, October 27 to November 1, 2009