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RESEARCH ARTICLE

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

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ABSTRACT

Introduction: Central Line associated Blood Stream Infection CLABSI as defined 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 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 and 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

Patients And Methods: 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 or taurolidine/citrate; TauroLock at the end of each dialysis session and continuously since catheter insertion.

Results: 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 respectitively . majority of patients have permenant Hemodialysis cathters and only 5 patients had temporary internal jugular cathter (1 in vancomycin group and 4 in taurollock group), total dialysis days in vancomycin group (202.83 ± 97.88 days) 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 ± 28.47day) than the vancomycin group (18.47 ± 22.75 days) without statistical significance p value (0.622) , episodes of infection per 1000 cathter dialysis days was slightly higher in vancomycin group (0.558±0.466 infection episode /1000 cathter dialysis days) than Taurolock group (0.528±0.380 infection episode /1000 cathter dialysis days) however statistically insignificant .

Discussion: Our results regarding the reduction of cathter related blood stream infection by using vancomycin based cathter lock solution come in accordance with the results of recent metaanalysis in january 2015 conducted by Macarena *et al* (21) , The key messages of his analysuis are consistent with the findings of the individual systematic reviews identified recommends its use only in patients with multiple central venous catheter related blood stream infections .

Conclusion: Up to our knowledge this is the 1st trial comparing the effectiveness of Taurolock versus vancomycin in prevention of cathter related blood stream infection and interpretation of the results showed that Taurolock have comparable efficacy on reducing the rate of infection and maintain cathter survival

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(1).

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).

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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 cathter 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 antibioitic against the gram positive organisms causing cathter related blood stream infection especially methicillin resistant staph aureus (MRSA) and emergence of the more resistant strains vancomycin resistant staph aureus necessitate the researchers for a non antibiotic based cathter 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/ Ml .(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 cathter 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 cathter lock solutions and in respect to its potency as effective treatment for the gram positive cathter related blood stream infection we considered studying the alternative cathter lock solution TAUROLOCK (taurouloidine 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 permenant cathter or internal jugular cathter either for initiation of Hemodialysis or after 2ry failure of AV fistula/graft , age 18 years old and older, sign the informed conscent 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 . (Cathter lumen volume 1.9 ml as recorded on cathter patch) .

We followed up the patients regarding total dialysis cathter days defined as the total days since cathter insertion till end of observation period . infection positive dialysis days defined as cathter days during episodes of infection since positive culture till clearance of infection and negative culture results. The infection negative cathter dialysis days are calculated as : (total cathter dialysis days – infection positive cathter dialysis days). Episodes of infection and culture results calculated , and incidence of cathter infection per 1000 cathter dialysis days calculated by dividing infection episodes by the total dialysis cathter 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 respectitively. Figure (2) showing the type of cathter s in the study groups where majority of patients have permenant Hemodialysis cathters and only 5 patients had

temporary internal jugular cathter (1 in vancomycin group and 4 in taurollock group).

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) 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 ± 28.47day) 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 grouops and showing that the majority of patients had less than 10 infection positive cathter dialysis days during the study period and the similarity between the 2 grouos indicating comparable effectiveness of Taurolock to vancomycin in preventing cathter related blood stream infection .

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

DISCUSSION

Our results regarding the reduction of cathter related blood stream infection by using vancomycin based cathter lock solution come in accordance with the results of recent metaanalysis in january 2015 conducted by Macarena *et al* who reviewed 8 meta analysis and 17 randomized trials on rule of antibiotic in prevention of the cathter related blood stream infection and he concluded that The key messages of his analysuis are consistent with the findings of the individual systematic reviews identified recommends its use only in patients with multiple central venous catheter related blood stream infections(21).

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 cathter 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 arecent trial comparing antibiotic lock solution with gentamycin against heparin showed better cathter 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).

FIGURES AND TABLES

Table 1 Demographics And Descriptive Statistics Of Study Groups

Group Statistics					
	Cathterlock solution	N	Mean	Std. Deviation	Std. Error Mean
age	V	18	59.38	15.69	3.698
	T	23	57.82	16.12	3.36
Total dialysis days	V	18	2.02	97.88	23.07
	T	23	1.891	99.41	20.73
Infection positive dialysis days	V	18	18	22.75	5.36
	T	23	22.08	28.47	5.93
Infection negative dialysis days	V	18	1.85	92.8	21.87
	T	23	1.67	95.36	19.88
Episodes of infection	V	18	1	1.28	0.3
	T	23	1.13	1.45	0.3
Infection episodes per 1000 cathter dialysis days	V	18	0.563	0.466	1.57
	T	23	0.528	0.38	2.04

Table 2 Comparison between study groups using independent T- test

	Vancomycin group (n 18)	Taurlock (n 23)	P- value for independent t test
Age yers (mean±sd)	59.39 ± 15.69	57.83 ± 16.12	0.757
Cathter dialysis days (mean±sd)	202.83 ± 97.88	189.17 ± 99.42	0.663
Infection positive cathter dialysis days (mean±sd)	18.47 ± 22.75	22.09 ± 28.47	0.622
Infection free cathter dialysis days (mean±sd)	185.83± 92.80	167.09±95.36	0.531
Infection episode/ patient (mean±sd)	1.00 ±1.28	1.13± 1.46	0.766
Episode of infection / 1000 cathter dialysis days (mean±sd)	0.55±0.466	0.528±0.38	0.597

*P value significant at 0.005; **p value highly significant at 0.001

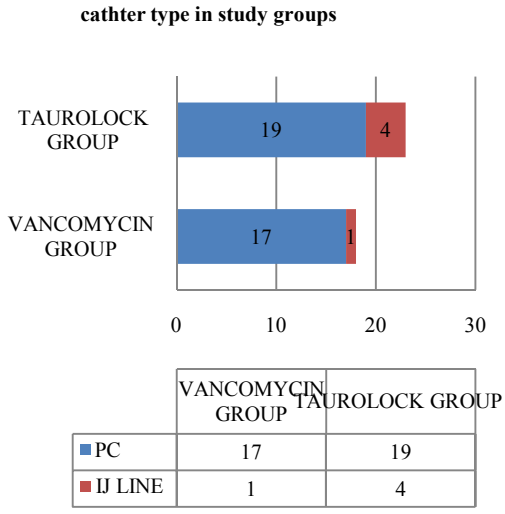
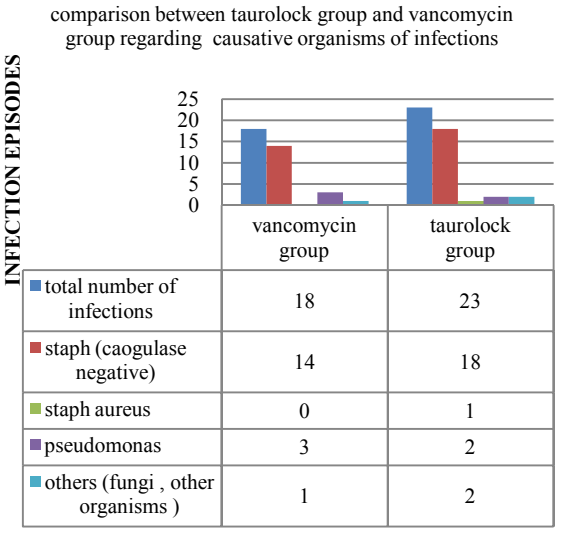


Figure 1 Cathter Type among Study Groups



	vancomycin group	taurolock group
total number of infections	18	23
staph (caogulase negative)	14	18
staph aureus	0	1
pseudomonas	3	2
others (fungi , other organisms)	1	2

Figure 2 causative organisms of infection episodes between study groups

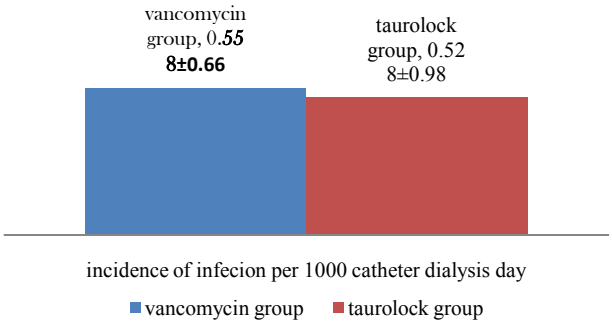


Figure 3 incidence of infection per 1000 cathter dialysis days

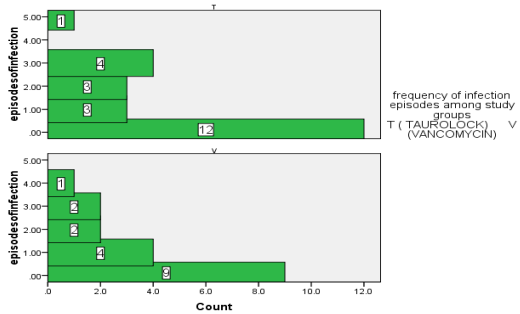


Figure 4 Frequency Of Occurrence Of Cathter Related Infecion Among The Study Groups

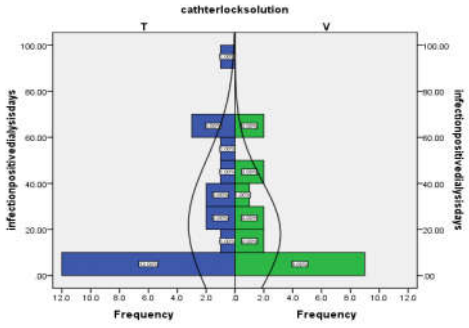


Figure 5 histogram showing frequency of distribution of infection positive cathter dialysis days

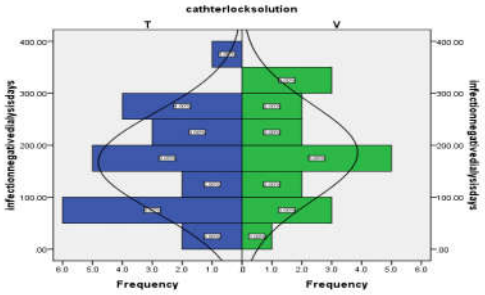


Figure 6 histogram showing frequency of distribution of infection negative cathter dialysis days

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 cathter related blood stream infection and interpretation of the results showed that Taurolock have comparable efficacy on reducing the rate of infection and maintain cathter survival as shown in the non significance difference between the studied groups in infection positive cathter dialysis days, rate of infection , infection episodes per 1000 cathter 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 cathter related blood stream infection notably in methicillin resistant staphylococci as a prophylaxis cathter 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 patteren of antibiotic strains and emergence of resistant strains with antibiotic lock solutions .

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