Taurolidine citrate and unfractionated heparin combination versus unfractionated heparin alone in prevention of inflammation in hemodialysis catheters

Thesis

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بسم الله الرحمن الرحيم

قالوا

سبحانك لا علم لنا
إلا ما علمتنا إنك أنت
العليم الحكيم

صدق الله العظيم

سورة البقرة الآية: ٣٢

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Contents

List of Abbreviations

ADPKD	Autosomal Dominant Polycystic Kidney Disease
AKI	Acute Kidney Injury
aPTT	Activated Partial Thromboplastin Time
AVF	Arteriovenous fistula
AVG	Arteriovenous graft
BC	Blood Culture
BFR	Blood Flow Rate
BSI	Bloodstream Infection
CDC	Centers for Disease Control and Prevention
CFU	colony-forming unit
CHD	Chronic Hemodialysis
CKD	Chronic Kidney disease
CLABSIs	Central Line Associated Blood Stream Infections
CRB	Catheter Related Bacteremia
CRBSI	Catheter Related Blood Stream Infection
CRI	Catheter related infection
CRP	C- reactive proteins
CVC	Central venous catheter
CVC-RBI	Central Venous Catheter Related bloodstream infection
CVC-RI	Central Venous Catheter Related Infection
CVC-RLI	Central Venous Catheter Related Local Infection
CVD	Cardiovascular disease
DM	Diabetes Mellitus
ELISA	Enzyme-Linked Immunosorbent assay
ESRD	End stage renal disease
FDA	Food and Drug Administration
FR	French
Hb	Hemoglobin
HD	Hemodialysis
HIA	Heparin Induced Antibodies
hsCRP	High-sensitivity CRP
HTN	Hypertension
IDSA	Infectious Disease Society of America
IJV	Internal Jugular vein
IL-6	Interleukin 6

KDIGO	Kidney Disease Improving Global Outcomes
KDOQI	Kidney Disease Outcome Quality Initiative
LTA	Lipoteichoic acid
MICS	Malnutrition Inflammation Cachexia Syndrome
NHSN	National Healthcare Safety Network
NTHCs	Non-tunneled hemodialysis catheters
PAI	Plasminogen Activator Inhibitor
PBMC	peripheral blood mononuclear cells
PD	Peritoneal dialysis
PEW	Protein Energy Wasting
PLT	Platelets
PreCLOT	Prevention of catheter lumen occlusion with rT-PA
P-value	Probability value
RRT	Renal replacement therapy
rT-PA	Recombinant Tissue Plasminogen Activator
SVC	Superior vena cava
TAT	Thrombin –Antithrombin
TCC	Tunneled Cuffed Catheter
TCHLS	Taurolidine Citrate Heparin Lock Solution
TDCs	Tunneled Dialysis Catheters
TIVAD	Totally implantable venous access devices
TLR	Toll-like receptor
URR	Urea Reduction Ratio
WBC	White blood cell

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Abstract

Introduction and Aims: 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 short term catheters represent 59.6% and 40.4% with long-term catheters. In this study we aim to assess the possible effect of using Taurolidine citrate and unfractionated heparin (Taurolock-hep500™) in comparison to unfractionated heparin, as a lock solution for temporary hemodialysis catheters, on inflammatory status in HD patients.

Methods: a randomized controlled clinical trial that included 60 stable HD patients recruited from Ain Shams University hospitals at the time of catheter insertion. They were divided into two groups, Group 1: 30 Patients received taurolidine and citrate (4%) and 500 i.u of heparin as a catheter lock solution after hemodialysis sessions, Group 2: 30 patients received unfractionated heparin (5000i.u) as a catheter lock solution after hemodialysis sessions.

Standard aseptic techniques were used in handling catheters. High sensitive C-reactive protein (hsCRP) and interleukin 6 (IL-6) were measured in serum for both groups and samples were obtained at baseline and after 1 month of using the lock solutions.

Results : Group 1 (mean age 39.5 ± 14, 46.7% males), Group 2 (mean of age 39.3 ±14,60% males). At base line, there was no significant difference between both groups regarding hsCRP (P=0.366) and IL-6 (p=0.900). While after 1 month of using the lock solution there was significant difference as regard levels of hsCRP (p=0.001) and IL-6 (p=0.018),with the higher levels of inflammatory markers showed in group 2.

Conclusions: we may conclude that the use of Taurolidine citrate and unfractionated heparin combination as a lock solution for HD catheters reduces the inflammatory markers, and the inflammatory status in HD patients when compared to the standard unfractionated heparin lock as demonstrated by reducing the levels of inflammatory markers (hsCRP and IL-6). This may have good clinical consequences regarding the quality of life in HD patients.

Keywords: highly sensitive c-reactive protein hs(CRP), end stage renal disease (ESRD),interleukin-6(IL-6),taurolidine citrate heparin lock solution (TCHLS).

Introduction

Chronic kidney disease occurs when one suffers from gradual and usually permanent loss of kidney function over time. This happens gradually, usually over months to years. With loss of kidney function, there is an accumulation of water, waste, and toxic substances in the body that are normally excreted by the kidney. It also causes other problems such as anemia, high blood pressure, acidosis (excessive acidity of body fluids), disorders of cholesterol and fatty acids, and bone disease. Chronic kidney disease may progress to end stage renal failure and the patients will undergo one of the renal replacement therapies. ***(Fogarty and Maxwell., 2013)***

Hemodialysis is a method that is used to achieve the extracorporeal removal of waste products such as creatinine and urea and free water from the blood in the state of renal failure. Hemodialysis is one of the renal replacement therapy modalities (others include renal transplant and peritoneal dialysis). **(*Rosner, 2010*)**

Adequate vascular access is essential for extracorporeal renal replacement therapy. Although an arteriovenous fistula (AVF) is the optimal vascular access for chronic dialysis, temporary dialysis catheters are frequently required when a permanent access is not mature at the time of initiation of hemodialysis or in the setting of access malfunction or thrombosis. Temporary dialysis catheters are also needed for the management of patients with acute renal failure requiring hemodialysis or continuous renal replacement therapy and for extra-

corporeal detoxification with hemoperfusion. Hemodialysis for the treatment of toxic ingestions and poisonings. Catheter access may also be necessary for the provision of therapeutic plasma exchange. ***(Grapsa and Pantelias, 2015)***

Catheter access for these extracorporeal therapies is usually achieved through cannulation of one of the three easily accessible central veins, the internal jugular, subclavian, or femoral veins. Subclavian venous cannulation is associated with high rates of central venous stenosis and thrombosis. This may result in severe venous hypertension in the ipsilateral arm and endanger the ability to use the arm for more permanent vascular access. For this reason, the subclavian vein should be avoided for temporary access in patients with chronic renal disease. Femoral venous catheters are associated with high rates of infectious and thrombotic complications and require limitation of ambulation. For these reasons, the internal jugular veins provide the most desirable site for placement of temporary dialysis catheters. ***(Delik, 2015)***

Vascular access is the patient's lifeline; access failure and access complications are a significant cause of morbidity and even mortality. Infection rates are linked with personal hygiene of the patient, experience of the staff and nature of the access. Education of patients and staff is crucial to minimize infection risks. ***(Bagdasarian, 2012)***

TauroLock-hep500™ is a catheter lock solution for tunneled and non-tunneled central venous access systems. It has to be instilled in the device lumens between treatments in order to make the internal flow passages

resistant to clot formation and hostile to bacterial and fungal growth. Active ingredients of TauroLock™ are the antimicrobial compound (cyclo)-taurolidine and citrate (4%) and 500 i.u of heparin as an anticoagulant.

For enhancing the flow, you can replace heparin by urokinase (TauroLock-U25000™) containing 25000 i.u of urokinase.

Before instilling TauroLock-hep 500™ the catheter has to be flushed with saline (10 or 20 ml). Before starting hemodialysis, lock solution has to be aspirated**.** ***(Al-Ali et al., 2017)***

Aim of work

To assess the efficacy of Taurolock-hep500™ as anticoagulant and antimicrobial catheter lock solution in comparison to unfractionated heparin as a lock solution to reduce incidence of catheter related blood stream infections (CRBSI), improve performance of hemodialysis catheters and quality of hemodialysis.

Hemodialysis and Vascular access

Chronic kidney disease (CKD) has been recognized as a worldwide health threat and understanding its complex pathophysiological mechanisms would help greatly in taking care of patients with CKD. The prevalence of CKD has reached epidemic proportions with 10%–12% of the population and 50% of elderly showing signs of kidney dysfunction, a condition associated with high morbidity and mortality. ***(Machowska et al., 2016)***

Kidney disease is among the 10 leading causes of premature mortality in the United States, persons with end-stage renal disease (ESRD) have a shortened life expectancy as compared to their peers without kidney disease. Examining trends related to death from this chronic condition is essential to guide and evaluate efforts in reducing the risk of death and increasing the potential life span. **(*United States Renal Data System, 2018)***

ESRD is a prevalent condition with impaired quality of life and survival. Given the scarcity of transplantable donor kidneys, hemodialysis remains the dominant form of renal replacement therapy in the developed world. Complications of uremia, associated comorbidities. The hemodialysis treatment itself contributes to the excess mortality associated with ESRD. ***(Lacson et al., 2010)***

Conventional HD remains the main modality of renal replacement therapy for patients with end-stage renal disease (ESRD) worldwide. Conventional HD is usually conducted over a 4-h duration three times per week for stable patients with ESRD. The dialyzer or filter used is