

## Observational Study of Need for Thrombolytic Therapy and Incidence of Bacteremia using Taurolidine-Citrate-Heparin, Taurolidine-Citrate and Heparin Catheter Locks in Patients Treated with Hemodialysis

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### ABSTRACT

Catheter-related blood stream infections may be reduced by interdialytic locking with Taurolidine, a nontoxic antimicrobial agent. A formulation of 1.35% Taurolidine in 4% citrate (TC) is associated with a greater need for thrombolysis to maintain catheter patency than 5000 U/ml heparin. Our aim was to determine whether addition of 500 Units/ml of heparin to TC reduces the need for thrombolysis. TCH (1.35% taurolidine, 4% citrate and 500 U/ml heparin) was compared to TC and Heparin 5000 U/ml using retrospective data. Hundred and six adult hemodialysis patients with internal jugular tunneled intravascular catheters using TCH were compared with 34 patients using TC and 34 patients using heparin 5000 U/ml

respectively. Outcomes were time to first use of thrombolysis and bacteremia rates. TCH reduced the need for thrombolysis compared to TC (hazard ratio, 0.2; 95%CI: 0.06, 0.5;  $p < 0.001$ ) and was not significantly different from heparin 5000 U/ml (hazard ratio, 1.4; 95%CI: 0.5, 3.9;  $p = 0.5$ ). The bacteremia rates from all causes were 1.33, 1.22 and 3.25 per 1000 catheter-days ( $p < 0.001$ ) in the TCH, TC and heparin groups respectively. Addition of 500 U/ml heparin to TC reduces the need for thrombolysis without increasing bacteremia and may achieve patency comparable to heparin 5000 U/ml.

Catheter-related blood stream infections (CRBSIs) is the second most common cause of morbidity and mortality in patients with hemodialysis (1). Several randomized clinical trials and meta-analyses have demonstrated the efficacy of antimicrobial catheter locks including gentamicin, vancomycin and chlorhexidine for the prevention of CRBSI (2-7). An early complication and an emergence of bacterial resistance are potential concerns with antibiotic locks. There are reports of gentamicin-resistant *enterobacteriaceae* species developing when gentamicin is employed as a lock (8-10).

Taurolidine is a broad-spectrum antimicrobial agent that has been reported to reduce bacteremia rates in patients with hemodialysis, antibiotic and gentamicin

resistance (11, 12). It acts by a direct effect on bacterial cell walls and has never been associated with resistance (12,14,15). In a recent multicenter double-blind randomized-controlled trial, we compared catheter locks containing 1.35% taurolidine in 4% citrate (TC) with heparin 5000 U/ml and demonstrated a need for reduced use of thrombolysis and a significant reduction in gram-negative bacteremia (17). The present study was aimed to assess the need for thrombolysis therapy for catheters in two problems. The combined results from these other randomized trials (12,14,15) show that a preparation of taurolidine with 500 U/ml of heparin (TCH) has become available. We wished to determine whether the addition of 500 U/ml heparin catheter lock was comparable with 5000 U/ml heparin without affecting antimicrobial activity. It was no longer considered possible to undertake a randomized comparison with heparin because the Royal Association and European Royal Free Practice have recommended that an antimicrobial agent should be included in catheter locks (16,20). We therefore compared prospectively different bacteremia rates and need for thrombolytic therapy using TCH with retrospective data from our original trial (17).

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