TAUROLOCK (TAUROLOUIDINE CITRATE) VERSUS VANCOMYCIN IN PREVENTION OF HEMODIALYSIS CATHETER RELATED BLOOD STREAM INFECTION

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INTRODUCTION

Catheter-related bloodstream infection renamed recently as Central Line associated Blood Stream Infection CLABSI as defined by the CDC (Centers for Disease Control, Atlanta, USA) is a clinical definition and based on microbiological criteria on the one hand (a single blood culture for organisms not commonly present on the skin and two or more blood cultures for organisms commonly present on the skin) and clinical signs on the other (fever, chills and fever and/or hypotension), in a patient who has a central line at the time of infection or within the 48-hour period before development of infection. CRBSI constitutes a major clinical and economic problem. Despite general hygienic measures and programs with certain reductions in the infection rates, it is estimated that 80,000 episodes of CRBSI occur annually on intensive care units in the United States (2). If all hospital wards, not just the intensive care units, are considered, the total number of CRBSI episodes in one year would be closer to 250,000 (3).

CRBSI constitutes a major clinical and economic problem.
Catheter-related blood stream infection (CRBSI) present a common cause of morbidity and mortality in patients on regular Hemodialysis through catheter (3) . Several randomised clinical trials and meta-analyses have demonstrated the efficacy of antimicrobial catheter locks including gentamicin, minocycline and cefotaxime for the prevention of CRBSI (4-6).

Moreover, exposure of hemodialysis patients to multiple courses of antibiotics is likely to select for the emergence of infections that are highly resistant to multiple antibiotics (7). Obviously the most useful measure that should reduce the frequency of catheter-related blood stream infection is to decrease the number of patients using a dialysis Catheter, however this goal still not achieved properly worldwide secondary to multiple barriers, including the late referral of patients with chronic kidney disease to nephrologists, high primary failure rate of new arteriovenous fistulas, and frequent failure of arteriovenous grafts (8).

Traditional preferred management of central line–associated bloodstream infections (CLABSIs) involves central venous catheter (CVC) removal and the administration of systemic antimicrobial therapy. Catheter removal, however, is not always feasible in patients with limited vascular access or those unable to tolerate an interventional procedure (9).

The use of antimicrobial lock therapy in combination with systemic antimicrobials is an option for treatment of CLABSIs when the CVC is retained or in a prophylactic modality after CVC Insertion , antimicrobial lock therapy is a technique that involves the instillation of a highly concentrated antimicrobial solution, with or without additives such as anticoagulants, into the catheter lumen. Solutions are allowed to dwell (i.e., are “locked”) in the catheter lumen for an extended period to overcome microbial biofilm, often the nidus of infection(10).

Antimicrobial lock therapy is commonly used for CVC management in a prophylactic modality in patients with protracted central venous access for hemodialysis (HD), chemotherapy, or total parenteral nutrition (11-12).

Vancomycin have been extensively studies among other antibiotics for catheter lock solution it have shown consistent evidence of reducing CRBSI in hemodialysis catheters , however the drawback of emergence of resistant strains and loss of potent antibiotic against the gram positive organisms causing catheter related blood stream infection especially methicillin resistant staph aureus (MRSA ) and emergence of the more resistant strains vancomycin resistant staph aureus necessitates the researchers for a non antibiotic based catheter lock solution , effective and safe (13-14) . compatibility has been demonstrated with solutions of vancomycin, at concentrations ranging from 0.1 to 10 mg/ mL, and heparin sodium 100–5000 units/ MI (9,15)

More studies have demonstrated the effectiveness and safety profile of the novel agent Taurolouidine. Taurolidine 13.5 mg/mL has been evaluated as an ALT solution, with no incompatibilities reported. With added trisodium citrate citrate 4%( taurolock ) as catheter lock solution with consistent good results in the literature (16-18). Zweich et al conducted atrial on a lock solution containing taurolidine 13 mg/mL, TSC 40 mg/ mL, and heparin sodium 500 units/ mL in patients on chronic HD for an average of 30.5 days, with no reported incompatibilities (19).

In view of the current evidence and as vancomycin was considered one of the most effective catheter lock solutions and in respect to its potency as effective treatment for the gram positive catheter related blood stream infection we considered studying the alternative catheter lock solution TAUROLOCK ( taurolouidine citrate ) for effectiveness and safety

PATIENTS AND METHODS

The study design is a prospective, open-label randomized trial conducted at a single medical center At Hemodialysis unit Ain Shams university hospital . 41 Patients were randomly assigned to receive interdialytic catheter locking with either vancomycin/ heparin (2.5 mg/ml vancomycin and 5,000 U/ml unfractionated heparin; ratio 1:3) (group V) or taurolidine/citrate (1.35% taurolidine and 4% sodium citrate; TauroLock TM, TauroPharm GmbH) (group T) at the end of each dialysis session and continuously since catheter insertion.

Inclusion crieteria included patient starting Hemodialysis through permanent catheter or internal jugular catheter either for initiation of Hemodialysis or after 2ry failure of AV fistula/graft , age 18 years old and older, sign the informed consent and patient records confidentiality was assured. The lock solution was prepared by dialysis nurses at the end of each dialysis session, immediately before instillation into the catheter lumen, according to clear instructions and each administration was reported in the patient’s dialysis chart. 5-ml syringes were used, used for instellation of both catheter lumens (0.5 ml of vancomycin and 1.5 ml of heparin for group V , 2 ml of Taurolock for group T . Catheter lumen volume 1.9 ml as recorded on catheter patch).

We followed up the patients regarding total dialysis catheter days defined as the total days since catheter insertion till end of observation period . infection positive dialysis days defined as catheter days during episodes of infection since positive culture till clearance of infection and negative culture results. The infection negative catheter dialysis days are calculated as : (total catheter dialysis days – infection positive catheter dialysis days ). Episodes of infection and culture results calculated , and incidence of catheter infection per 1000 catheter dialysis days calculated by dividing infection episodes by the total dialysis catheter years ( days /365 ) Data was then tabulated, computerized statistically analyzed using SPSS 16 program.

RESULTS

Demographic data shown in table (1) showing no significant difference in study groups regarding age distribution with age 59.39 ± 15.69 and 57.83 ± 16.12 for vancomycin and Taurolock groups respectively. Figure (2) showing the type of catheter s in the study groups where majority of patients have permanant Hemodialysis catheters and only 5 patients had
DISCUSSION

As shown in Table 2, the comparison between the groups in the study using Student T-test for two independent variables showed that: the total dialysis days in vancomycin group (202.83 ± 97.88 days) was higher than in Taurolock group (189.17 ± 99.42 days) but without significant difference p value (0.663). And that there was infection positive dialysis days was higher in Taurolock group (22.09 ± 28.47 days) than the vancomycin group (18.47 ± 22.75 days) without statistical significance p value (0.622). Figure (5) showing the distribution of frequency between the two groups and showing that the majority of patients had less than 10 infection positive catheter dialysis days during the study period and the similarity between the two groups indicating comparable effectiveness of Taurolock to vancomycin in preventing catheter related blood stream infection.

Also in Table 2, the comparison between the study groups regarding episodes of infection per 1000 catheter dialysis days was slightly higher in vancomycin group (0.558 ± 0.466 infection episode /1000 catheter dialysis days) than aurolock group (0.528 ± 0.380 infection episode /1000 catheter dialysis days) however statistically insignificant. Both values are lower than detected with conventional heparin alone (1.68 episodes /1000 catheter days) and similar to gentamicin (0.45 episodes /1000 catheter days) antibiotic lock solution shown in anecent trial by Carol et al. (20)

FIGURES AND TABLES

Table 1 Demographics And Descriptive Statistics Of Study Groups

<table>
<thead>
<tr>
<th>Group Statistics of Catheter lock solution</th>
<th>N</th>
<th>Mean</th>
<th>Std. Deviation</th>
<th>Std. Error</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vancomycin group (18)</td>
<td>18</td>
<td>59.38</td>
<td>15.69</td>
<td>3.698</td>
</tr>
<tr>
<td>Taurolock (n 23)</td>
<td>23</td>
<td>57.82</td>
<td>16.12</td>
<td>3.36</td>
</tr>
<tr>
<td>Total dialysis days</td>
<td>T</td>
<td>23</td>
<td>1.891</td>
<td>20.73</td>
</tr>
<tr>
<td>Infection positive dialysis days</td>
<td>V</td>
<td>18</td>
<td>2.02</td>
<td>97.88</td>
</tr>
<tr>
<td>Infection negative dialysis days</td>
<td>T</td>
<td>23</td>
<td>22.08</td>
<td>28.47</td>
</tr>
<tr>
<td>Infection days</td>
<td>V</td>
<td>18</td>
<td>22.75</td>
<td>5.36</td>
</tr>
<tr>
<td>Infection days</td>
<td>T</td>
<td>23</td>
<td>92.8</td>
<td>21.87</td>
</tr>
<tr>
<td>Episodes of infection</td>
<td>T</td>
<td>23</td>
<td>1.28</td>
<td>0.3</td>
</tr>
<tr>
<td>Infection episodes per 1000 catheter dialysis days</td>
<td>V</td>
<td>18</td>
<td>0.563</td>
<td>0.466</td>
</tr>
</tbody>
</table>
| *p value significant at 0.005; **p value highly significant at 0.001

Table 2 Comparison between study groups using independent T-test

<table>
<thead>
<tr>
<th>Group Statistics of Infection positive catheter dialysis days</th>
<th>N</th>
<th>Mean</th>
<th>Std. Deviation</th>
<th>Std. Error</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age years (mean ±sd)</td>
<td>59.39 ± 15.69</td>
<td>57.83 ± 16.12</td>
<td>0.757</td>
<td></td>
</tr>
<tr>
<td>Catheter dialysis days (mean ±sd)</td>
<td>202.83 ± 97.88</td>
<td>189.17 ± 99.42</td>
<td>0.663</td>
<td></td>
</tr>
<tr>
<td>Infection positive catheter dialysis days (mean ±sd)</td>
<td>18.47 ± 22.75</td>
<td>22.09 ± 28.47</td>
<td>0.622</td>
<td></td>
</tr>
<tr>
<td>Infection free catheter dialysis days (mean ±sd)</td>
<td>185.83 ± 92.80</td>
<td>167.09 ± 95.36</td>
<td>0.531</td>
<td></td>
</tr>
<tr>
<td>Infection episode / patient (mean ±sd)</td>
<td>1.00 ± 1.28</td>
<td>1.13 ± 1.46</td>
<td>0.766</td>
<td></td>
</tr>
<tr>
<td>Episode of infection / 1000 catheter dialysis days (mean ±sd)</td>
<td>0.55±0.466</td>
<td>0.528±0.38</td>
<td>0.597</td>
<td></td>
</tr>
</tbody>
</table>

The current practice guideline states that current evidence supports its use, but more trials are lacking with more patients and more homogeneity in the therapy implemented (10). Taurolouidine citrate (Taurolock) have been studied for safety and efficacy as catheter lock solution the use of premixed low dose trisodium citrate 4% have been studied for its safety and efficacy without reported hypocalcemia or incidental arrhythmias that was found with higher citrate solutions (22-23).

Carol et al, conducted anecent trial comparing antibiotic lock solution with gentamycin against heparin showed better catheter survival and reduced mortality with the gentamycin group however the author concluded that The instillation of an antibiotic solution into the catheter during the interdialytic period can reduce the bacterial colonisation of the lumen and therefore prevent the development of a biofilm. Due to the leakage of the lock solution into the bloodstream, however, the prophylactic use of antibiotics is not recommended because of the resistance development of micro organisms and the corresponding side-effects (2).
Taurolock (Taurolouidine Citrate) Versus Vancomycin In Prevention Of Hemodialysis Catheter Related Blood Stream Infection

CONCLUSION

This study evaluated the comparative effectiveness of taurolouidine citrate (Taurolock) and a prophylactic antibiotic lock solution vancomycin on clinical outcomes in a hemodialysis population with a high incidence of CRBSI. Our findings confirm the results of prior work, which showed a significant reduction in CRBSI from the use of the same prophylactic antibiotic lock and comparable efficacy of both groups in preventing infection. Up to our knowledge this is the 1st trial comparing the effectiveness of Taurolock versus vancomycin in prevention of catheter related blood stream infection and interpretation of the results showed that Taurolock have comparable efficacy on reducing the rate of infection and maintain catheter survival as shown in the non significance difference between the studied groups in infection positive catheter dialysis days, rate of infection, infection episodes per 1000 catheter dialysis days.

Add on is the emergence of resistant strains of bacteria that can develop while using vancomycin which is an effective antibiotic for treatment for catheter related blood stream infection notably in methicillin resistant staphylococci as a prophylaxis catheter lock solution. Weak points of our study was the small sample size (41 patients), open randomization and short follow up period (mean 228 days), we suggest larger studies with higher sample size and longer follow up period with statistical analysis of the pattern of antibiotic strains and emergence of resistant strains with antibiotic lock solutions.

References

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