بسم الله الرحمن الرحيم

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تم رفع هذه الرسالة بواسطة / سلوي محمود عقل

بقسم التوثيق الإلكتروني بمركز الشبكات وتكنولوجيا المعلومات دون أدنى مسئولية عن محتوى هذه الرسالة.

ملاحظات:
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A randomized controlled clinical trial of Trisodium Citrate 30 % versus Heparin as a lock solution for the prevention of catheter-related infections in adult hemodialysis patients

A Thesis

Submitted For Partial Fulfilment Of Master Degree In Internal Medicine

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2022


بسم الله الرحمن الرحيم
قَالوُاسُبحَانَك لاَعِلمَ لنَا إلا مَاعَلمتَناَ
إنكَ أَنتَ العَلِيمُ الحَكِيمُ
صدق الله العظيم
(سورة البقرة – الآية ٣٢)

Acknowledgement

First of all, thanks GOD, the merciful, the beneficent for helping me during this work.

I would like to express my indebtedness and deepest gratitude to **Prof. Dr. Magdy Mohamed EL-Sharkawy,** Professor of internal medicine and nephrology, Faculty of Medicine, *Ain shams* University for his valuable advice, guidance and constructive criticism, also for the invaluable assistance and efforts he devoted in the supervision of this study.

I'll never forget, how co-operative was **Dr. Lina Essam Khedr**, Lecturer of internal medicine and nephrology, Faculty of Medicine, *Ain shams* University, also she was encouraging all the time. It is honorable to be supervised by her.

I would like also, to express my great thanks to **Dr. Ahmed Abdelmoniem Emara**, Lecturer of internal medicine and nephrology; Faculty of Medicine – *Ain shams* University. His valuable advises and continuous support facilitated completing this work.

I would like to thank all the staff members of the internal medicine and nephrology department.

Finally, I would like to express my appreciation and gratitude to all my family, especially my caring and loving parents who enlighten my life.

Ahmed Kamal Abdelhamid

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AVF	arteriovenous fistula
AVG	arteriovenous graft
CATD	carbon transcutaneous hemodialysis access device
CBC	Complete blood count
CKD	Chronic kidney disease
CLABSIs	central line–associated bloodstream infections
CRB	catheter-related bacteremia
CRBSIs	catheter-related bloodstream infections
CVC	Central venous catheters
CVS	central venous stenosis
DOPPS	Dialysis Outcomes and Practice Patterns Study
ESI	exit-site infection
ESRD	End-stage renal disease
GN	glomerulonephritis
HD	hemodialysis
IJ	internal jugular
NHSN	National Healthcare Safety Network
PTFE	polytetrafluoroethylene
RRT	renal replacement therapy
TDCs	tunneled dialysis catheters
TIVAD	Totally implantable venous access devices
TSC	trisodium citrate
U.S	United States
VA	vascular access

ABSTRACT

Background; Central venous catheters (CVC) are the only option when hemodialysis is needed for patients without definitive vascular access. However, CVC is associated with complications, such as infection, thrombosis, and dysfunction, leading to higher mortality and expenditures. Interdialytic hemodialysis catheter-locking solutions could contribute to reduction of catheter-related complications, especially infections, **Aim and objectives;** to assess the possible effect of using Trisodium citrate 30% (TSC 30%) in comparison to unfractionated heparin , as a lock solution for hemodialysis catheters, on inflammatory status in HD patients, **Subjects and methods;** This was a randomized controlled clinical trial, conducted on 70 patients on regular hemodialysis , selected from hemodialysis unit in Nasser Institute Hospital in Cairo government , divided into two groups: (Citrate Group); 35 patients received trisodium citrate, (Heparin Group); 35 patients received unfractionated heparin (5000i.u) as a hemodialysis lock solution after the end of HD session and followed up for 3 months , **Result;** In our study , the catheter-related bacteremia episodes were significantly lower in the Citrate group when compared with those in the Heparin group. Only 2 patients (5.7%) in Citrate group had CRBSI, whereas in Heparin group, 8 patients (22.9%) had CRBSI (P=0.04). Also, Bacteremia-free time was longer in the Citrate group. The mean bacteremia free time in Citrate group was 10.97 ± 2.36 weeks, while in Heparin group it was 9.43 ± 3.91 weeks (P=0.032). At base line, there was no significant difference between both groups regarding hsCRP (P=0.596) and WBCs (P=0.528). While after 3 months of using TSC 30% as a lock solution, there was a *significant difference* as regards levels of hsCRP (P=0.030) and WBCs (P=0.036), with the higher levels of inflammatory markers showed in Heparin group. There was no difference between the two studied groups regarding thrombosis, however, catheter performance was higher in citrate group after 3 months assessed by URR (P=0.005) compared to baseline (P=0.108), **Conclusion;** we found that Trisodium citrate 30% may be a better alternative to heparin as a catheter lock solution as it reduces the inflammatory markers and CRBSI incidence. We therefore believe that TSC 30% may be used safely as catheter lock solution in Hemodialysis **Keywords; Catheter-related bloodstream infection;Citrate; heparin; Hemodialysis; Lock solutions.**

INTRODUCTION

End-stage renal disease (ESRD) requiring renal replacement therapy (RRT) has become a major health problem worldwide. Approximately 2.5 million people were estimated to be receiving chronic RRT in 2010 ***(Liyanage et al, 2015)***. There were 726,331 prevalent cases of end-stage renal disease (ESRD) in 2016 among the United States (U.S.) population (crude prevalence of 2,160.7 per million), with 87.3% of incident individuals beginning RRT with hemodialysis (HD) ***(USRDS, 2018)***. The prevalence of ESRD requiring RRT in Europe in 2016 was 823 per million, with hemodialysis being the modality for renal replacement therapy for 84% of such patients ***(Kramer et al, 2019)***.

ESRD requiring HD has significant effects on morbidity and mortality. Although mortality rates have declined over the last 15 years, the mortality rate for patients on HD is significantly higher than the general population. In 2016, the adjusted mortality rates in dialysis patients were 166 per 1000 patients ***(USRDS, 2018)***.

Infection is the second leading cause of death in patients on HD ***(US Renal Data System, 2014*)**. The use of a CVC is the major risk factor for bacteremia in HD, which can result in life-threatening complications in over 10 % of cases, such as septic shock, endocarditis, septic arthritis, osteomyelitis, and epidural abscesses. The relative risk of hospitalization for infection and death is 2–3 times greater in patients using CVC compared with patients with AVF or vascular graft ***(Dhingra RK et al, 2001)*** with consequent increase in health expenditures

Central venous catheters (CVC) are the only option when hemodialysis is needed for patients without definitive vascular access.

However, CVC is associated with complications, such as infection, thrombosis and dysfunction, leading to higher mortality and expenditures (***FC Barcellos et al, 2017***).The quality of sealing a catheter directly affects the establishment of vascular access, and thus the outcome of treatment and the quality of life of patients in the intensive care unit. Therefore, maintaining the patency of vascular access, ensuring adequate blood flow, and avoiding complications of vascular access are important ***(Vazquez-Padron et al, 2016).***

Patients on hemodialysis (HD) using dialysis catheters have significantly higher rates of morbidity and mortality which has been associated with chronic inflammatory state. In Egypt, 6.6% of HD patients use catheters, of which temporary catheters represent 59.6% and 40.4% with permanent catheters ***(M El Sharkawy et al, 2019).***

Sealing catheters with an anticoagulant plays a role in establishing vascular access, hemodialysis treatment, and preventing complications ***(TW El Said et al, 2018).***At present, commonly used catheter lock solutions in clinical practice include heparin and sodium citrate. Heparin has several important functions ***(F Zia et al, 2016).*** It enhances the affinity between antithrombin III and thrombin, and accelerating inactivation of thrombin***(Van Walderveen et al,2010)*** inhibiting adhesion and aggregation of platelets***(RB Eslam et al,2011),***enhancing the activity of protein C, and stimulating vascular endothelial cells to release anticoagulant and fibrinolytic substances***(Van Walderveen et al, 2010)*** **.**Heparin overflow can increase the risk of systemic anticoagulation***(***Greinacher A, 2015**).Therefore, finding a safe and effective alternative catheter lock solution is required.

Studies have shown that sealing catheters with sodium citrate can reduce the incidence of catheter-related bloodstream infections,while reducing the risk of bleeding in patients***(M Szymczak, et al,2009).***Citrate is considered as an effective 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 ***(Bruyère R et al,2014).***Studies have also shown that citrate has certain antibacterial activity ***(Liu Jet al, 2015) .***

Although the comparisons between citrate and heparin lock for the prevention of hemodialysis catheter-related complications have been reported in previous systematic reviews, the results are not consistent. In one study, it was reported that citrate lock containing antimicrobial agents is more effective in preventing CRBI while citrate alone fails to show a similar advantage ***(Zhao Y al, 2014)***.On the contrary, a meta-analysis showed that the use of citrate alone can reduce the occurrence of CRBI, hemorrhage, and exit-site infection ***(Liu J al, 2015).***

Citrate 4% lock solution is equally effective as heparin in maintaining catheter patency in dialysis patients. It may have a favorable effect on prevention of catheter-related infection due to its additional antiseptic properties as compared to heparin. Citrate-based locking solutions are a promising alternative to unfractionated heparin as a locking solution for dialysis catheters ***(TW El Said et al,2018)***

Citrate as compared to heparin has a significant lower rate of CRI in patients of end stage renal disease on hemodialysis. However, heparin may be used in routine practice***(B Javaid et al, 2019).*** The solution 4% sodium citrate can effectively reduce the risk of catheter obstruction, bleeding, infection, and leakage better than sodium heparin in patients

with long-term intravenous indwelling catheters. Reducing catheter-associated complications using 4% sodium citrate versus sodium heparin as a catheter lock solution ***(H Huang et al, 2019)***

Aim Of The Work

The aim of this study is to assess the possible effect of using Trisodium citrate 30% in comparison to unfractionated heparin, as a lock solution for hemodialysis catheters, on inflammatory status in HD patients.