Lock solutions (also called block solutions) are designed to fill or "seal" the inner lumen of catheters and port systems when they are not in use. They should have the following major effects:

1. Prevent catheter-related infections and biofilm formation
2. Maintain the patency of the access system

Since some leakage of lock solution from the catheter into the bloodstream is inevitable, an additional requirement of a modern lock solution is the fact that it is safe even if instilled into the patient.

Physiological saline solution has none of both major effects listed above. It should therefore be used only for rinsing or flushing the access system in order to remove any residual blood or medication.

Heparin has been the classical lock solution for decades and is still in use in various concentrations. The debates in professional societies and publications about the "correct" concentration have meanwhile attained an "inflationary level". In dialysis, it is most common to use a concentrated heparin solution containing 5,000 IU/ml. The heparin concentrations used in oncology and parenteral nutrition access devices are significantly lower (100 IU/ml).

It is quite obvious that the heparin concentration needed are lower in catheter and port systems without regular blood flow. Sometimes heparin is completely omitted in these areas. The use of high heparin concentrations of 10,000 IU/ml, which are common mainly in the USA, is not recommended. There is no evidence of improved patency due to the use of very high heparin concentrations. In contrast, the bleeding tendency is increased due to heparin being spilled out from the catheter into the bloodstream. Heparin, as such, cannot prevent catheter-related infections, though. Moreover, since it is an oligosaccharide, heparin is an ideal nutrient for microbes and also accelerates the formation of biofilms on the inner surface of catheters and port-a-cath systems.

These experiences promoted the search for alternative lock solutions. There was some impression in the first clinical studies to indicate that citrate-containing lock solutions (4%, 5%, 10%, and 30%) might attain approximately the same catheter patency as heparin solutions.\textsuperscript{1a, b, c, d, 4} More recent studies of Power and Solomon compare heparin (5,000 IU/ml) to heparin-free lock solutions that are based solely on citrate as their anticoagulant component. Both 4% and 46.7% citrate solutions double the urokinase needs as compared to heparin.\textsuperscript{2, 3} As a result, many dialysis catheters with difficult flow conditions are therefore being blocked with heparin, whereas catheters with less significant difficulties are blocked with a heparin-free citrate-containing lock solutions.

Citrate-based lock solutions are popular especially for their antimicrobial activity. However, this does not apply to low concentrated citrate solutions (4%).\textsuperscript{1} Despite recurring claims that low concentration citrate solutions show antimicrobial activity under in vitro conditions, 4% citrate solution has never been observed to reduce catheter-associated infections in clinical studies. It was
therefore an obvious step to use highly concentrated citrate lock solutions to attain not only catheter patency but antimicrobial activity in addition. Indeed, 30% sodium citrate solution is reducing the incidence of catheter-related infections in clinical studies.\(^3\)

The addition of antibiotics to 4% citrate solutions reduces the incidence of catheter-associated infections massively. Gentamycin, Vancomycin or Cephalosporin derivatives have been used for this purpose in clinical studies. The most success was attained with gentamycin/citrate. However, after some months of use the development of resistancy was observed. As a result, the study was discontinued.\(^1\) The prophylactic use of antibiotic lock solutions is therefore assessed with some criticism in the hygiene guidelines complementing the German Dialysis Standard.\(^4\)

The hygiene guideline complementing the German Dialysis Standard recommend the use of lock solutions with an antimicrobial effect since 2008, since these solutions reduce the incidence of catheter-related infections compared to the use of heparin. For this purpose highly concentrated citrate solutions and taurolidine-citrate solutions are recommended. The antimicrobial substance of Taurolidine (which is not an antibiotic) is combined with 4% citrate in these solutions. Taurolidine has been known in Europe for a long time as a substance with bactericidal efficacy with an extremely broad range of action that includes both gram-positive and gram-negative pathogens. MRSA and VRE are also included in the range of action.\(^1\)

**TauroLock\(^\text{TM}\)-Hep500**

Especially preferred for use in haemodialysis catheters is **TauroLock\(^\text{TM}\)-Hep500**. Taurolidine, 4% citrate and 500 IU/ml heparin are combined in this solution. It has been demonstrated in a major clinical study that **TauroLock\(^\text{TM}\)-Hep500** is equivalent to concentrated heparin (5,000 IU/ml) and superior to the heparin-free **TauroLock\(^\text{TM}\)** variant with regard to maintaining catheter patency.\(^5\) For the blocking of port systems and Broviac or Hickman catheters in use for parenteral nutrition, it is preferable to use the heparin free **TauroLock\(^\text{TM}\)**. The use of **TauroLock\(^\text{TM}\)-Hep100** in catheter and port systems of paediatric oncology patients has been associated with a reduction of more than 80% in the incidence of catheter-associated infections.\(^8\)

Recent studies show a dramatic reduction in the incidence of catheter-associated infections both in adults and children.\(^9, 10, 11\)

In terms of the safety of lock solutions, the risk of bleeding associated with heparin-containing lock solutions has for a long time been the focus of attention. In fact, the use of heparin in HIT patients is contraindicated. For this reason, the use of heparin-containing lock solutions must be scrutinised very closely. Current study situation seems to suggest that addition of heparin significantly increases catheter patency.

The use of highly concentrated citrate-containing lock solutions has been associated with some dramatic adverse effects resulting from leakage of the solution from the catheter into the bloodstream.\(^13, 14\) Cardiac risks need to be mentioned in this regard. Since the density of highly concentrated citrate solutions is much higher than the density of blood, the solution cannot be prevented from entering into the right atrium\(^15\). In particular over-instillation of the lock solution may cause hypercalcaemia with possible life-threatening outcome.\(^14\)

Davenport reported in 2010 embolic complications from Central Venous Hemodialysis Catheters used with Hypertonic Citrate Locking solution (46.7%)\(^13\)

Schilcher et al. showed that contact of blood and highly concentrated citrate solutions (>12%) precipitate proteins from the blood with the potential to contribute to the pathophysiology of reported embolisms.\(^16\)

Accordingly, 10 catheters each were filled with 4%, 20% and 46.7% citrate under in vivo conditions. Protein precipitation was detected in none of the catheters filled with 4% citrate, whereas precipitated proteins were detected in all catheters filled with 20% or 46.7% citrate. Filtration tests through a 20 μm-mesh filter show that the resulting crystals have the potential to be responsible for the embolic complications. The risk-benefit profile of lock solutions based on highly concentrated citrate must therefore be assessed very critically. One commercial supplier of 30% citrate solutions already

The hygiene guideline supplementing the German dialysis standard has recommended the use of lock solutions with an antimicrobial effect since 2008, because these solutions reduce the incidence of catheter-related infections as compared to heparin.
stopped the manufacturing and distribution of this solution. The citrate concentration in TauroLock™ is only 4% and conforms to the recommendation of the FDA. Overinstillation of 4% citrate into the catheter or “flushing” are not associated with dramatic adverse effects as compared to highly concentrated citrate (30% and 46.7%) such as metallic taste, thromboembolic events and cardiac arrhythmia.13-17 Tauroldidine is degraded in the blood within a period of 2 hours through enzymatic hydrolysis to produce the natural amino acid, taurine.

Summary
The use of Antimicrobial Lock Solutions have been recommended in the “Hygiene Guideline complementing the German Dialysis Standard” and in the Position statement of European Renal Best Practice (ERBP”). Pure heparin solutions containing no antimicrobial agent do not meet this criterion. Antibiotics are associated with the development of resistancy which is a major drawback. Highly concentrated citrate solutions and taurolidine-citrate solutions are therefore conceivably useful in this application. With regard to catheter patency, the use of heparin-free lock solutions obviously increases the need for fibrinolytics to re-open the catheter. Highly concentrated citrate solutions (30% and 46.7%) cause major adverse effects that are a significant risks for the patient. Antimicrobial lock solutions such as TauroLock™-Hep500 have proven useful in dialysis for many years and have meanwhile become established in the prevention of catheter-related infections.

Literature / Sources:
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