Taurolidine-Citrate-Heparin
the superior lock solution

Clinical Evidence
for central venous catheters in haemodialysis
Catheter-related infections and dysfunction are the main catheter complications causing morbidity and mortality in haemodialysis patients. Over the years, many lock solutions - often based on sodium citrate - have been discussed as best alternative to 5,000 IU/mL Heparin. Suppliers of 4% Citrate containing lock solutions even claim it is antimicrobial. However, there is no supporting clinical evidence.

“\textbf{In the prevention of catheter-related infections... citrate alone fails to show a similar advantage compared to an antimicrobial-containing citrate lock.}”

"\(^1\)"
Expert Recommendations

According to the European Renal Best Practice (ERBP 2010), in two studies (McRae, Grudzinski), no benefit regarding infectious complications had been observed for 4% citrate. 2,3

<table>
<thead>
<tr>
<th>4% Citrate vs Heparin³</th>
<th>Heparin 5000 IU/ml</th>
<th>4% sodium citrate</th>
</tr>
</thead>
<tbody>
<tr>
<td>CRBSI rate per 1.000 catheter days</td>
<td>3.3</td>
<td>2.2</td>
</tr>
<tr>
<td><strong>Not significant</strong></td>
<td></td>
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</tbody>
</table>

Antibacterial lock solutions should ... be preferred. ... taurolidine-citrate solutions can be used.⁴

<table>
<thead>
<tr>
<th>Taurolidine-Citrate vs Heparin⁴</th>
<th>Heparin 5000 IU/ml</th>
<th>Taurolidine + 4% Sodium Citrate</th>
</tr>
</thead>
<tbody>
<tr>
<td>CRBSI rate per 1.000 catheter days</td>
<td>5.6</td>
<td>decreased by about 90%</td>
</tr>
<tr>
<td>Bacteremia-free survival at 90 days ( p&lt;0.001 )</td>
<td>47%</td>
<td>94%</td>
</tr>
</tbody>
</table>

“**Allon recommended in 2003: Because of a number of incidences of clotting, the possibility of adding Heparin to the Taurolidine/Citrate as soon as the catheter is inserted, should be investigated.**”⁵
In 2012: Solomon confirmed “…the addition of 500 IU/ml of Heparin to Taurolidine-Citrate may achieve patency comparable to Heparin 5000 U/ml.”

“...The most promising results are obtained when antibacterial compounds are added to citrate or heparin.”

TauroLock™-Hep500 contains the antimicrobial compound Taurolidine, 4% sodium citrate and 500 IU/mL Heparin.
The utilisation of TauroLock™-Hep500 as an antimicrobial lock solution in dialysis has shown a significant reduction of catheter related bloodstream infections (CRBSI) in many different studies.\(^8,9,10\)

Even better results are achieved with the so called 2+1 protocol: Twice per week TauroLock™-Hep500 and once per week TauroLock™-U25.000.

<table>
<thead>
<tr>
<th></th>
<th>TauroLock™-Hep500</th>
<th>2+1 protocol</th>
</tr>
</thead>
<tbody>
<tr>
<td>CVC exchanges</td>
<td>due to thrombosis and infection</td>
<td>7</td>
</tr>
<tr>
<td>Patency</td>
<td>rt-PA consumption per 1.000 catheter days</td>
<td>4.3</td>
</tr>
<tr>
<td>Infection</td>
<td>CRBSI per 1.000 catheter days</td>
<td>0.3</td>
</tr>
</tbody>
</table>

Study authors: Al-Ali, F. et al. \(^{11}\)

Study location: Qatar

Patients enrolled: 164

Journal and publication date: Nephrology Dialysis Transplantation (ndt), 2017

Keynotes: “Taurolock™-U25.000 is a safe and effective tunnelled dialysis catheter lock solution, with low rate of catheter exchange.”

“No reported serious adverse event or bleeding related to the lock solution was encountered during the study period in either group.”
Expert recommendations

The German guideline of infection prevention and hygiene and the US dialysis guideline (KDOQI) recommend urokinase for the prophylactic use in central venous catheters.

“...Urokinase with or without taurolidine is a reasonable option for overproportional rates of bloodstream infections.”

TauroLock™-U25.000 fulfills the above mentioned guideline recommendations and contains Urokinase to ensure patency and provides infection control in the device.

TauroLock™-U25.000 contains the antimicrobial compound Taurolidine, 4% Citrate and Urokinase (25,000 IU).
Best practice & cost efficiency

<table>
<thead>
<tr>
<th>Clinical outcomes</th>
<th>Sodium Citrate 4%</th>
<th>2+1 protocol</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patency</td>
<td>catheter dysfunction per 1,000 catheter days</td>
<td>44.3</td>
<td>18.7</td>
</tr>
<tr>
<td></td>
<td>rt-PA Rate per 1,000 catheter days</td>
<td>9.8</td>
<td>3.8</td>
</tr>
<tr>
<td>Bloodstream Infection</td>
<td>CRI per 1,000 catheter days</td>
<td>2.7</td>
<td>0.67</td>
</tr>
<tr>
<td>Hospitalisation</td>
<td>CRI events in days</td>
<td>15.8</td>
<td>3.7</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Costs per year</th>
<th>Sodium Citrate 4%</th>
<th>2+1 protocol</th>
<th>43 % cost savings</th>
</tr>
</thead>
<tbody>
<tr>
<td>costs of lock solution (purchase accumulated)</td>
<td>187.- USD</td>
<td>1.485.- USD</td>
<td>Use of alteplase included!</td>
</tr>
<tr>
<td>Costs for complication management (dysfunction, CRI)</td>
<td>4.309.- USD</td>
<td>1.063.- USD</td>
<td></td>
</tr>
</tbody>
</table>

Study authors: Winnicki, W. et al. 13
Study location: Vienna, Austria
Patients enrolled: 106
Journal and publication date: Kidney International, 2017
Keynotes: “significant catheter-related cost savings of 43% in the taurolidine group vs. citrate group when overall expenses per patient and year were compared”

“use of taurolidine-based catheter lock solutions containing heparin and urokinase significantly reduced complications related to tunneled hemodialysis catheters when compared to four percent citrate solution and was overall more cost-efficient”
1 Citrate versus heparin lock for hemodialysis catheters: a systematic review and meta-analysis of randomized controlled trials. 

2 Sodium citrate 4% locking solution for central venous dialysis catheters-an effective, more cost-efficient alternative to heparin. 

3 Citrate 4% versus Heparin and the Reduction of Thrombosis Study (CHARTS) 
MacRae Jennifer M, Ivana Djordjevic, Ognjenka Djurdjev, Beverly Jung, Steven Shalansky, Adeera Levin and Mercedeh Kiaii. CJASN March 2008, 3 (2) 369-374

4 Dialysis standard 2016, German Society of Nephrology in cooperation with the Association of German Kidney Centers as well as the Society of Paediatric Nephrology

5 Prophylaxis against Dialysis Catheter-Related Bacteremia with a Novel Antimicrobial Lock Solution. 
Allon M, Clinical Infectious Diseases, 2003;36:1539-44

6 Observational study of need for thrombolytic therapy and incidence of bacteremia using taurodine-citrate-heparin, taurodine-citrate and heparin catheter locks in patients treated with hemodialysis. 

7 Any use for alternative lock solutions in the prevention of catheter-related blood stream infections? 

8 A new haemodialysis catheter-locking agent reduces infections in haemodialysis patients. 

9 Tunneled catheters with taurodine-citrate-heparin lock solution significantly improve the inflammatory profile of hemodialysis patients. 

10 Taurodine-citrate-heparin catheter lock solution reduces staphylococcal bacteraemia rates in haemodialysis patients. 

11 Safety and efficacy of taurodine/urokinase versus taurodine/heparin as a tunneled catheter lock solution in hemodialysis patients: a prospective, randomized, controlled study. 
Guideline for infection prevention

12 Guideline for infection prevention and hygiene 2019 in addition to the dialysis standard. 
German society for nephrology e.V. 2701.2020

13 Taurodine-based catheter lock regimen significantly reduces overall costs, infection, and dysfunction rates of tunneled hemodialysis catheters. 