



Half dose of TauroLock; does it work?

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ABSTRACT

Introduction: Bacteremia is one of the most important complications in central vein catheter used in hemodialysis. TauroLock is known as an effective catheter lock solution (antimicrobial plus anticoagulant solution) in preventing catheter-related bacteremia (CRB). However, its cost is high and not covered by the most insurance companies.

Objectives: The aim of this study is to investigate the effect of the medication as a half dose for its economic advantages.

Patients and Methods: In this clinical trial study, 152 patients were divided into case (n=62) and control groups (n=90). In the case group, for 1 year, TauroLock and heparin were injected into the catheter's lumen (equal dose), but in the control group, only heparin was injected. For detecting bacteremia, blood cultures were obtained.

Results: According to the results, there was a significant difference in CRB between the two groups, at the base time, 3, 6 and 12 months after injection of TauroLock ($P < 0.05$). There was a significant difference in CRB, at the base time, 3, 6 and 12 months, after injection of TauroLock for the case group ($P < 0.05$), but there was no significant difference for the control group ($P < 0.05$). A positive effect in decreasing CRB was seen in the patients, based on age, sex, BMI, duration of hemodialysis, level of serum albumin, diabetes mellitus history and serum ferritin.

Conclusion: The catheter lock solution TauroLock, even in half dose, after each hemodialysis session, could significantly decrease the rate of CRB in hemodialysis patients

Implication for health policy/practice/research/medical education:

Usage of TauroLock as an antimicrobial drug that prevents CRB has been recommended in most studies, but the high cost of the drug prevents its widespread use in hemodialysis patients. Therefore, in this study the effect of TauroLock as a half dose for its economic advantages was investigated.

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Introduction

Hemodialysis is the most common renal replacement therapy in end-stage renal disease (ESRD). Vascular access is required to conduct hemodialysis and one of the most predominant ways is central venous catheter (CVC), while heparin lock is used to prevent thrombosis in catheters (1). Applying central venous catheter increases catheter-related bacteremia (CRB). A report stated that CRB rate was 2.5-5.5 times for every 1000-day dialysis that is equivalent to 0.9-2 times in performing one-year dialysis (2). CRB occurrence is related to the time distance between using catheters. In one study CRB has been reported 35% within 3 months and 48%

during 6 months of catheter insertion (3). This infection increases mortality, morbidity and extra costs for health care system. CRB may be predisposed to metastatic infections like osteomyelitis, endocarditis, septic arthritis and epidural abscess in 5%-10% of patients with catheter insertion (2,3). In fact, using catheters increasingly results in metastatic infections (4). The most common risk factor for CRB occurrence is the time of applying catheter. Other risk factors include recent surgery, diabetes mellitus, iron overload, immunosuppression and hypoalbuminemia (5,6). Using antibiotic lock solutions for preventing CRB is effective, especially in patients who are high risk. In a meta-analysis, it was detected that this method had a high

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risk of antibiotic resistance (7,8). TauroLock (Taurolidine and 4% citrate) was used in several studies while a meta-analysis that indicated its effectiveness and accordingly no side effects were reported (9,10).

It seems that the catheters locked by Taurolidine are an effective and safe way to reduce catheter-caused septicemia. Taurolidine contains a simple and general antibacterial effect. In vitro examinations with sub-inhibitory doses of Taurolidine did not cause the microorganism resistance (11). Therefore, it is unlikely that long-time TauroLock injection in dialysis line results to increase bacterial infections resistant to the drug. No side effects were reported for TauroLock, and this compound is quickly metabolized to Taurine and carbon dioxide. Using Taurolidine for a long-time is possible with no toxicity and its anti-adherence property results in protecting against bacteria and fungi adhering to central venous catheter (12).

Objectives

In this study, the preventive effect of the drug in patients with catheter in dialysis center of Imam Khomeini and Imam Reza hospitals in Kermanshah were assessed. For its economic advantages, TauroLock was used to fill a half catheter lumen (half dose) after each dialysis session, and the rest of the catheter lumen space was filled with heparin, by the impression that by a suitable response to this drug with half dose, we can prevent CRB occurrence at a lower cost, which is beneficial modality.

Patients and Methods

Study population

During 1 year, 152 patients including 62 in the case group (40.8%) and 90 in the control group (59.2%) were considered. Variables were as follows; age, gender, body mass index (BMI), time of using catheter (less or more than one year), using TauroLock, catheter infection, diabetes mellitus history, iron overload (ferritin >300 ng/mL), CRP and hypoalbuminemia (albumin >4 g/dL). The symptoms of CRB included fever and chills during dialysis, in the absence of other causes. For this category of patients, two blood cultures from catheters were done to the time interval of fifteen minutes. If the cultures were positive, CRB would be confirmed. The information about

patients like demographic data was analyzed in SPSS. Inclusion criteria were; patient under hemodialysis by catheter in dialysis center of Imam Khomeini and Imam Reza hospitals. They agreed to participate in this study. Accordingly, exclusion criteria were; IV drug abuse, changing dialysis from catheter to AVE, patients with surgical history and immunosuppression. After choosing patients, they were assimilated based on field variables. Causal layered analysis was conducted when they were not assimilated by goals.

Ethical issues

The research followed the tenets of the Declaration of Helsinki. The study was approved by the institutional ethics committee of Kermanshah University of Medical Sciences and was registered in Iranian Registry of Clinical Trials (identifier: IRCT2016020221066N2; <http://www.irct.ir/trial/18554>). Written informed consent was obtained from all participants too.

Data analysis

Quantitative data were reported by mean \pm standard deviation (SD) and qualitative data by percentage and frequency. Two groups were compared based on Mann-Whitney U and chi-square tests and were checked for assimilation by chi-square and independent t test. The significance level was 0.05. The data were analyzed by SPSS, version 22. Mann-Whitney U test was applied to compare the intervention and control groups for CRB, levels CRP, albumin level and ferritin level in dialysis patients with catheter during base time, 3, 6 and 12 months after injection of TauroLock. Chi-square test was applied to compare the intervention with the control group for CRB in dialysis patients with catheter based on age, gender, dialysis time, and diabetes mellitus history, level of serum albumin and ferritin.

Results

The results of descriptive properties and comparing age, gender, body mass index (BMI), time of using catheter and diabetes mellitus between case and control groups were shown in Table 1. There was no significant difference in mentioned terms between two groups ($P > 0.05$). Table 2 shows frequencies and comparing CRP and CRB in

Table 1. Descriptive properties and comparing age, sex, Body Mass Index (BMI), time of using catheter, diabetes mellitus history and bacteremia history resulted from catheter in dialysis patients of case and control groups

Feature		Group		P value
		Case	Control	
Age	Mean \pm SD	61.03 \pm 16.91	55.23 \pm 18.43	0.205
Sex	Male, No. %	32 (51.6)	63 (70.0)	0.192
	Female, No. %	30 (48.4)	27 (30.0)	
BMI	Mean \pm SD	22.48 \pm 4.46	24.17 \pm 4.27	0.115
Duration of use of catheter	Mean \pm SD	11.9 \pm 30.81	27.60 \pm 45.17	0.718
Diabetes mellitus history	Yes, No. %	18 (29.0)	27 (30.0)	1
	No, No. %	44 (71.0)	63 (70.0)	

dialysis patients with catheter in case and control groups during base time, 3, 6 and 12 months after injection of TauroLock. Intergroup comparison showed a significant difference in 6 ($P=0.046$) and 12 months ($P=0.002$) between two groups for CRP. Therefore the frequency of CRP in the case group was less than the control group. In addition, intergroup comparison showed a significant difference in 3 ($P=0.018$), 6 ($P=0.011$) and 12 months ($P=0.001$) between two groups for CRB; therefore, the frequency of CRP in the case group was less than the control group. Intragroup comparison showed that changings of frequency of CRP and CRB during time had just a significant difference in case group ($P=0.024$ and $P=0.002$, respectively) that the frequency with time had a reverse correlation.

Table 3 shows descriptive properties and comparing level of albumin and ferritin in two groups during base time, 3, 6 and 12 months after injection of TauroLock. Intergroup comparison showed no significant difference all times between two groups ($P>0.05$) for albumin and ferritin levels. Intragroup comparison showed just the changes of albumin level in case group during time had a significant difference ($P=0.027$) with a direct relationship.

Frequencies and comparing CRB in dialysis patients with catheter in two groups based on age, gender and BMI were shown in Table 4. There was a difference for CRB frequency between two groups in terms of age (<50 and >50 years: $P=0.037$ and $P=0.008$ respectively), gender (male and female: $P=0.002$ and $P=0.430$), and BMI (<25 and >25 kg/m^2 ; $P=0.035$ and $P=0.014$ respectively).

Frequencies and comparing CRB in dialysis patients with catheter in two groups based on dialysis time, diabetes, serum albumin and serum ferritin levels were shown in Table 5. There was a difference for CRB frequency between two groups in terms of time of dialysis (<1 and >1 years: $P=0.010$ and $P=0.033$ respectively), diabetes (yes and no: $P=0.031$ and $P=0.014$ respectively), base albumin level (<4 and >4 g/dL ; $P=0.015$ and $P=0.047$ respectively), and base ferritin level (<300 and >300 ng/mL ; $P=0.033$ and $P=0.004$ respectively).

Discussion

There was no significant difference among age, gender, BMI, time of using catheter and history of diabetes mellitus between the case and control groups. According to the most significant results, injecting TauroLock - with

Table 2. Frequencies and comparing CRP and CRB in dialysis patients with catheter in case and control groups during base time, 3, 6 and 12 months after injection of TauroLock

Variable	Measuring time	Group		Intergroup comparisons		
		Case, No. (%)	Control, No. (%)	Testing statistics	P value	
CRP	0	20 (32)	35 (39)	0.89	0.3734	
	3 months	16 (26)	35 (39)	1.71	0.0872	
	6 months	13 (19)	30 (33.3)	2	0.046	
	12 months	6 (9.7)	25 (27.7)	2.98	0.002	
	Intergroup comparisons	Testing statistics	9.45	3.76		
		P value	0.024	0.288		
CRB	3 months	10 (16.1)	27 (30.0)	2.08	0.018	
	6 months	8 (17.8)	28 (31.1)	6.73	0.011	
	12 months	6 (9.7)	30 (33.3)	11.36	0.001	
	Intergroup comparisons	Testing statistics	12	0.483		
		P value	0.002	0.786		

Table 3. Descriptive properties and comparing level of albumin and ferritin in case and control groups during base time, 3, 6 and 12 months after injection of TauroLock

Variable	Measuring time	Group		Intergroup comparisons	
		Case, Mean \pm SD	Control, Mean \pm SD	Testing statistics	P value
Albumin	0	3.62 \pm 0.25	3.52 \pm 0.4	1.1	0.27
	3 months	3.67 \pm 0.38	3.6 \pm 0.38	0.536	0.592
	6 months	3.8 \pm 0.43	0.68 \pm 0.38	0.106	0.106
	12 months	3.75 \pm 0.38	3.72 \pm 0.3	0.547	0.584
	Intergroup comparisons	Testing statistics	9.15	4.13	
	P value	0.027	0.248		
Ferritin	0	377 \pm 209.01	312.16 \pm 100.54	0.859	0.391
	3 months	358.9 \pm 145.01	324.16 \pm 93.37	1.108	0.272
	6 months	383.37 \pm 236.44	349.33 \pm 83.23	0.57	0.569
	12 months	399.19 \pm 324.31	356.06 \pm 90.71	0.902	0.367
	Intergroup comparisons	Testing statistics	3.68	2.93	
	P value	0.298	0.051		

Table 4. Frequencies and comparing CRB in dialysis patients with catheter in case and control groups based on age, sex and BMI

Variable	Feature	CRB	Group		P value
			Case, No. (%)	Control, , No. (%)	
Age (y)	Less than 50	Yes	0 (0.0)	8 (28.6)	0.037
		No	14 (100)	20 (71.4)	
	More than 50	Yes	6 (12.5)	22 (35.5)	0.008
		No	62 (87.5)	40 (64.5)	
Sex	Male	Yes	0 (0.0)	23 (31.9)	0.002
		No	19 (100)	49 (68.1)	
	Female	Yes	6 (14.0)	7 (38.9)	0.43
		No	37 (86.0)	11(61.1)	
BMI	Less than 25	Yes	2 (6.3)	8 (28.6)	0.035
		No	30 (93.8)	20 (71.4)	
	More than 25	Yes	4 (13.3)	22 (39.3)	0.014
		No	26 (86.7)	34 (60.7)	

Table 5. Frequencies and comparing CRB in dialysis patients with catheter in case and control groups based on dialysis time, diabetes, level of serum albumin and level of serum ferritin

Variable	Feature	CRB	Group		P value
			Case, No. (%)	Control, , No. (%)	
Time of dialysis	Less than 1 year	Yes	4 (8.3)	20 (28.2)	0.01
		No	44 (91.7)	51 (71.8)	
	More than 1 year	Yes	2 (14.3)	10 (52.6)	0.033
		No	12 (85.7)	9 (47.4)	
Diabetes	Yes	Yes	2 (10.5)	13 (39.4)	0.031
		No	17 (89.5)	20 (60.6)	
	No	Yes	4 (9.3)	17 (29.8)	0.014
		No	39 (90.7)	40 (70.2)	
Level of base albumin (mg/dL)	Less than 4	Yes	4 (9.5)	19 (31.1)	0.015
		No	38 (90.5)	42 (68.9)	
	More than 4	Yes	2 (10.0)	11 (37.9)	0.047
		No	18 (90.0)	18 (62.1)	
Level of base ferritin	Less than 300	Yes	6 (17.6)	20 (40.0)	0.033
		No	28 (82.4)	30 (60.0)	
	More than 300	Yes	0 (0.0)	10 (25.0)	0.004
		No	28 (100.0)	30 (75.0)	

half dose - and heparin decreased CRB in dialysis patients with catheter. The positive effects of compounding TauroLock (half dose) and heparin on decreasing CRB were observed in patients with following features; less or more than 50 years old age, male or female, with BMI less or more than 25, dialysis time less or more than one year, with or without diabetic history, with albumin level less or more than 4 g/dL and ferritin level less or more than 300 ng/mL ($P < 0.05$). Therefore, age, gender, BMI, duration of dialysis, duration of use of catheter, diabetes mellitus history, levels of albumin and ferritin had no effect on the performance of TauroLock.

To the best of our knowledge, no study investigated the effect of TauroLock -with half dose- and heparin on CRB in hemodialysis patients with catheter. But in recent studies, the positive effect of TauroLock on catheter related infections was reported among dialysis patients (13,14). Some studies have shown the prevention effect of TauroLock in CRB among hemodialysis patients. Al Malki et al found that compounding TauroLock and

heparin prevents CRB in hemodialysis patients (15). Fontseré et al stated that compounding TauroLock and heparin is effective in decreasing CRB in hemodialysis patients with catheter (16). Stein et al concluded that CRB in hemodialysis patients receiving TauroLock and heparin is less than patients who received just heparin (17). Similarly, Zwiech et al found that compounding TauroLock and heparin, compared to heparin, affected decreasing CRB among hemodialysis patients with catheter (18). Furthermore, Solomon et al concluded that adding 500 U/mL heparin to TauroLock can decrease the need for thrombolysis without increasing bacteremia (19). Liu et al found that antimicrobial solution like TauroLock with heparin could be the best preventative factor for CRB in hemodialysis patients (20). Likewise, Murray et al reported that using throline-citrate – heparin instead of heparin can be related to central venous catheter, as the catheter lock solution with 56% decrease in hemodialysis related infections (21). The results of this study are compatible with other mentioned studies.

Kavosi et al, in a meta-analysis, found that CRB in hemodialysis patients who used TauroLock, was less than hemodialysis patients who used heparin. However, they showed an unequal result that, TauroLock in comparison to the combination of heparin and gentamicin is not the preferable strategy to prevent CRB than TauroLock alone (22).

Solomon et al found no difference between bacteremia episodes in hemodialysis patients who used throline-citrate and who received heparin. In fact, using throline-citrate does not decrease bacteremia and needs thrombolytic therapy (23). The densities of throline, applied for lock solutions, are 1.35% to 2%. Still no studies have reported throline decrease in lumen catheter or the relationship between throline density and CRB (24).

Conclusion

According to the findings, medication of half-dose TauroLock, after each dialysis session, can decrease CRB among dialysis patients with central catheter. Under the positive effect of TauroLock in preventing catheter-related infections in dialysis patients, prescribing it beside other effective drugs in hemodialysis patients with catheter could be recommended.

Limitations of the study

Given the contradicting results of this and other studies, larger-scale studies are recommended to be conducted on the long-term effects of contrast agents on renal function.

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Authors' contribution

SG conducted the research and contributions to the conception and design of the research. HRO prepared the primary draft. NA contributed to the acquisition of data. ES contributed to the analysis of data. MRZ contributed to the drafting of the manuscript and final approval of the manuscript.

Conflicts of interest

The authors declare that they have no competing interest.

Ethical considerations

Ethical issues (including plagiarism, misconduct, data fabrication, falsification, double publication or submission, redundancy) have been completely observed by the authors.

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