

# A Randomised Double-blind Trial of Taurolidine-Citrate Catheter Locks for the Prevention of Bacteraemia in Cuffed and Tunnelled Haemodialysis Catheters

Laurie R Solomon1 FRCP, John C Cheesbrough2 FRCP, Leonard Ebah1 MRCP, Tamer Al-Sayed1 MRCP, Michael Heap1 RGN, Nick Millband1 MBChB, Dee Waterhouse3 RGN, Sandip Mitra3 FRCP, Alan Curry4 PhD, Rema Saxena 5 MRCP, Rammoan Bhat 5 MRCP, Michael Schultz5 FRCP, Peter Diggle PhD6

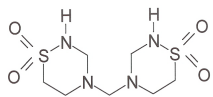
1Renal Unit and 2Department of Microbiology, Lancashire Teaching Hospitals, Royal Preston Hospital, Sharoe Green Lane, Fulwood, Preston, Lancashire PR2 9HT, UK  
 3Renal Unit, Manchester Royal Infirmary, Oxford Road, Manchester, M13 9WL, UK  
 4Health Protection Agency, Clinical Sciences Building, Manchester Royal Infirmary, Oxford Road, Manchester, M13 9WL, UK  
 5Renal Unit, Royal Liverpool Hospitals, Prescot Street, Liverpool L7 8XP  
 6CHICAS, Division of Medicine, School of Health & Medicine, B7 Faraday Building, University of Lancaster, Lancaster LA1 4YB

## Haemodialysis –related bacteraemia

Haemodialysis-related bacteraemia usually occurs in patients with tunneled catheters and is associated with morbidity, hospitalisation and mortality.

Antibiotic locks reduce infection but may be associated with antibiotic resistance.

## Taurolidine



## Properties

Taurine Derivative  
 Non-toxic  
 Bactericidal  
 Active against MRSA  
 Fungicidal  
 Anti-inflammatory  
 Does not cause antibiotic resistance  
 Has been available many years and been administered intravenously

## Taurolidine-citrate (Uncontrolled Studies)

Very low bacteraemia rate in nutrition catheters  
 Reduces infection rates in paediatric central venous access  
 May eradicate catheter-related blood stream infections unresponsive to systemic antibiotics

## Taurolidine-citrate (haemodialysis studies)

One non-randomised trial in established catheters found reduced bacteraemia but increased need for thrombolytic therapy  
 Several anecdotal reports of reduced infection rates  
 No randomised trial  
 The increased need for thrombolytic therapy may have been due to pre-existing biotin

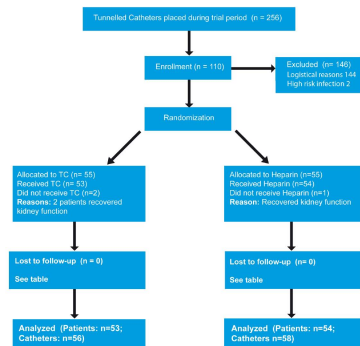
## Hypothesis

Taurolidine-citrate (TC) reduces the incidence of bacteraemia in haemodialysis patients using tunneled intravascular catheters compared to standard heparin locks and that, if started at the time of catheter insertion, might not be associated with more occlusions requiring thrombolytic therapy.

## Trial Protocol

1.35% Taurolidine in 4% Citrate versus Heparin 5000 U/ml  
 Double blind  
 Tunnelled and Cuffed Catheters only  
 1:1 Randomised permuted blocks of 10  
 Stratified by Centre  
 From time of line insertion  
 3 Main and 10 Satellite Dialysis Units  
 No change to standard clinical practice  
 Every positive blood culture counted (i.e. all cause bacteraemia)  
 All use of thrombolytics recorded  
 Replacement catheters could continue in same arm of trial

## Trial Flow Diagram



## Demographics

| Patient Details                |              |              |        | Catheter Type        |    |         |
|--------------------------------|--------------|--------------|--------|----------------------|----|---------|
|                                | TC           | Heparin      | P      |                      | TC | Heparin |
| No. Patients                   | 53           | 56           | 0.7    | Number of Patients   | 53 | 54      |
| Sex: Male                      | 52           | 53           | 0.7    | Number of Catheters  | 58 | 58      |
| Age (Mean±SD)                  | 59.8 (±14.7) | 56.7 (±13.4) | 0.3    | <b>TC Catheters</b>  |    |         |
| Male                           | 29           | 41           | 0.009  | Lock users (n/total) |    |         |
| Race: White                    | 47           | 49           | 0.8    | Anti-Spirt Cath      | 31 | 34      |
| Asian                          | 4            | 5            | <0.001 | Distal Catheters     | 1  | 1       |
| Black                          | 1            | 0            | <0.001 | Circlet              | 2  | 2       |
| Mixed/Other                    | 1            | 0            |        | Circlet-C            | 0  | 0       |
| Years on dialysis (Mean range) | 0.75 (0-13)  | 0.59 (0-6)   | 0.4    | Hemodialysis         | 8  | 6       |
| Cause of ESRD                  |              |              |        | Phen-Cath            | 0  | 1       |
| Diabetic (5)                   | 5            | 7            | 0.8    | Total                | 14 | 15      |
| Diabetic (7)                   | 7            | 7            | 0.8    | <b>Lockless</b>      |    |         |
| CKD (7)                        | 7            | 7            | 0.8    | Internal Jugular     | 66 | 67      |
| CKD (9)                        | 9            | 9            | 0.8    | Subclavian           | 1  | 1       |
| Other (11)                     | 11           | 11           | 0.8    |                      |    |         |
| Other (30)                     | 30           | 28           | 0.8    |                      |    |         |

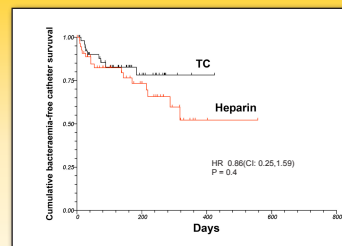
## Results (Intention to Treat)

|                      | Bacteraemic episodes |         |                             |                                  |                    |  |
|----------------------|----------------------|---------|-----------------------------|----------------------------------|--------------------|--|
|                      | TC                   | Heparin | TC (per 1000 catheter-days) | Heparin (per 1000 catheter-days) | P (based on ratio) |  |
| No. Patients         | 53                   | 54      |                             |                                  |                    |  |
| Bacteraemic Episodes | 11                   | 23      | 1.4                         | 2.4                              | 0.1                |  |
| Gram Pos             | 9                    | 12      | 1.1                         | 1.2                              | 0.8                |  |
| MSSA                 | 5                    | 6       |                             |                                  |                    |  |
| MRSA                 | 1                    | 2       |                             |                                  |                    |  |
| Other                | 3                    | 4       |                             |                                  |                    |  |
| Gram Neg             | 2                    | 11      | 0.2                         | 1.1                              | 0.02               |  |
| No. Catheter Days    | 8129                 | 9642    |                             |                                  |                    |  |

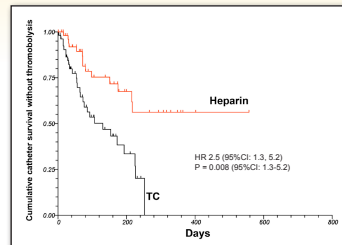
| Details of organisms         | Number of Bacteraemic Episodes per Patient |         |             |                  |
|------------------------------|--|---------|-------------|------------------|
|                              | TC   | Heparin | TC (n = 53) | Heparin (n = 54) |
| Staphylococcus aureus (MSSA) | 5  | 6       |             |                  |
| Staphylococcus aureus (MRSA) | 1  | 2       |             |                  |
| Escherichia coli             | 2  | 2       |             |                  |
| Klebsiella oxytoca           | 1  | 1       |             |                  |
| Stenotrophomonas maltophilia | 1  | 1       |             |                  |
| Enterobacter aerogenes       | 1  | 1       |             |                  |
| Campylobacter jejuni/jejuni  | 2  | 4       |             |                  |
| Haemophilus parainfluenzae   | 1  | 1       |             |                  |
| Serratia marcescens          | 1  | 1       |             |                  |
| Serratia liquefaciens        | 1  | 1       |             |                  |
| Streptococcus multiplies     | 1  | 1       |             |                  |
| Enterococcus faecalis        | 1  | 1       |             |                  |

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Time to First Bacteraemic Episode



Time to First Use of Thrombolytic Therapy



## Exit Site Infection

|                     | TC | Heparin |
|---------------------|----|---------|
| Staph aureus (MSSA) | 5  | 2       |
| Staph aureus (MRSA) | 2  | 2       |
| Coliforms           |    |         |
| TOTAL               | 7  | 6       |

## Reasons for Catheter Removal or Trial Termination

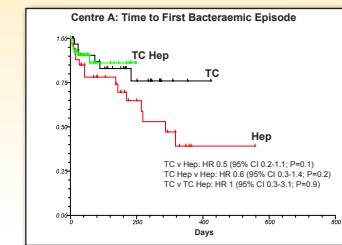
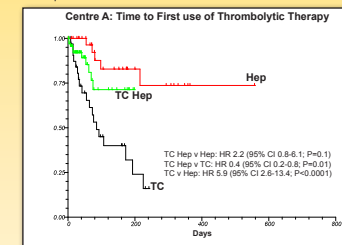
|                                   | TC | Heparin | P    |
|-----------------------------------|----|---------|------|
| Number Patients                   | 53 | 54      |      |
| Number Lines                      | 56 | 58      |      |
| Bacteraemia                       | 2  | 8       | 0.1  |
| Exit Site Infection               | 2  | 3       | 0.8  |
| Occlusion/flow problems           | 8  | 3       | 0.06 |
| Patient Choice                    | 2  | 2       | 0.8  |
| Physician Choice                  | 1  | 0       | 0.2  |
| Heparin induced thrombocytopenia  | 1  | 0       | 0.2  |
| Recovered Renal Function          | 4  | 4       | 0.7  |
| Alternative Access Available      | 17 | 15      | 0.3  |
| Conversion to PD                  | 3  | 1       | 0.2  |
| Transplanted                      | 1  | 2       | 0.7  |
| Transfer to another Dialysis Unit | 3  | 4       | 0.9  |
| Catheter Fell Out                 | 0  | 1       | 0.3  |
| Deaths                            | 11 | 8       | 0.2  |
| <b>Causes of Death:</b>           |    |         |      |
| Unknown                           | 6  | 4       |      |
| Cardiac                           | 2  | 1       |      |
| Staph Sepsis                      | 1  | 1       |      |
| Cirrhosis                         | 1  | 1       |      |
| Miliary tb                        | 1  | 1       |      |
| Myeloma                           | 1  | 1       |      |
| Unknown                           | 4  | 4       |      |
| Infected Toe                      | 1  | 1       |      |
| Mesothelioma                      | 1  | 1       |      |
| Myeloma                           | 1  | 1       |      |
| Peripheral Ischaemia              | 1  | 1       |      |

## Comparison Between Centres

|                   | Centre A |      | Centre B |      | Centre C |      |
|-------------------|----------|------|----------|------|----------|------|
|                   | TC       | Hep  | TC       | Hep  | TC       | Hep  |
| No. Pts           | 34       | 34   | 10       | 10   | 9        | 10   |
| Pt-days           | 5718     | 6470 | 1352     | 1846 | 1059     | 1326 |
| Bacteraemias      | 7        | 21   | 3        | 0    | 1        | 2    |
| Staph aureus      | 4        | 8    | 1        | 0    | 1        | 0    |
| Bact/1000 Pt-Days | 1.22     | 3.25 | 2.21     | 0    | 0.94     | 1.51 |

## Taurolidine-Citrate + 500 U/ml Heparin

Since March 2009 Centre A has used TC + 500 U/ml Heparin  
 72 consecutive patients  
 Open Label  
 Compared to retrospective data from Centre A



## Limitations

Small Numbers  
 All Cause Bacteraemia – not specific for Catheter-Related Bacteraemia  
 Other measures to reduce infections introduced over same time period

## Conclusions

Taurolidine citrate (TC) reduces the incidence of bacteraemia due to exogenous gram negative organisms in haemodialysis patients using tunneled cuffed catheters

TC does not reduce exit-site infections

TC is associated with a greater need for thrombolytic therapy

The size of benefit depends on the background rate of bacteraemia and may be greatest in patients at highest risk of infection

The addition of 500 U/ml heparin reduces need for thrombolytic therapy without increasing bacteraemia rates

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