

Catheter Related Infection (CRI): Comparison of Heparin Versus Citrate

Bilal Javaid, Adil Manzoor, Irfan Elahi, Salman Javaid

ABSTRACT

Objective: To compare heparin versus citrate in cases with end stage renal disease (ERSD) maintaining on hemodialysis. **Study Design:** Randomized Controlled Trial. **Settings:** Nephrology Department of Allied Hospital, Faisalabad-Pakistan. **Duration:** 01-09-2017 to 01-03-2018. **Methodology:** A total of 70 cases on hemodialysis were enrolled. Randomization was done for division of patients in two groups. Heparin was given in Group-A cases while citrate in B Group. Follow up of patients was done till next session of hemodialysis. We sent blood cultures to see any episode of CRI. **Results:** CRI was present in 37.1%(n=13) v/s 14.3%(n=5) in Group A & B, p: 0.029. **Conclusion:** Citrate as compared to heparin is having significant lower rate of CRI in cases on hemodialysis with ERSD. However, heparin may be used in routine practice.

Keywords: End stage renal disease, Hemodialysis, Catheter related infection, Citrate and heparin.

Corresponding Author

Submitted for Publication: 28-12-2018

Accepted for Publication: 16-03-2019

DR. BILAL JAVAID, Assistant Professor, Nephrology, Faisalabad Medical University, Allied Hospital, Faisalabad-Pakistan

Contact / Email: +92 321-7612484, dr.bilaljavaid160@gmail.com

Citation: Javaid B, Manzoor A, Elahi I, Javaid S. Catheter Related Infection (CRI): Comparison of Heparin Versus Citrate. APMC 2019;13(2):94-6.

INTRODUCTION

Worldwide, the rate of stage V chronic kidney disease (CKD) is increased on alarming figures.¹ Hemodialysis is initiated in these cases through central venous catheter.² Different kind of catheters and stents are also used in urological patients which results ultimately in increased incidence of infection.³ For vascular access, central venous catheters are commonly used in these cases. Unfortunately, around 25% to 50% failure of CVCs is recorded within first 12 months of insertion. Due to significant antibiotic exposure and longer hospital stay increases the healthcare cost, furthermore, higher rate of mortality is also associated with CVCs.⁴

Various studies emphasizes that relative risk (RR) is significantly higher for infection and mortality in CVCs as compared those with arteriovenous fistula.¹ Recent prospective trials reveal a greater risk of catheter-related bloodstream infection (CRBSI) in these cases and association of higher morbidity attributed to at least 10% of mortality rate.²

Various alternatives are considered to reduce the risk of catheter related infection i.e. chemical substances when used as locking solutions in the interdialytic period.¹ However, this practice reduces the risk of infection catheter related infection during dialysis session.

The use of Tunneled catheters (TCs) is frequent in cases requiring temporary/long-term hemodialysis (HD). Unfortunately, various complications relating to TC including infection and dysfunction are recorded. It prolongs hospital stay and higher mortality.⁵ Catheter locks are included in preventing strategies of catheter related infection and dysfunction, however, citrate and heparin are commonly used for this purpose.⁶

The use of heparin locks is indicated in cases with renal replacement therapy with reference to non-tunneled

haemodialyss catheter. However, unfractionated heparin is widely used as locking solution, it may be associated with a several complications including allergic reactions and heparin induced thrombocytopenia.⁷ It is difficult to handle anticoagulant effect of heparin in ICU due to association of bleeding and development of heparin-induced thrombocytopenia.⁷

Citrate is considered as an effect alternate to heparin for catheter lock solution. It exerts the anti-coagulant effect through its ability to chelate calcium. However, bacterial resistance is not recorded with the use of citrate as catheter lock solution.⁸

A study reported the Catheter related blood stream infections in 65% cases in the Heparin Group and in 35% cases in the Citrate Group.¹

Heparin is an anticoagulant and is usually used as catheter lock solution in CKD patients on HD. Rate of CRI is very high with heparin. Trisodium citrate is a good locking solution that can be used to reduce CRI episodes. But in routine often this is not administered. So, we want to conduct this study to prove that Citrate can prevent patient from developing CRI. Issue is important, however there is paucity of information as for as local data is concerned.

METHODOLOGY

Study Design: Randomized Controlled Trial.

Settings: Nephrology Department, Allied Hospital, Faisalabad-Pakistan.

Duration: 01-09-2017 to 01-03-2018.

Methods: Where a total of 70 cases (35 in each group) of either gender with diagnosis of ERSD on hemodialysis having central venous catheters inserted for hemodialysis of any age were included in the study. Whereas all cases with deranged LFTs (ALT>40IU, AST>40IU), medical record of current malignant diseases, pregnant females, severe anemia (Hb <7 g/dl), having

chronic hypertension (BP \geq 140/90mmHg on medical record), medical record of cardiac problems and INR \geq 2 were excluded from the study. A certificate from institutional ethical review committee was obtained, consent of the patients was also taken. Randomization was done in 2 equal groups. Patients in group A were given Heparin while patients in B group were given citrate. In group A, at the end of each haemodialysis session, each port of the catheter was filled with 5000 U/mL of unfractionated heparin solution according to the volume of the ports. In group B, dialysis catheter lumens were locked with citrate 30%. Upon completion of each dialysis session, all the citrate locks were instilled into both lumens of the dialysis catheter, and withdrawn immediately prior to the next dialysis session. Patients were followed up for next hemodialysis session. Blood cultures were obtained when catheter-related bacteraemia was clinically suspected (by fever and purulent discharge from catheter insertion site) and sent to the laboratory of the hospital. Reports were assessed and CRI episodes were noted. The data analysis contained mean values of age, serum creatinine, duration of hemodialysis and GFR whereas gender and catheter related infection episodes were recorded in form of frequency (%).

RESULTS

Most of the cases in both groups were recorded with >40 years of age, mean age was calculated as 51.37 \pm 12.116 in both groups. Table 1

Table 1: Age distribution (n=70)

		Group		Total
		Heparin	Citrate	
Age Distribution	\leq 40 years	12 34.3%	8 22.9%	20 28.6%
	> 40 years	23 65.7%	27 77.1%	50 71.4%
Total		35	35	70

Chi square value = 1.12, p-value = 0.29

Male gender was common by calculating 60% (n=21) and 65.7% (n=23) in Group A & B. Table 2

Table 2: Gender distribution (n=70)

		Group		Total
		Heparin	Citrate	
Gender	Male	21 60.0%	23 65.7%	44 62.9%
	Female	14 40.0%	12 34.3%	26 37.1%
Total		35	35	70

Chi square value = 0.245, p-value = 0.621

Comparison of Catheter Related Infection (CRI) in both groups was done, where it was recorded in 37.1% (n=13) versus 14.3% (n=5) in Group A & B, p: 0.029 i.e. <0.05. Table 3

Table 3: Comparison of catheter related infection (CRI) in both groups (n=70)

		Group		Total
		Heparin	Citrate	
CRI Episode	Present	13 37.1%	5 14.3%	18 25.7%
	Absent	22 62.9%	30 85.7%	52 74.3%
Total		35	35	70

Chi square value = 4.786, p-value = 0.029

DISCUSSION

Various trials reveal the superiority of citrate when combined with other antimicrobials over heparin for avoidance of catheter related bacteria. We recorded the use of citrate-alone lock solutions is associated with a lower rate of catheter related infection, in contrast, a previous study⁹ failed to find a benefit of citrate-alone solutions. However, of four trials on catheter related infection, only one study revealed a difference in heparin lock and citrate.⁸

Zhao et al¹⁰ also favoured citrate-containing locking solution, however, the citrated with combined with other antimicrobial agents.

Another study included a larger population and compared the efficacy and safety of citrate versus heparin and concluded that catheter dysfunction was lower in patients with citrate group.¹¹ In a randomized controlled trial¹² comparing heparin 1:5000 units and 30% citrate had an incidence of 23% CAB episodes in heparin group. In this study by Weijmer et al the 30% citrate resulted in a reduction of CAB events by 74% (event rate was 6% in citrate 30% group).

In a previous study by Bevilacqua et al¹ revealed that infection rate of 22% (11/49) in heparin group and 13.95% (6/43) in citrate group, that is comparable with our study. Grudzinski et al¹¹ recorded (46.7%) citrate concentration can induce fatal cardiac arrest, and thus the US Food and Drug Administration stated that it should not be used as a catheter-locking solution.

In a previous Quasi-experimental study by Parienti et al⁶ in which 46.7% citrate lock solution was used (Dura Lock-C). The use of C-Lock was associated with less catheter colonization than the heparin lock solution. This observation is consistent with the anticoagulant and antibacterial activity across a broad spectrum of microbes. Of note, thrombosis and bacterial growth within biofilm are closely related in the physiopathology of catheter-related infections.

Among the 464 patients who received Heparin lock solution, the overall cumulative incidence of catheter colonization was 27.6%. Among the 132 patients who received C-Lock, the overall cumulative incidence of catheter colonization was 14.4%.

The hypothesis of our study that “**citrate is superior to heparin in prevention of CRI in patients of end stage renal disease on hemodialysis**” is justified and we are of the view that citrate may be used in routine to prevent patient from developing CRI. However, further local studies are required to authenticate the findings of our study.

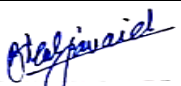


CONCLUSION

We concluded that citrate as compared to heparin is having significant lower rate of CRI in patients of end stage renal disease on hemodialysis. However, heparin may be used in routine practice.

REFERENCES

1. Bevilacqua JL, Gomes JG, Santos VF, Canziani ME. Comparison of trisodium citrate and heparin as catheter-locking solution in hemodialysis patients. *J Bras Nefrol.* 2011;33(1):86-92.
2. Maki DG, Ash SR, Winger RK, Lavin P, AZEPTIC Trial Investigators. A novel antimicrobial and antithrombotic lock solution for hemodialysis catheters: a multi-center, controlled, randomized trial. *Crit Care Med.* 2011;39(4):613-20.
3. Javed MS, Subhani GM, Tahir S, Javed SH. Significance of Indwelling Time for Bacterial Colonization of Double J Stents. *APMC.* 2016;10(1):36-40.
4. Liu J, Wang C, Zhao H, Zhang J, Ma J, Hou Y, et al. Anticoagulant therapies versus heparin for the prevention of hemodialysis catheter-related complications: systematic review and meta-analysis of prospective randomized controlled trials. *Int J Clin Exp Med.* 2015;8(8):11985-95.
5. Lee T, Lok C, Vazquez M, Moist L, Maya L, Mokrzycki M. Minimizing hemodialysis catheter dysfunction: an ounce of prevention. *Int J Nephrol.* 2012;2012(15):170857-66.
6. Parienti JJ, Deryckère S, Mégarbane B, Valette X, Seguin A, Sauneuf B, et al. Quasi-experimental study of sodium citrate locks and the risk of acute hemodialysis catheter infection among critically ill patients. *Antimicrob Agents Chemother.* 2014;58(10):5666-72.
7. Grudzinski A, Agarwal A, Bhatnagar N, Nesrallah G. Benefits and harms of citrate locking solutions for hemodialysis catheters: a systematic review and meta-analysis. *Can J Kidney Health Dis.* 2015;2:13.
8. Bruyère R, Soudry-Faure A, Capellier G, Binquet C, Nadji A, Torner S, et al. Comparison of heparin to citrate as a catheterlocking solution for non-tunneled central venous hemodialysis catheters in patients requiring renal replacement therapy for acute renal failure. (VERROU-REA study): study protocol for a randomized controlled trial. *Trials.* 2014;15:449.
9. Zhao Y, Li Z, Zhang L, Yang J, Yang Y, Tang Y et al. Citrate versus heparin lock for hemodialysis catheters: a systematic review and meta-analysis of randomized controlled trials. *Am J Kidney Dis.* 2014;63(3):479-90.
10. Grudzinski L, Quinan P, Kwok S, Pierratos A. Sodium citrate 4% locking solution for central venous dialysis catheters—an effective, more cost-efficient alternative to heparin. *Nephrol Dial Transplant.* 2007;22(2):471-6.
11. Weijmer MC, van den Dorpel MA, Van de Ven PJ, ter Wee PM, van Geelen JA, Groeneveld JO, et al. CITRATE Study Group: Randomized, clinical trial comparison of trisodium citrate 30% and heparin as catheter-locking solution in hemodialysis patients. *J Am Soc Nephrol.* 2005;16(9):2769-77.

AUTHORSHIP AND CONTRIBUTION DECLARATION

AUTHORS	Contribution to The Paper	Signatures
Dr. Bilal Javaid Assistant Professor, Nephrology Faisalabad Medical University, Faisalabad	Conception and Design, Acquisition of Data, Analysis and Interpretation of Data, Drafting Article	
Dr. Adil Manzoor Consultant Nephrologist & Transplantation Medicine King Fahd Hospital Madina, Saudi Arabia	Revising it Critically Important Intellectual Content	
Dr. Irfan Elahi Assistant Professor, Nephrology KEMU, Mayo Hospital, Lahore	Revising it Critically Important Intellectual Content	
Dr. Salman Javaid Assistant Professor, Neonatology Children Hospital, Faisalabad	Conception and Design, Drafting and Revising Important Intellectual Content	