Les verrous pour cathéters d'hémodialyse chronique

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Les 2 principaux problèmes des cathéters en hémodialyse

Thrombose

- De la veine
- De la lumière du CVC
  - 50% - 91% de dysfonctionnement à 1 an
  - Dose de dialyse insuffisante (débit sanguin réduit, séances écourtées)
  - Morbidité liée aux changements de cathéters
  - Coût de désobstruction
  - Augmente le risque d'infection

Infection

- Risque de bactériémie
  x 10-20 / FAV
- Incidence bactériémies
  0,5 – 10 / 1000 jours
- Localisations secondaires
  5-10 % des patients avec KT
  10-40% si S. aureus
- Risque de décès x 2-3 / FAV

Prévention des dysfonctionnements des cathéters

- Qualité du cathéter : gros calibre, court, architecture de l'extrémité
- Positionnement de l'extrémité du cathéter : OD, jonction VCS-OD
- VJID > VJIG > VF
- Verrou

Les verrous disponibles en France

Verrou	Prix pour 2 lumières
NaCl 0,9%	0,07 €
NaCl 10%	0,08 €
HBPM (Tinzaparine 2500 UI/voie)	4,48 €
Héparine non fractionnée (5000 UI /voie)	0,77 €
Citrate 4%	2,7 €
Citrate 46,7% (Duralock ou citralock)	2,7 €
Taurolidine + citrate 4% (Taurolock)	≈ 7 €
Taurolidine + citrate 4% + héparine 500 UI (Taurolock-Hep500)	≈ 7 € x2
Taurolidine + citrate 4% + héparine 1000 UI	≈ 7 € x2
Taurolidine + urokinase 25,000UI (Taurolock-U25,000)	28 € x2
Urokinase 100,000 UI (Actosolv / therasolv 100,000 UI / voie)	85 € x2
Alteplase (Actilyse 1 mg/ voie)	54 €
Antibiotiques + héparine	
Ethanol + HBPM	

L'héparine est à risque hémorragique

Randomized, Clinical Trial Comparison of Trisodium Citrate 30% and Heparin as Catheter-Locking Solution in Hemodialysis Patients

J Am Soc Nephrol 16: 2769–2777, 2005

Marcel C. Weijmer,*# Marinus A. van den Dorpel,† Peter J.G. Van de Ven,† Pieter M. ter Wee,* Jos A.C.A. van Geelen,‡ Johannes O. Groeneveld,§ Brigitte C. van Jaarsveld,‖ Marjon G. Koopmans,¶ Caatje Y. le Poole,** Anita M. Schrander-Van der Meer,†† Carl E.H. Siegert,‡‡ Koen J.F. Stas;§§ for the CITRATE Study Group

Table 3. Adverse and bleeding events

Locking Procedures	No. of Events		*P* Value
	TSC Group (*n* = 6208)	Heparin Group (*n* = 6416)	
Adverse event			
paresthesia, "metallic taste," tingling in fingers immediately after locking	9	4	0.26
thrombopenia of unknown origin	2	4	0.44
withdrawal for medical reasons (persistent bleeding disorder)	0	1	0.49
Bleeding events			
persistent bleeding after insertion	6	19	0.005
severe	0	2	0.24
major bleeding episodes during follow-up			
total	5	16	0.010
no. per 1000 catheter-days	0.60	2.0	
gastrointestinal bleeding	1	7	0.034
exit-site bleeding	0	5	0.028
hemorrhagic ascites after peritoneal dialysis catheter removal	1	1	0.74
hematuria	0	1	0.49
postoperative bleeding	2	2	0.68
hemoptysis in pulmonary malignancy	1	0	0.51

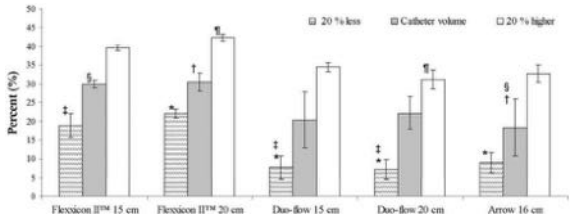
Passage systémique du verrou

Nephrol Dial Transplant (2007) 22: 3533–3537
doi:10.1093/ndt/gfm452
Advance Access publication 26 September 2007

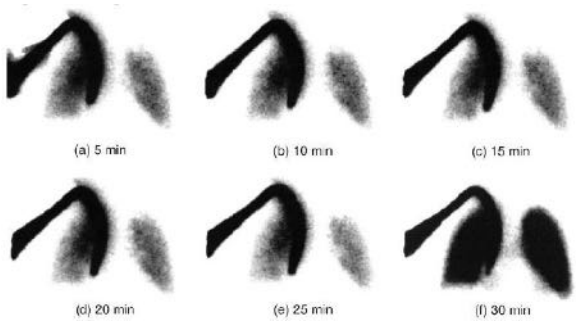
Original Article

Exit of catheter lock solutions from double lumen acute haemodialysis catheters—an *in vitro* study*

Murat Sungur[1], Emel Eryuksel[2], Sinan Yavas[1], Azra Bihorac[1], A. Joseph Layon[1,2,3] and Lawrence Caruso[1,2]



Passage systémique du verrou



Nephrol Dial Transplant (2006) 21: 1135

L'héparine est à risque hémorragique

Nephrol Dial Transplant (2001) 16: 2072–2074

Nephrology Dialysis Transplantation

Technical Note

Risk of heparin lock-related bleeding when using indwelling venous catheter in haemodialysis

Hüseyin Karauslan, Pierre Peyronnet, Daniel Benevent, Christian Lagarde, Michel Rince and Claude Leroux-Robert

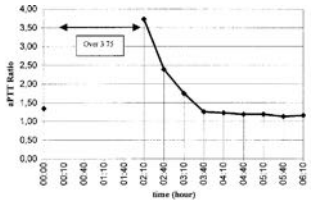


Fig. 1. aPTT changes after a 2 ml heparin locking over a 6-h period in one patient.

Table 2. Estimated volumes of arterial and venous catheters and the aPTT ratio before and after heparin locking according to estimated volumes

Patients	Arterial lumen volume (ml)	Venous lumen volume (ml)	aPTT* ratio before heparin locking	aPTT* ratio after heparin locking
1	1.2	1.2	2.17	3.09
2	1.2	1.2	0.96	2.88
3	ND	ND	ND	ND
4	1.2	1.2	1.52	2.55
5	1.3	1.2	1.82	3.26
6	1.2	1.5	1.40	2.58
7	1.1	1.3	1.29	1.68
8	1.4	1.5	1.20	1.36
9	1.2	1.4	1.05	1.08
10	1.3	1.1	1.39	2.51
11	1.1	1.3	1.46	3.49
12	1.4	1.4	1.36	2.20
13	1.1	1.2	1.20	1.44
14	1.1	1.2	1.34	2.18
15	1.3	1.2	1.24	3.17
16	1.0	1.2	1.06	1.89
17	1.4	1.4	1.67	>3.75
18	1.1	1.2	0.94	2.99
19	1.1	1.0	1.46	2.05
20	1.3	1.2	1.76	3.21

Les mécanismes de la dysfonction

Causes précoces

- Mauvaise position
- Plicature
- Hypovolémie sévère

Causes tardives

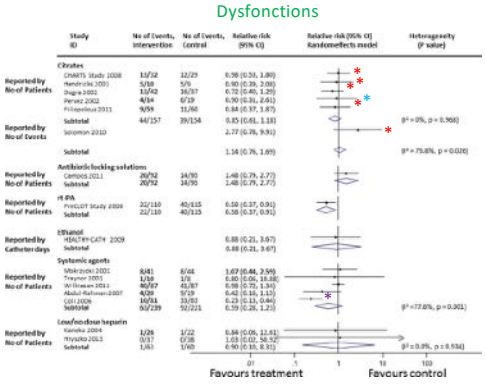
- Thrombus intraluminal
- Thrombus péri-cathéter
- Manchon fibrineux engainant le cathéter
- Hypovolémie

Mécanismes d'action des verrous

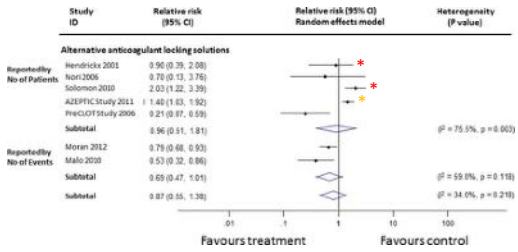
- Citrate : chélation du calcium qui est un cofacteur indispensable à plusieurs réactions enzymatiques de la coagulation
- Taurolodine : aucun effet
- Urokinase, alteplase : thrombolyse, pas d'effet anticoagulant

Stratégies de prévention des dysfonctions

Dysfonctions



Utilisation de thrombolytiques

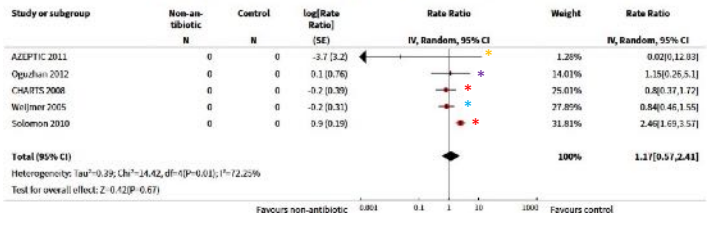


* Citrate 3-4%
* Citrate 47%
* INR 1,8-2,5 + ticlopidine
* Citrate 7% + bleu méthylène + parabènes

Wang Y, Ivany JN, Perkovic V, Gallagher MP, Woodward M, Jardine MJ.
Anticoagulants and antiplatelet agents for preventing central venous haemodialysis catheter malfunction in patients with end-stage kidney disease.
Cochrane Database of Systematic Reviews 2016, Issue 4. Art. No.: CD009631.
DOI: 10.1002/14651858.CD009631.pub2.

Stratégies de prévention des dysfonctions

Analysis 5.8. Comparison 5 Non-antibiotic antimicrobial lock solutions versus control, Outcome 8 Subgroup analysis: thrombosis (per 1000 catheter-days) in tunnelled catheters.



* Citrate 4%
* Citrate 47%
* NaCl 27%
* Citrate 7% + bleu méthylène + parabènes

Arechabala MC, Catoni MI, Claro JC, Rojas NP, Rubio ME, Calvo MA, Letelier LM.
Antimicrobial lock solutions for preventing catheter-related infections in haemodialysis.
Cochrane Database of Systematic Reviews 2018, Issue 4. Art. No.: CD010597.
DOI: 10.1002/14651858.CD010597.pub2.

Efficacité des verrous sur les dysfonctions

- Beaucoup d'études, méthodologie souvent moyenne
- Critères de jugement = débit, survie cathéter ou consommation de thrombolytiques

- En résumé :
  - Citrate toute concentration et taurolodine + citrate ne font pas vraiment mieux que l'héparine
  - Avec le citrate il est montré une diminution du risque hémorragique, qui doit exister aussi avec la taurolidine

Intérêt d'une thrombolyse hebdomadaire préventive ?

- Plusieurs études le suggèrent
- Méthodologie souvent bien supérieure aux études habituelles sur les verrous

Prevention of Dialysis Catheter Malfunction with Recombinant Tissue Plasminogen Activator

Brenda R. Hemmelgarn, M.D., Ph.D., Louise M. Moist, M.D., Charmaine E. Lok, M.D., Marcello Tonelli, M.D., S.M., Braden J. Manns, M.D., Rachel M. Holden, M.D., Martine LeBlanc, M.D., Peter Faris, Ph.D., Paul Barre, M.D., Jianguo Zhang, M.Sc., and Nairne Scott-Douglas, M.D., Ph.D., for the Prevention of Dialysis Catheter Lumen Occlusion with rt-PA versus Heparin (PreCLOT) Study Group

- HD chronique sur cathéter central tunnellisé
- Au moins 3 séances / semaine
- Cathéters incidents

- Héparine 5000 U/ml 3x
- Vs
- Héparine 1ère et 3ème séance + altéplase 1 mg à la 2ème séance

N ENGL J MED 364;4 NEJM.ORG JANUARY 27, 2011

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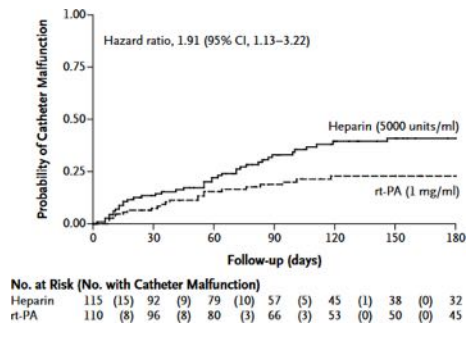

Table 2. Adverse Events.*

Event	rt-PA Group (N=139)	Heparin-Only Group (N=115)	P Value†
	no. (%)		
Any serious adverse event	23 (20.9)	34 (29.6)	0.14
Bleeding			0.93
Minor	7 (6.4)	9 (7.8)	
Clinically important nonmajor	3 (2.7)	2 (1.7)	
Major	3 (2.7)	4 (3.5)	
Fatal	0	1 (0.9)	
Hospitalization			0.15
For ischemic heart disease	3 (2.7)	5 (4.3)	
For congestive heart failure	3 (2.7)	0	
For arrhythmia	2 (1.8)	0	
For cerebrovascular disease	1 (0.9)	2 (1.7)	
For infection			
Related to central venous catheter	2 (1.8)	4 (3.5)	
Not related to central venous catheter	5 (4.5)	3 (2.6)	
For bleeding event	1 (0.9)	3 (2.6)	
For other event	8 (7.3)	18 (15.7)	
Death			0.72
Cardiovascular-related	1 (0.9)	0	
Infection-related	1 (0.9)	1 (0.9)	
Bleeding-related	0	1 (0.9)	
Other‡	1 (0.9)	3 (2.6)	

N ENGL J MED 364;4 NEJM.ORG JANUARY 27, 2011

Prevention of tunneled cuffed catheter dysfunction with prophylactic use of a taurolidine urokinase lock: A randomized double-blind trial

Florence Bonkain[1,2], Jean-Claude Stolear[3], Concetta Catalano[4], Dominique Vandervelde[2], Serge Treille[5], Marie M. Couttenye[6], Annemieke Dhondt[7], Mark Libertalis[2], Mandelina Allamani[1,4], Philippe Madhoun[3], Amaryllis H. Van Craenenbroeck[8], Floris Vanommeslaeghe[7], Freya Van Hulle[1], Philippe Durieux[3], Ingrid Van Limberghen[1], Christian Tielemans[1], Karl Martin Wissing[1]*

- HD chronique sur KT central tunnellisé
- Au moins 3 séances /sem
- Cathéter prévalents avec dysfonction nécessitant 2 thrombolyses lors des 6 derniers mois

Lock composition	Monday Tuesday	Wednesday Thursday	Friday Saturday	Group
Taurolidine-citrate-heparin500	X	X	X[1]	
Placebo			X[2]	TaurolockHep500 (control group)
Taurolidine-citrate-heparin500	X	X		
Taurolidine-citrate			X[2]	TaurolockU
Urokinase 25000 U			X[2]	

PLOS ONE | https://doi.org/10.1371/journal.pone.0251793 May 20, 2021

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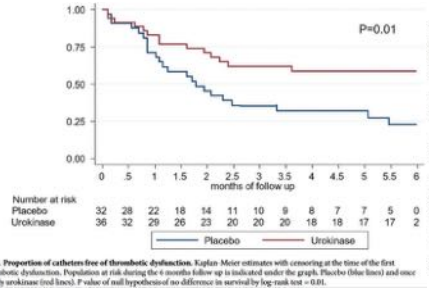

Fig 2. Proportion of catheters free of thrombotic dysfunction. Kaplan-Meier estimates with censoring at the time of the first thrombotic dysfunction. Population at risk during the 6 months follow up is indicated under the graph. Placebo (blue lines) and once weekly urokinase (red lines). P value of null hypothesis of no difference in survival by log-rank test = 0.01.

Table 3. Primary and secondary efficacy outcomes.

Outcomes	TaurolockU N = 36	TaurolockHEP N = 32	P-value
Primary outcome			
Total number of thrombotic dysfunctions (TD)	24	59	0.0012[a]
Incidence rate (N/1000 catheter days)	4.8	12.3	
Incidence rate ratio (95% CI)	0.39 (0.23–0.64)		<0.0001
TD with reduction of blood flow[2]	13	46	
Incidence rate (N/1000 catheter days)	2.6	9.5	
Incidence rate ratio (95% CI)	0.27 (0.14–0.51)		<0.0001
TD with impossibility to start dialysis therapy[2]	11	13	
Incidence rate (N/1000 catheter days)	2.2	2.7	
Incidence rate ratio (95% CI)	0.82 (0.33–1.98)		0.32
Secondary outcomes			
Refractory thrombosis (total)[a]	9 (25%)	4 (12.5%)	0.23
Catheter removal for refractory thrombosis	0	2	0.218
Systemic fibrinolysis	4	0	0.116
Refractory thrombosis (without catheter removal or fibrinolysis)	5	2	0.454
Catheter-related bloodstream infection	1	0	1

PLOS ONE | https://doi.org/10.1371/journal.pone.0251793 May 20, 2021

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Table 6. Costs of prophylactic and therapeutic catheter locks per patient during the 6-month study period [1].

	Treatment group	Control group	P- value[3]
TaurolockHEP500[2]	150 (79.3–156)	207 (160.1–216)	NA[4]
TaurolockU[2]	375 (198.2–390)		NA[4]
Total cost prophylaxis	525 (277.5–546)	207 (160.1–216)	<0.0001
Therapeutic urokinase locks	0 (0–192)	384 (0–576)	0.0012
	Range (0–768)	Range (0–1344)	
Total cost	546 (481.5–547.5)	554.4 (234–781.1)	0.96
Total cost/week[5]	21 (21–33.4)	23.1 (9–30.3)	0.35

PLOS ONE | https://doi.org/10.1371/journal.pone.0251793 May 20, 2021

KDOQI CLINICAL PRACTICE GUIDELINE FOR VASCULAR ACCESS: 2019 UPDATE

AJKD Vol 75 | Iss 4 | Suppl 2 | April 2020

Statements: Pharmacologic Prevention of CVC Dysfunction

CVC Connectors to Prevent CVC Dysfunction or Bacteremia

21.2 KDOQI considers it reasonable to have an individualized approach to use special CVC connectors based on the clinician's discretion and best clinical judgment. *(Expert Opinion)*

21.3 KDOQI considers it reasonable to use an antimicrobial barrier cap to help reduce CRBSI in high-risk patients or facilities; the choice of connector should be based on clinician's discretion and best clinical judgment. *(Expert Opinion)*

Intraluminal Agents to Prevent CVC Dysfunction

21.4 KDOQI considers it reasonable that the choice to use citrate or heparin as a CVC locking solution be based on the clinician's discretion and best clinical judgment, as there is inadequate evidence to demonstrate a difference in CVC survival or complications between these locking solutions. *(Expert Opinion)*

21.5 KDOQI suggests the use of low-concentration citrate (<5%) CVC locking solution, if feasible, to help prevent CRBSI and CVC dysfunction. *(Conditional Recommendation, Low Quality of Evidence)*

21.6 KDOQI suggests that TPA may be prophylactically used as a CVC locking solution once per week to help reduce CVC dysfunction. *(Conditional Recommendation, Low Quality of Evidence)*

21.7 There is inadequate evidence for KDOQI to make a recommendation on the comparative use of the following CVC locking agents for CVC dysfunction or infection prophylaxis: tinzaparin versus unfractionated heparin, taurolidine/citrate versus heparin with or without gentamicin, neutral valve connector (Tego [ICU Medical]) versus citrate (46.7%) locking solution.

Systemic Agents to Prevent CVC Dysfunction

21.8 KDOQI recommends against the routine use of prophylactic systemic anticoagulants (eg, warfarin) for the sole purpose of maintaining or improving CVC patency, as there is inadequate evidence of benefit for CVC patency but suggestion of increased risk of harm. *(Conditional/Strong Recommendation, Low Quality of Evidence)*

21.9 KDOQI suggests that low-dose aspirin may be used to maintain tunneled CVC patency in patients with low bleeding risk. *(Conditional Recommendation, Low Quality of Evidence)*

Note: CVC refers to tunneled hemodialysis CVCs unless otherwise specified.

Que faire en cas de dysfonction ?

- D'abord identifier la cause de la dysfonction
- Voir ce qui se passe en inversant les voies
  - Hypovolémie : PA basse quelle que soit la voie qui aspire. Etonnant si l'extrémité est dans l'OD. PVC basse, amélioration après remplissage, lever de jambes
  - Thrombus intraluminal : la même voie dysfonctionne, un problème de PA devient PV et PV devient PA
  - Gaine de fibrine : souvent c'est la PA qui pose problème, on injecte assez bien. Pas d'amélioration après lever de jambes. Problèmes récurrents.
  - Thrombus péri-cathéter : On peut avoir un peu tout. Pas d'amélioration après lever de jambes. Problèmes récurrents. Phléboscan VCS++.

Prise en charge du thrombus intra-luminal

= verrou thrombolytique

- Fibrinolytiques autorisés:
  - Urokinase, ACTOSOLV®
    - 5.000-10.000 UI/ml pdt 15-30', renouvelable 1-4x
    - Si échec, perfusion 20.000 UI/h pdt >1h ou reperméabilisation
  - Urokinase, THERASOLV®
    - 5,000-25,000 UI / voie pdt 20-60'
    - Si échec, perfusion de 250,000 en 90-180' à concentration de 1000-2500 UI/ml
  - Altéplase, ACTILYSE® 2mg
    - 2 mg/2ml pendant 120 minutes, renouvelable 1x

Efficacy of alteplase 1 *versus* 2 mg dose in restoring haemodialysis catheter function (Alte-dose 2): A randomized double-blind controlled study

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[1]Wayne State University, College of Nursing, Detroit, Michigan, USA, [2]Cleveland Clinic Abu Dhabi, Abu Dhabi, UAE, [3]Windsor Regional Hospital, and [4]Care for Kidneys Foundation, Windsor, Ontario, Canada

HD chronique sur TCC
Thrombose de cathéter

Randomisé, double aveugle
Alteplase 1 mg/2 ml
Vs
Altéplase 2 mg/2 ml

CP = perméabilité restaurée

48 patients inclus

Perméabilité restaurée :
Altéplase 1 mg : 84,9%
Altéplase 2 mg : 85,7%

Table 2 Comparison of correlated observation between the two tPA dosing groups

Variable	Clustered Observations			*P*
	2 mg (*n* = 126)	1 mg (*n* = 126)	Total (*N* = 252)	
tPA repeats per occlusion (*n* (%))				
1 time	112 (88.9)	107 (84.9)	219 (86.9)	0.350
2 times	14 (11.1)	19 (15.9)	33 (13.1)	
Pre tPA blood flow (M(SD)) mL/min	236 (50)	234 (53)	235 (51)	0.743
Post tPA Blood flow (M(SD)) mL/min	339 (41)	329 (53)	334 (47)	0.115
Previous occlusion of HDC (*n* (%))	110 (87.3)	106 (84.1)	216 (85.7)	0.147
Platelets (M(SD)) x 10^9/L	189.9 (57.3)	196.4 (62.7)	193.1 (60.0)	0.391
Haemoglobin (M (SD)) g/dL	11.3 (1.2)	10.9 (1.3)	11.1 (1.3)	0.077
Catheter site (*n* (%))				0.407
Right internal jugular	92 (73)	86 (68.3)	178 (70.6)	
Left internal jugular	34 (27)	40 (31.7)	74 (29.4)	

Nephrology 25 (2020) 491–496

Thrombosis of Tunneled-Cuffed Hemodialysis Catheters: Treatment With High-Dose Urokinase Lock Therapy

Gabriele Donati, Luigi Colì, Giuseppe Cianciolo, Gaetano La Manna, Vania Cuna, Mara Montanari, Francesco Gozzetti, and Sergio Stefoni

Randomisée
AVK, INR cible 1,8-2,5
Thrombose / dysfonction
Temps de contact = 1h
Objectif > 250 ml/min
Fraxiparine pdt HD
Verrou HNF

TABLE I. *Baseline patient characteristics*

	Group A	Group B	*P*
Patients (*n*)	32	40	ns
Age (years)	73 (66–85)	75 (65–87)	ns
Males/female	15/17	18/22	ns
Dialysis vintage (months)	36 (12–61)	37 (13–60)	ns
Causes of ESRD %			
Hypertension	55	60	ns
Glomerulonephritis	25	22	ns
Diabetes	15	14	ns
Other	5	4	ns
Hb (g/%)	11.1 ± 1.1	10.8 ± 1.3	ns
Platelets (n × 10^3/mm^3)	235 ± 61	244 ± 53	ns
INR	1.5 ± 0.2	1.1 ± 0.3	ns
aPTT	0.9 ± 0.2	0.7 ± 0.3	ns
CRP	0.6 ± 0.2	0.5 ± 0.4	ns
Fibrinogen	335 ± 61	344 ± 43	ns
Kt/V	1.3 ± 0.2	1.2 ± 0.2	ns
Dry weight (kg)	65.4 ± 8.6	68.7 ± 7.5	ns

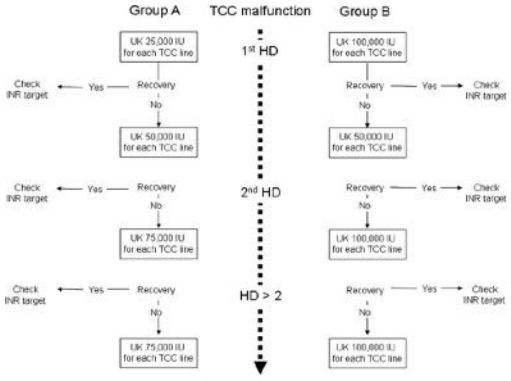


FIG. 1. UK lock therapy schedules.

Artif Organs, Vol. 36, No. 1, 2012

Thrombosis of Tunneled-Cuffed Hemodialysis Catheters: Treatment With High-Dose Urokinase Lock Therapy

Gabriele Donati, Luigi Colì, Giuseppe Cianciolo, Gaetano La Manna, Vania Cuna, Mara Montanari, Francesco Gozzetti, and Sergio Stefoni

TABLE 3. *Results of the two UK schedules*

HD session	Group A	Group B	*P*
1st			
Patency rate after UK lock	4/29 (13.7%)	36/36 (100%)	0.01
Additional 50 000 IU UK lock	25/29 (86.3%)	0/36	0.001
2nd			
Repeated UK lock	25/29 (86.3%)	12/36 (33.3%)	<0.05
>2			
Repeated UK lock	14/29 (48.2%)	3/36 (8.3%)	0.01

TABLE 4. *BFR (mL/min) with the two UK schedules*

HD session	Group A	Group B	*P*
1st	226 ± 32	305 ± 34	<0.05
7th	265 ± 21	315 ± 14	<0.05
14th	285 ± 19	310 ± 23	ns
30th	265 ± 15	300 ± 15	ns

TABLE 5. *Extracorporeal arterial pressure (mm Hg) with the two UK schedules*

HD session	Group A	Group B	*P*
1st	−173 ± 32	−125 ± 32	<0.05
7th	−151 ± 40	−121 ± 22	<0.05
14th	−147 ± 45	−120 ± 41	ns
30th	−135 ± 42	−120 ± 35	ns

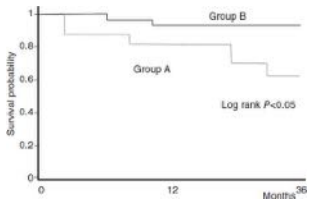


TABLE 6. *Biocompatibility*

	Prelock	Postlock	After 7 days
Group A			
Fibrinogen (mg/dL)	325 ± 51	314 ± 44	326 ± 54
INR	1.4 ± 0.2	1.5 ± 0.3	2.0 ± 0.3
aPTT (ratio)	0.8 ± 0.2	0.9 ± 0.3	0.9 ± 0.4
Hb (g%)	11.0 ± 1.3	10.9 ± 1.2	11.2 ± 1.2
Group B			
Fibrinogen (mg/dL)	314 ± 43	318 ± 41	337 ± 44
INR	1.3 ± 0.4	1.4 ± 0.4	2.1 ± 0.2
aPTT (ratio)	0.9 ± 0.2	0.7 ± 0.4	0.9 ± 0.5
Hb (g%)	10.8 ± 1.3	11.5 ± 1.6	11.4 ± 1.3

Artif Organs, Vol. 36, No. 1, 2012

Alteplase vs. urokinase for occluded hemodialysis catheter: A randomized trial

Viviane POLLO, Danielle DIONÍZIO, Edwa Maria BUCUVIC, João Henrique CASTRO, Daniela PONCE

- Inclusion de cathéters tunnelisés complètement occlus
- Altéplase 1 mg/ml vs Urokinase 5000 Ui/ml + citrate 4%
- Pdt 40 minutes

Table 1 Baseline patient characteristics with occluded tunneled central venous catheter for hemodialysis

Characteristics	All patients N = 100	Alteplase N = 44	Urokinase N = 56	P
Male gender %	54 (54%)	25(56.8)	29(51.8)	0.35
Age (years)	59.6 ± 12.6	59 ± 13	60 ± 12	0.71
Etiology of CKD(%)				
Diabetes	60 (60%)	29(65.9)	31(55.3)	0.07
Hypertension	19 (19%)	7 (15.9)	12 (21.4)	0.19
Others	21 (21%)	8 (18.2)	13 (23.2)	0.22
Comorbidity (%)				
Diabetes	62 (62%)	31(70.4)	31(55.3)	0.08
CVD	20 (20%)	10 (22.7)	10 (17.8)	0.38
Catheter site (%)				
Internal jugular vein	59 (59%)	24(54.3)	35(62.5)	0.57
Femoral vein	31 (31%)	16 (36.3)	15 (26.8)	0.56
Time on dialysis (days)	638 ± 194	678 ± 203	548 ± 189	0.77
Days since catheter insertion	246 ± 61	278 ± 63	218 ± 59	0.67

Table 2 Treatment success at the end of hemodialysis and at the next 10 hemodialysis sessions after urokinase or alteplase use

	Alteplase N = 44	Urokinase N = 56	P
Treatment success after one dose (%)	42(95)	46 (82)	0.06
Treatment success after two doses (%)	43 (98)	49 (88)	0.075
Catheter removal due to no success	1(2.5)	7 (12.5)	0.049
Blood flow post declotting (ml/min)	278 ± 31	264 ± 27	0.29
Catheter function at the next 10 sessions (%)	40 (93)	42 (85.7)	0.23

Données confirmées:
Eyrich, Am J Health Syst Pharm 2002
Zacharias, Ann Pharmacother 2003

Mais la dose d'Urokinase est trop faible

Hemodialysis International 2016; **20**:378–384

Alteplase for blood flow restoration in hemodialysis catheters: a multicenter, randomized, prospective study comparing "dwell" versus "push" administration

Lavern M. Vercaigne[1], James Zacharias[2], Keevin N. Bernstein[2]
and the PUSH Protocol Investigators

Alteplase dwell:
2 mg/2 ml of alteplase dilué dans NaCl 0,9%
/lumière : volume lumière
Après 30', vérification perméabilité puis rinçage,
Si non fonctionnel, nouvelle administration de 90'.

Alteplase push:
2 mg/2 ml of alteplase dilué dans NaCl 0,9%
/lumière : volume lumière+ 0.1 ml
Bolus 0.3 ml NaCl 0,9% /10', 2x
Après 30' vérification permébilité

Catheter dysfunction was defined :
- Inability to aspirate the catheter to initiate dialysis
- Inability to maintain a blood flow (pump speed) of 200 ml/min on dialysis with arterial and venous pressures not exceeding ± 250 mmHg, respectively.
- The dialysis nurses assessed all other possible causes of
catheter dysfunction including the patients' positioning, problems with the dialysis tubing, fluid status and hypotension before patients were considered for treatment with alteplase.

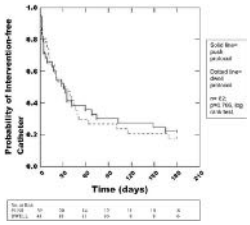
Critère de jugement =
% Cathéters débitant ≥300 ml/min

Clinical Nephrology, Vol. 78 – No. 4/2012 (287-296)

Alteplase for blood flow restoration in hemodialysis catheters: a multicenter, randomized, prospective study comparing "dwell" versus "push" administration

Lavern M. Vercaigne[1], James Zacharias[2], Keevin N. Bernstein[2]
and the PUSH Protocol Investigators

- Résultats non significatifs mais il y a une tendance en faveur de « Push »:
  - Débit ≥300 ml/min : 82% vs 65% (p=0,08)
  - Débit moyen obtenu : 318 ± 56 ml/min vs 302 ± 81 ml/min
  - Gain de débit : 194 ± 88 ml/min vs 157 ± 110 ml/min



Clinical Nephrology, Vol. 78 – No. 4/2012 (287-296)

Options thérapeutiques pour le manchon fibrineux

- 1ère intention = Thrombolyse
  - urokinase 250,000 U dans 250 ml de NaCl 0,9% à 30 ml/h sur chaque voie (4h)
  - rt-PA 2,5 mg dans 50 ml à 17 ml/h sur chaque voie (3h)
  - *Protocole perso : 100.000 unités d'urokinase ou 2 mg d'altéplase dans 50 ml de NaCl 0,9% à passer à un débit de 50 ml/h sur chaque voie à traiter en 1 heure*
- En cas d'échec:
  - Ablation et repose dans une autre veine
  - Changement sur guide
  - Changement sur guide avec destruction du manchon par angioplastie
  - Stripping par voie fémorale
  - Souvent un résultat immédiat intéressant mais des dysfonctions à répétition ensuite…

Gray, JVIR 2000
Savader, J Vasc Interv Radiol 2000
Oliver, CJASN 2007
Janne d'Othée, J Vasc Interv Radiol 2006

Thrombus mural

- A l'endroit où le cathéter frotte la paroi veineuse (TVBC ou VCS)
- Souvent associé à un cathéter jug gauche trop court qui butte contre la paroi de la VCS
- Peut donner une dysfonction de cathéter qui doit être retiré ± anticoagulation
- Diagnostic par angiographie ou angioscanner

Thrombose de veine

- Fémorale, Jugulaire, sous-clavière, TBC ou VCS
- Favorisée notamment par un état procoagulant et la malposition de l'extrémité
- Clinique =
  - thrombose de veine de membre ou de VCS
  - embolie pulmonaire
  - asymptomatique
- Pas forcement de dysfonction du cathéter si l'extrémité est dans l'OD

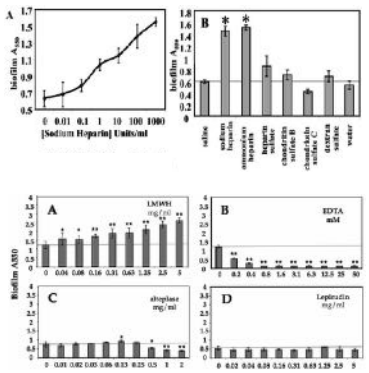
Thrombose de veine

- Diagnostic par échodoppler ou angioscanner
- Si symptomatique ou infection associée :
  - Anticoagulation 3 mois + retrait du cathéter
  - Si cathéter laissé en place par obligation, durée de l'anticoagulation ? jusqu'au retrait du cathéter ?
- Si asymptomatique
  - Anticoagulation discutée

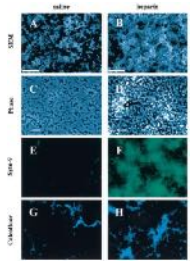
Prévention des infections liées aux cathéter

- Limiter l'utilisation des cathéters
- Cathéters tunnelisés > non tunnelisés
- Hygiène ++ à la pose et lors des manipulations (masque, gants stériles, charlotte)
- Désinfection à la chlorhexidine alcoolique 2% > povidone iodée
- Traitement de surface du cathéter : rien de démontré
- Bouchons : clearguard intéressant
- Verrous

Héparine et biofilm



S. Aureus



Shanks, Infect Immun 2005; Shanks, NDT 2006

Citrate et biofilm

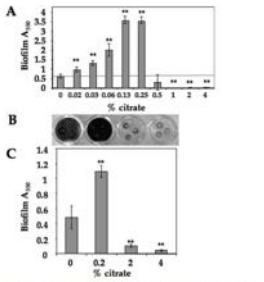


Fig. 1. Sodium citrate inhibits biofilm formation above 0.5%, but strongly stimulates biofilm formation at lower concentrations. (A) Biofilm formation of *S. aureus* strain MZ100 on polystyrene microtitre plates at 8 h in response to increasing concentrations of sodium citrate. (**B** and **C**) Biofilm formation was determined on silicon elastomer coupons as a function of citrate concentrations. Three coupons were attached to the bottom of each well of a 24-well polystyrene dish. At 20 h non-adherent bacterial cells were removed and biofilms were stained with crystal violet. (**B**) A digital photograph shows biofilm formation on polystyrene and silicon with respect to citrate concentration. (**C**) Coupons were removed, crystal violet was solubilized and measured spectrophotometrically (A550). The average crystal violet staining of nine coupons is shown. Error bars show one SD; ***P*-value of <0.01.

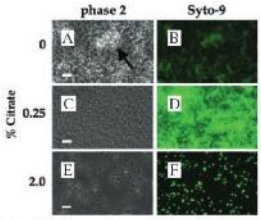
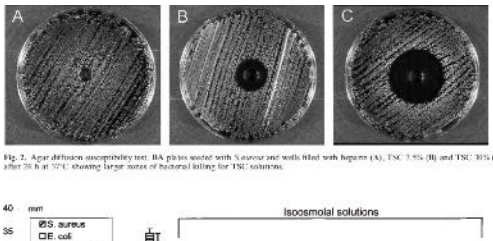


Fig. 2. Microscopic analysis of citrate exposed biofilms. Micrographs of 4 h biofilms formed on polystyrene in response to citrate concentration, shown as citrate percent (wt/vol). Images magnified 400 x were observed with phase microscopy (**A**, **C**, **E**) and stained with a fluorescent dye, Syto 9, that preferentially stains living bacterial cells (**B**, **D**, **F**). Bars = 2 μ.

Shanks, NDT 2006

Citrate et croissance bactérienne



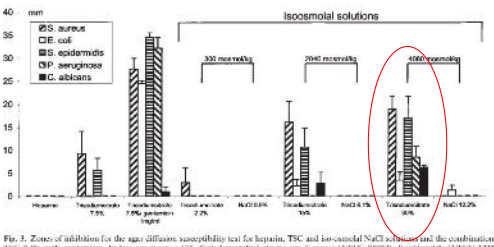
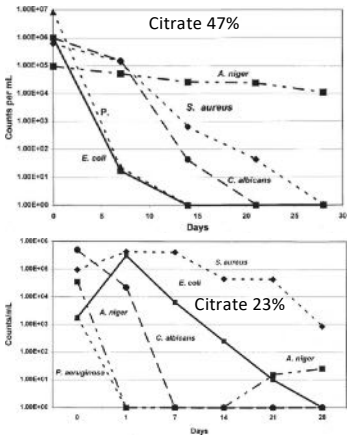


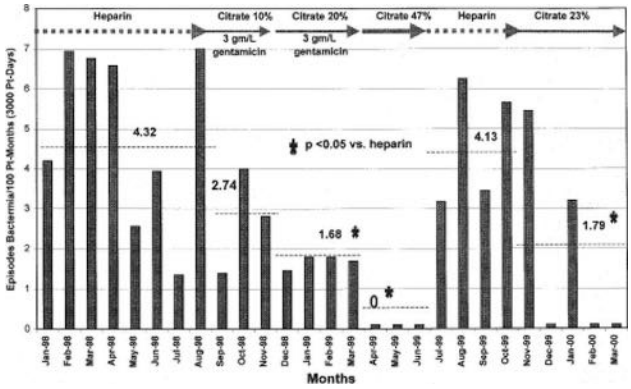
Fig. 3. Zones of inhibition for the agar diffusion susceptibility test for heparin, TSC and iso-osmolal NaCl solutions and the combination of TSC 7.5% with gentamicin. Values are means ± SD. Tested microbial strains are *S.aureus* (ATCC 25923), *S.epidermidis* (ATCC 12228), *P.aeruginosa* (ATCC 25922), *E.coli* (ATCC 25853) and *Ca.albicans* (ATCC 90028).

Weijmer, NDT 2002



Ash, Hemodial Int 2000

Efficacité du citrate concentré sur les bactériémies



Ash, Hemodial Int 2000

DOI: 10.1111/aor.14331

HISTORY

Artificial Organs WILEY

Concentrated sodium citrate catheter lock: "The best laid schemes o' mice an' men..."

Stephen R. Ash[1,2,3]

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[2]HemoCleanse Technologies, LLC, Lafayette, Indiana, USA
[3]Ash Access Technology, Inc., Lafayette, Indiana, USA

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Stephen R. Ash, HemoCleanse Technologies, LLC, 3601 Sagamore Parkway North, Suite B, Lafayette, IN 47904, USA.
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Abstract

Our laboratory's in vitro studies showed that sodium citrate at concentrations from 23% to 47% is antibacterial, and a non-randomized clinical trial showed that its use as a lock solution in dialysis catheters greatly decreased the incidence of CRBSI. The licensee placed 30 ml bottles of 47% sodium citrate in kits containing the Ash Split Cath, with *clear* instructions to dilute the solution and inject *only* the catheter volume as a catheter lock. Gross misuse of the solution by one physician led to a serious adverse outcome. FDA instructed the company to remove the product from the market and issued a warning not to use concentrated citrate off-label. Sodium citrate at 23%–30% is widely used in Europe, without major complications or side effects. However, our EPO patent was contested by a Dutch company and they eventually prevailed.

In our original publication on concentrated sodium citrate as a catheter lock, we included an elaborate safety analysis, to determine what would be the expected toxicity from a citrate lock solution if, somehow, the sodium citrate lock was injected directly to the bloodstream. We predicted that 2 ml of 23% sodium citrate would cause no symptoms at all. This was confirmed by rapid injection to a "normal" volunteer (guess who?). A review of animal studies in the literature showed that injection of 10 catheter volumes (20 ml) of 23% sodium citrate would be expected to cause only transient hypotension and possibly some cardiac arrhythmias.[5] I felt that concentrated sodium citrate (23%) could greatly diminish the incidence of CRBSI in dialysis patients, improve their health and well-being, and save the cost and stress of catheter removal and replacements. I knew that the product would be safe in general use, as long as instructions were followed and common sense prevailed.

Taurolidine et croissance bactérienne

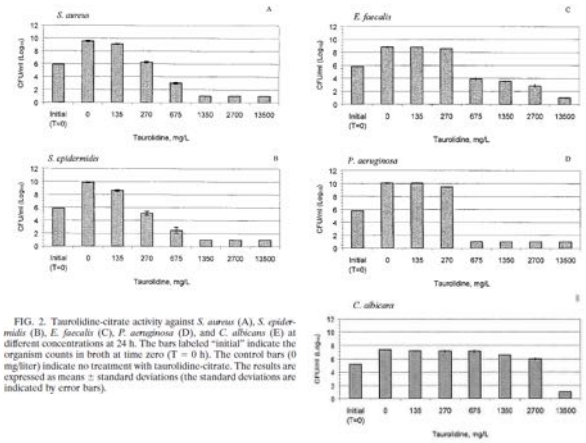


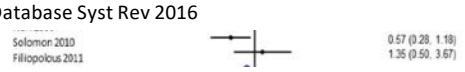
FIG. 2. Taurolidine-citrate activity against *S. aureus* (A), *S. epidermidis* (B), *E. faecalis* (C), *P. aeruginosa* (D), and *C. albicans* (E) at different concentrations at 24 h. The bars labeled "initial" indicate the organism counts in broth at time zero (T = 0 h). The control bars (0 mg/liter) indicate no treatment with taurolidine-citrate. The results are expressed as means ± standard deviations (the standard deviations are indicated by error bars).

Shah, Antimicrob Agents Chemother 2002

Efficacité des verrous sur les bactériémies

- De nombreuses études, de méthodologie souvent médiocre
  - Beaucoup d'études avant-après$
  - Effectifs faibles
  - Cathéters tunnelisés ou non
  - Cathéters prévalents ou incidents
  - CKD et/ou AKI
- Quelques méta-analyses
- Résultats divergents selon les critères de jugement, par exemple:
  - Zhao, AJKD 2014

  - Wang, Cochrane Database Syst Rev 2016

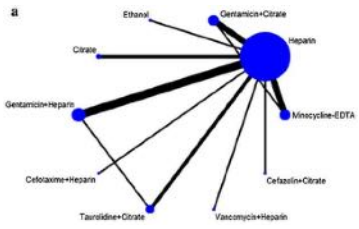


Int Urol Nephrol
DOI 10.1007/s11255-016-1490-x

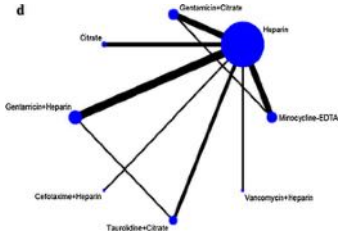
NEPHROLOGY - ORIGINAL PAPER

Does antimicrobial lock solution reduce catheter-related infections in hemodialysis patients with central venous catheters? A Bayesian network meta-analysis

Jun Zhang[1] · Bo Wang[2] · Rongke Li[1] · Long Ge[3] · Kee-Hsin Chen[4,5,6] · Jinhui Tian[3]



18 essais



Sensitive analysis, 16 essais

Int Urol Nephrol
DOI 10.1007/s11255-016-1490-x

NEPHROLOGY - ORIGINAL PAPER

Does antimicrobial lock solution reduce catheter-related infections in hemodialysis patients with central venous catheters? A Bayesian network meta-analysis

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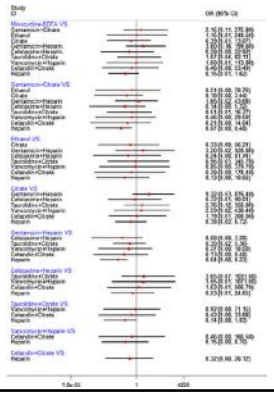
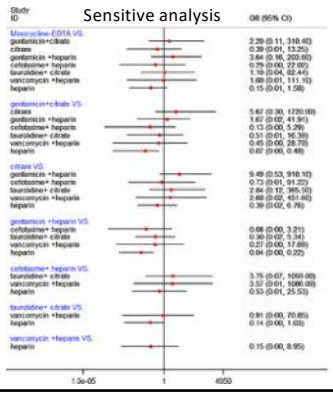
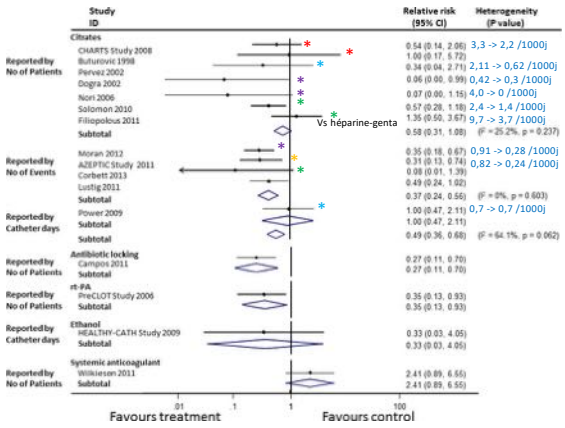


Sensitive analysis



Stratégies de prévention des bactériémies

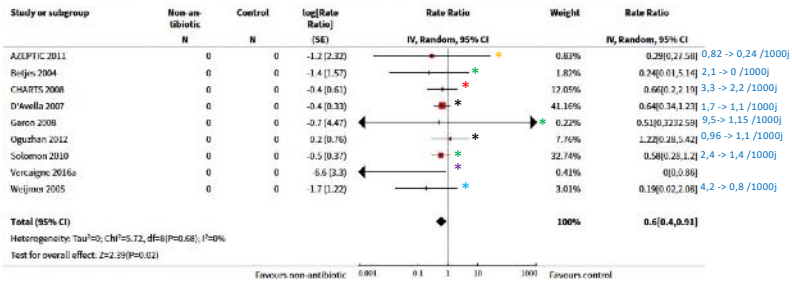


* Citrate 4%
* Citrate 47%
* Citrate 4% + gentamycine
* Citrate 4% + taurolidine
* Citrate 7% + bleu méthylène + parabènes

Wang Y, Ivany JN, Perkovic V, Gallagher MP, Woodward M, Jardine MJ.
Anticoagulants and antiplatelet agents for preventing central venous haemodialysis catheter malfunction in patients with end-stage kidney disease.
Cochrane Database of Systematic Reviews 2016, Issue 4. Art. No.: CD009631.
DOI: 10.1002/14651858.CD009631.pub2.

Stratégies de prévention des bactériémies

Analysis 5.6. Comparison 5 Non-antibiotic antimicrobial lock solutions versus control, Outcome 6 Subgroup analysis: catheter-related infection (per 1000 catheter-days) in tunnelled catheters.



* Citrate 4%
* Citrate 30%
* Citrate 4% + ethanol 30%
* Citrate 4% + taurolidine
* Citrate 7% + bleu méthylène + parabènes
* NaCl 18%-27%

Arechabala MC, Catoni MI, Claro JC, Rojas NP, Rubio ME, Calvo MA, Letelier LM.
Antimicrobial lock solutions for preventing catheter-related infections in haemodialysis.
Cochrane Database of Systematic Reviews 2018, Issue 4. Art. No.: CD010597.
DOI: 10.1002/14651858.CD010597.pub2.

Efficacité des verrous sur les bactériémies

- Les verrous antibiotiques fonctionnent très bien mais exposent à un risque de résistance, d'ototoxicité, etc.
- Citrate seul et taurolidine - citrate font probablement mieux que l'héparine, si on l'applique dès la pose, sauf si on a un taux de bactériémie déjà très bon (<1/1000 jours)
- Entre taurolidine et citrate, pas de différence évidente d'efficacité, mais de coût
- Sur le plan purement microbiologique et in vitro, le citrate concentré fait mieux que le citrate 4%

Intérêt de thrombolyses préventives ?

- Hemmelgarn, NEJM 2011
  - Alteplase 1mg/voie 1x/sem + HNF 5000 UI /voie 2x/sem vs HNF 3x/sem
  - Cathéters tunnelisés incidents
  - Réduction par 2 des dysfonctions et par 3 des bactériémies
  - Manns, JASN 2014 :
    - pas de différence significative de coût global
    - Avantage économique de l'alteplase si taux de bactériémie élevé (>2/1000j)

- Winnicki, Kidney Int 2018
  - Taurolock-U 1x/sem + Taurolock-Hep 2x/sem vs citralock 4% 3x/sem
  - Cathéters tunnelisés incidents
  - Réduction de 75% des infections (que des gram neg) et de 60% des dysfonctions
  - Réduction des coûts de 43%

- Bonkain, Plos One 2021
  - Taurolock-U 1x/sem + Taurolock-Hep 2x/sem vs Taurolock-Hep 3x/sem
  - Réduction des thrombolyses de 63%
  - Pas d'infection

➢ La thrombolyse hebdomadaire systématique réduit donc les dysfonctions et les bactériémies ainsi que probablement les coûts

KDOQI CLINICAL PRACTICE GUIDELINE FOR VASCULAR ACCESS: 2019 UPDATE

AJKD Vol 75 | Iss 4 | Suppl 2 | April 2020

Intraluminal Strategies

24.3 KDOQI suggests that the selective use of specific prophylactic antibiotic locks can be considered in patients in need of long-term CVC who are at high risk of CRSBI (eg, multiple prior CRSBI), especially in facilities with high rates of CRBSI (eg, >3.5/1,000 days). *(Conditional Recommendation, Low-Moderate Level of Evidence)*

Note: Under these circumstances and given the current data, KDOQI considers it reasonable for prophylactic use of specific antibiotics: cefotaxime, gentamicin, or cotrimoxazole (TMP-SMX). KDOQI cannot support the routine prophylactic use of antibiotic locks with very low supporting evidence (Table 24.1).

24.4 KDOQI suggests that the selective use of specific prophylactic antimicrobial locks can be considered in patients in need of long-term CVC who are at high risk of CRSBI, especially in facilities with high rates of CRBSI (eg, >3.5/1,000 days). *(Conditional Recommendation, Low-Moderate Quality of Evidence)*

Note: Under these circumstances and given the current data, KDOQI can support the prophylactic use of methylene blue. KDOQI cannot support the routine prophylactic use of antimicrobial locks with very low supporting evidence (Table 24.1).

24.5 KDOQI suggests that the selective use of once weekly prophylactic CVC locking with thrombolytic agent (recombinant TPA) can be considered in patients in need of long-term CVC who are at high risk of CRSBI, especially in facilities with high rates of CRBSI (eg, >3.5/1,000 days). *(Conditional Recommendation, Moderate Quality of Evidence)*

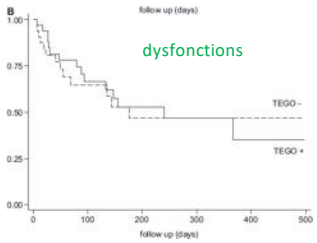
Note: Under these circumstances and given the current data, KDOQI can support the prophylactic use of recombinant TPA.

Note: High-risk patients refers to those with prior multiple CRSBI, S aureus nasal carriers.

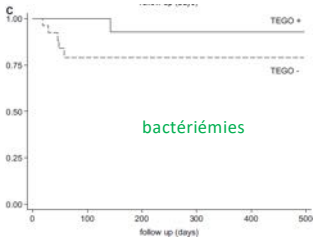
Et les bouchons ou autres dispositifs ??

Prevention of Tunneled Cuffed Hemodialysis Catheter–Related Dysfunction and Bacteremia by a Neutral-Valve Closed-System Connector: A Single-Center Randomized Controlled Trial

Florence Bonkain, MD,[1] Judith Racapé, PhD,[1] Isabelle Goncalvez,[1] Micheline Moerman,[1] Olivier Denis, MD, PhD,[2] Nadia Gammar,[1] Karine Gastaldello, MD,[1] and Joëlle L. Nortier, MD, PhD[1]



dysfonctions



bactériémies

66 patients patients incidents ou prévalents
Citrate 46,7% vs Tego + NaCl 0,9%

Table 2. Incidence Rates of Outcomes

Complication	No. of Events	Events/100 Person-Years	RR (95% CI)	*P*
Dysfunction or bacteremia	16 vs 18	63.56 vs 71.51	0.72 (0.37-1.42)	0.3
Dysfunction	15 vs 13	59.59 vs 51.64	0.94 (0.45-1.97)	0.9
Bacteremia	1 vs 5	3.97 vs 19.86	0.16 (0.02-1.39)	0.06

Note: Data shown as intervention group versus control group.

Am J Kidney Dis. 2013;61(3):459-465

Dialysis Catheter–Related Bloodstream Infections: A Cluster-Randomized Trial of the ClearGuard HD Antimicrobial Barrier Cap

Jeffrey L. Hymes, MD,[1] Ann Mooney, MSN, RN, CNN,[2] Carly Van Zandt, MS,[2] Laurie Lynch, PhD,[3] Robert Ziebol, BS,[3] and Douglas Killion, MBA[3]

Am J Kidney Dis. 2016;

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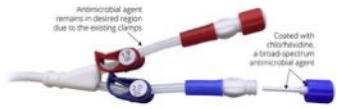

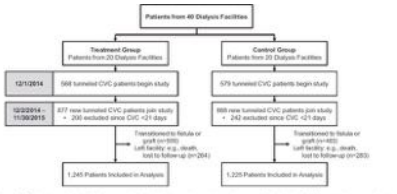

Figure 2. Patient count during follow-up period for the intervention and control groups. Abbreviation: CVC, central venous catheter.

Pratiques standards:
- masque, charlotte, gants stériles
- Désinfection systématique de l'émergence à la chlorehexidine 2% alcoolique
- Désinfection 15 secondes à l'alcool 70% des extrêmités à chaque déconnexion
- Vérrou Héparine – NaCl

Table 2. Twelve-Month Comparison of Rates for Bloodstream Infections, Cause-Specific Hospitalizations, and IV Antibiotics

	Episodes/1,000 CVC-Days		Poisson Regression	
	Intervention Group	Control Group	IRR (95% CI)	*P*
Primary end point: positive blood culture episodes	0.26	0.59	0.44 (0.23-0.83)	0.01
Secondary end points				
No. of hospital admissions for BSI	0.28	0.47	0.60 (0.37-0.97)	0.04
No. of hospitalization-days for BSI	3.24	4.68	0.69 (0.41-1.16)	0.2
No. of IV antibiotic starts	1.68	1.78	0.94 (0.74-1.19)	0.6

Abbreviations: BSI, bloodstream infection; CI, confidence interval; IRR, incidence rate ratio; IV, intravenous.

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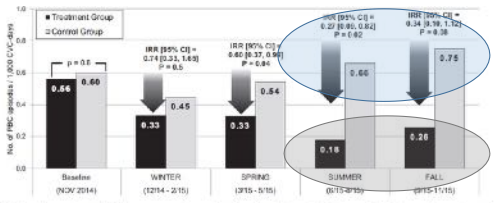

Effet de la chaleur et de la sudation ?

Disparition des anciens KT, ne restent plus que les incidents

Figure 4. Baseline and quarterly follow-up comparison of positive blood culture (PBC) rates for the intervention and control groups. Abbreviations: CI, confidence interval; CVC, central venous catheter; IRR, incidence rate ratio.

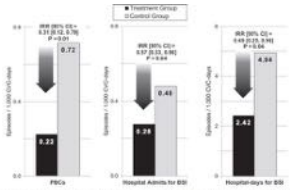

Figure 5. Comparison of sustained rates (last 6 months) for positive blood cultures (PBCs), hospital admissions for bloodstream infection (BSI), and hospitalization-days for BSI for the intervention and control groups. Abbreviations: CI, confidence interval; CVC, central venous catheter; IRR, incidence rate ratio.

Cluster-Randomized Trial of Devices to Prevent Catheter-Related Bloodstream Infection

Steven M. Brunelli,[1] David B. Van Wyck,[2] Levi Njord,[2] Robert J. Ziebol,[3] Laurie E. Lynch,[3] and Douglas P. Killion[3]

[1]DaVita Clinical Research, Minneapolis, Minnesota; [2]DaVita, Inc., Denver, Colorado; and [3]Pursuit Vascular, Inc., Maple Grove, Minnesota

Randomisation par centre

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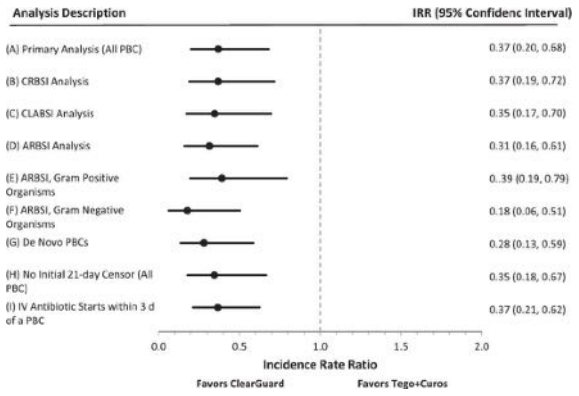

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U-plug

- Conception française (Caen)
- Résultats préliminaires intéressants

- Mais l'entreprise qui le fabrique a fait faillite…

Pour finir, mon opinion

- Pour un patient a faible risque infectieux, à faible risque hémorragique, dans un centre de dialyse avec une incidence faible d'infections, un verrou héparine fera l'affaire
  - Mais pour réduire les dysfonctions je ferais quand même une thrombolyse hebdomadaire
- Mais qui connait son taux d'incidence de bactériémies ?
- Combien de patients dialysés sur cathéter sont à faible risque hémorragique et infectieux ?
- Est-ce qu'il est bien d'utiliser plusieurs verrous dans un même centre ?
- L'héparine il faut la préparer, le citrate est prêt à l'emploi
- Le citrate ne coûte pas cher et in-vitro il est largement meilleur que l'héparine sur le plan microbiologique, notamment le citrate concentré
- Innocuité totale du citrate concentré lorsqu'il est utilisé comme recommandé
- Chez nous j'ai proposé l'utilisation de citrate 47% en standard avec une thrombolyse hebdomadaire systématique par taurolock-U
- Pour les désobstructions, urokinase 100.000 UI / voie en 30'
- Si suspicion de gaine de fibrine, Urokinase IVSE 100.000/50ml/1h/voie
- Clearguard : doit être appliqué dès la pose, semble très efficace pour prévenir les bactériémies mais ne règle pas le problème des dysfonctions