بسم الله الرحمن الرحيم

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

ملاحظات: لا يوجد

The Effect of Taurolidine-Citrate-Heparin Combination on The Inflammatory Response and Hemodialysis Adequacy in Hemodialysis Patients

Thesis

Submitted for Partial Fulfillment of Master Degree in Internal Medicine & Nephrology

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قالوا

سبحانك لا علم لنا
إلا ما علمتنا إنك أنت
العليم الحكيم

صدق الله العظيم

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Omar El-Sayed

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List of Abbreviations

Abb	Full Term
AVF	arteriovenous fistula
AVG	arteriovenous graft
CATD	carbon transcutaneous hemodialysis access device
CDC	
CKD	Chronic kidney disease
CRB	Catheter-related bacteremia
CRBSIs	Catheter-related bloodstream infections
CRP	
CVC	central venous catheters
CVD	Cardiovascular diseases
CVS	central venous stenosis
EDTA	ethylenediaminetetraacetic acid
ESRD	end- stage renal disease
HD	Hemodialysis
NHSN	National Healthcare Safety Network
PTA	percutaneous transluminal angioplasty
PTFE	Polytetrafluoroethylene
RRT	Renal Replacement Therapy
rt-PA	Recombinant Tissue Plasminogen Activator
TLC	Total Leukocytic Count
TIVAD	Totally Implantable Venous Access Devices
TLS	Taurolidine Lock Solutions

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ABSTRACT

Background; Catheter-related bloodstream infections (CRBSIs) are a significant cause of morbidity and mortality in critically ill patients, contributing to prolonged hospital stays and increased costs. Whether taurolidine lock solutions (TLS) are beneficial for the prevention of CRBSIs remains controversial.

Aim and objectives to assess the effect of Taurolock-hep500™ as a lock solution on the incidence of Catheter Related Blood Stream Infections (CRBSI), performance of hemodialysis permanent catheters, and haemodialysis adequacy.

Subjects and methods; This study was Randomized Controlled Trial, was carried out on 60 patients at Al-Zaitoun Specialized Hospital -Ministry of Health & Al-Demerdash Hospital – Ain Shams University divided into 2 groups: **Taurolidine Group (Group 1):** included 30 Patients received Taurolock-hep500™, (Taurolidine, 4% citrate and 500 IU/ml heparin are combined in this solution), **Heparin Group(Group 2))**: included 30 Patients will receive unfractionated heparin (heparin sodium 5000i.u/ml) as a permanent catheter lock solution**.** Patients were followed up for 1 month for monitoring hemodialysis adequacy and incidence of CRBSI.

Result; CRP was significantly increased in heparin group more than Taurolidine Group. One case with CRBSIs was in Taurolidine Group, whereas five cases in heparin group.

Conclusion; The use of Taurolidine–citrate–heparin lock solution may be associated with better hemodialysis adequacy, lower incidence of Catheter Related Blood Stream Infections (CRBSI) and lower inflammatory markers in comparison to the use of Heparin.

Keywords; Catheters, CRBSI, taurolidine, inflammation, dialysis adequacy, **Taurolidine.**

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 extracorporeal 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, there is available (TauroLock-U25000™) containing 25000 i.u of urokinase, where heparin is replaced by urokinase.

Aim of the Study

To assess the effect of Taurolock-hep500™ as a lock solution on the incidence of Catheter Related Blood Stream Infections (CRBSI), performance of hemodialysis permanent catheters, and haemodialysis adequacy

Chapter (1)

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 usually of the low-flux type, and the filtered molecules are water-soluble, small-size (molecular weight <500 Dalton) compounds. **(*Karkar, 2012)***

Conventional HD treatment had, over many years, improved the survival rate of patients with ESRD. However, this basic modality of dialysis is far from replacing the function of the normal kidneys. In fact, conventional HD prescription provides only about 10% of the clearance power of the natural kidneys. Although it is capable of removing excess water and small size uremic toxins, yet, conventional HD is not capable of removing middle and large size (>500 Dalton) and protein-boundtoxic molecules. These middle and large-size molecules include β_2-microglobulin (β_2 -M), which is strongly associated with carpal tunnel syndrome and dialysis-related amyloidosis. Others include pro-inflammatory cytokines and severe vasoactive molecules such as *p*-cresol and uridine adenosine tetraphosphate. ***(Ledebo andBlankestijn, 2010)***

The accumulation and retention of all types and sizes of uremic compounds (and excess water), which have concentration-dependent toxicity, results in increased morbidity and mortality. ***(Ledebo and Blankestijn, 2010)***

- **History of vascular access**

Vascular access for hemodialysis is closely associated with the history of dialysis. Glass needles were employed as vascular access when hemodialysis came into view in 1924. The first haemodialysis treatment in humans was carried out by Haas G. who used glass cannulae to acquire blood from the radial artery and reverting it to the cubital vein. Venipuncture needles were used as means for blood acquisition from the femoral artery and its reinfusion to the patient by vein puncture, in 1943

by Kolff W. Regular hemodialysis treatments were possible in 1950s through the use of a medical apparatus (Kolff 's twin-coil kidney), thus projecting the problem of a reliable, capable of repeated use vascular access. Nowadays, the artery-side-to-vein-end-anastomosis has become a standard procedure. In 1952, Aubaniac had described the puncture of the subclavian vein **(Hentschel et al., 2016).**

In 1977, Gracz KC et al created the "proximal forearm fistula for maintenance hemodialysis", a variant of an AV anastomosis. An adjustment of this AVF became quite significant in the old, hypertensive and diabetic patients on the grounds that it allows a proximal anastomosis with a low risk of hypercirculation. In 1979 Golding A.L. et al developed a "carbon transcutaneous hemodialysis access device" (CATD), commonly known as "button", by which, blood access does not require needle puncture. As a procedure of third choice, these devices were expensive and never gained widespread acceptance. Shapiro F.L. described another type of "button", a device similar to that developed by Goldin **(Ndinya, 2016).**

-Scribner Shunt

The inventor of shunt dialysis, Belding H Scribner invented a device credited with saving the lives of over one million patients with kidney failure worldwide. Although his work was laughed at initially, it was his invention's extraordinary success that sparked an ethical dilemma of epic proportion.proportion.

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