Comparison of Streptokinase and Urokinase for Thrombolysis in Blocked Tunnel Cuffed Catheter Among the Patients of Chronic Renal Failure Undergoing Hemodialysis

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ABSTRACT

Objective: To compare the efficacy of Streptokinase and Urokinase for thrombolysis in blocked tunnel cuffed catheter among the patients with chronic renal failure undergoing hemodialysis.

Study Design: Comparative prospective study.

Place and Duration of Study: Department of nephrology Pak Emirates Military Hospital Rawalpindi Pakistan, from Aug 2019 to Mar 2020.

Methodology: A total of 100 cases were included in the study which was undergoing hemodialysis in the nephrology department and had a poorly functioning or blocked tunnel cuffed catheter. These patients were either given Urokinase or Streptokinase in standard doses for thrombolysis. The lottery method was used to designate the patient either in the Streptokinase or Urokinase groups. The primary endpoint was the resolution of blocking and regain of proper functioning of the catheter.

Results: In our study, 54 (54%) patients were males, and 46 (46%) were females. The mean age of the study participants was 44.63 ± 3.782 years, and the mean duration of chronic kidney disease was 2.19 ± 6.814 years. 43 (43%) patients were given Urokinase, while 57 (57%) were given Streptokinase. After applying the logistic regression, we found that the use of Streptokinase had a significant association with the resolution of blocking and regain of proper functioning of the catheter compared to the use of Urokinase.

Conclusion: This study concluded that most catheters regain the proper functioning after thrombolysis with either Urokinase or Streptokinase. However, Streptokinase emerged as a better agent for this purpose in our study.

Keywords: Catheter, Chronic kidney disease, Hemodialysis, Thrombolysis.

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INTRODUCTION

Renal diseases, especially chronic renal disease, has been a source of interest for clinicians and researchers from all domain of medical science as the effects of this disease does not confine to one system but affect the overall physiology of the body.[1] Recent studies done to look for the epidemiology of this devastating illness concluded that no part of the world has been spared, and may it be developing or the developed countries, all have high incidence and prevalence of CKD.[2,3] Management strategies for the CKD patients may include supportive medications, different types of dialysis or the renal transplant.[4]

Hemodialysis has usually been the treatment on which most patients with chronic renal disease remain for a long time. Few may have to stay on it for months or years.[5] This procedure is life-saving and supports the patient until any definitive management of his underlying condition; it still has specific side effects.[6] Few complications have been related to the underlying condition or the limitations of hemodialysis, but few complications have been linked to the procedure itself. Usually, a fistula is made in the patients on long-term dialysis, but sometimes patients have to undergo this procedure via a catheter which has its implications.[6]

Blocking or malfunctioning of the catheter with which the patient has been undergoing the procedure of hemodialysis is a fairly common complication. Various agents have been used for thrombolysis and make the catheter functional again. Bahardoust *et al,* published a study in 2017 highlighting the use of Streptokinase as a low-cost, safe and effective option for restoring patency to hemodialysis central venous catheters.[7] Clase *et al,* in 2001 published a systematic review on this subject and summed up their findings as 1-2 mg/lumen tissue plasminogen antigen (tPA) is a suitable dose for catheter installation and likely to be

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more effective than 5000 units/lumen Urokinase. Systemic lysis with 5-10 mg tPA is likely safe and effective in suitably selected patients. More research is needed to ascertain these findings and form the protocol.[8] Zacharias *et al,* 2003 performed a study to compare the efficacy of Alteplase (recombinant tissue plasminogen activator) versus Urokinase in reestablishing adequate blood flow through partially or completely occluded vascular catheters. They concluded that Alteplase, administered via the 30-minute push protocol, is an effective thrombolytic for restoring hemodialysis catheter patency. In our study sample, Alteplase was generally more effective than Urokinase in restoring blood flow through catheters, especially those that were completely occluded.[9] Mockrzycki *et al,* in 2010 discussed various traditional and nontraditional strategies to optimize catheter function and concluded that lumen-locking agents, oral anticoagulants, and mechanical intervention are the foundations of prevention and management of this problem and all could be effective depending upon the underlying cause of blocking.[10]

In a developing country like ours, where the transplant is offered to limited patients, hemodialysis is a widely practiced option for managing CKD. Fistulas usually are the preferred option, but there is a long waiting list for that, and they may block, or sometimes patients prefer the use of a catheter instead of a fistula. Therefore, catheter care and ensuring adequate flow become of supreme importance for the treating physicians. The use of expensive agents like tPA may not be the option for most patients in our setup. Therefore, we planned this study to compare the difference in efficacy of Streptokinase and Urokinase for thrombolysis in blocked tunnel cuffed catheters among the patients with chronic renal failure undergoing hemodialysis.

METHODOLOGY

This comparative prospective study was conducted at the Nephrology Department in Military Hospital Rawalpindi from Aug 2019 to March 2020. The sample size was calculated by the WHO sample size calculator with a population prevalence proportion of 85%.[8] Sample size was 196 or more for this study. Non-probability consecutive sampling technique was used to gather the sample.

Inclusion Criteria: All the patients of CKD who were undergoing hemodialysis between the age of 18 and 65 years and had blocked or malfunctioning catheters were included in the study.

Exclusion Criteria: Patients with kinking of the catheter or physical blockage due to reasons other than thrombus were excluded from the study. Patients undergoing dialysis for any reason other than CKD were also not included in the analysis. Patients with catheter malfunctioning but still having a flow of more than 200ml/minute were also excluded from the study.

Diagnosis and staging of CKD were made as per the National Kidney Foundation/Kidney Disease Outcome Quality Initiative (NKF/KDOQI) 2002.[11] Catheter obstruction or malfunctioning was defined as the flow of less than 200mls/min during two successive dialysis sessions.[12]

The Ethical Review Board Committee of the hospital was approached to get the ethical approval for this study. It was granted via letter no A/28/EC/77. Written informed consent was taken from all the potential participants of this study before the start of the study after a complete description of the study. Patients with ESRD with Catheter obstruction or malfunctioning having flow less than 200 ml/in fulfilling the above-mentioned inclusion and exclusion criteria were included in the study. Once the flow became less than 200ml/minute, they were evaluated in detail for all the causes of obstruction or catheter malfunctioning. A chest X-ray and relevant physical examination were performed to rule out all other causes of catheter malfunctioning. When all the causes were ruled out and it was established that thrombolysis of the catheter is required in the patient, they were allocated to either the Streptokinase group or the Urokinase group via a lottery method. Urokinase was given at a dose of 25000 units in each lumen, making 50000 units. In comparison, Streptokinase was given 250000 units in each lumen, making a total of 500000 units.[13,14] Success in thrombolysis and restoration of functioning of the catheter was defined as flow rate achieved more than 200ml/min.

Characteristics of participants and the distribution of the patients with successful thrombolysis of the catheter were described using descriptive statistics. Statistical analysis was performed using Statistics Package for Social Sciences version 24.0 (SPSS-24.0). Chi-square was applied to look for the correlation of age, gender, stage of CKD and type of thrombolytic used (Streptokinase vs. Urokinase) with the achievement of successful thrombolysis among the target population. Differences between groups were considered significant for both chi square if *p*-values were less than or equal to 0.05.

RESULTS

After applying inclusion and exclusion criteria and ensuring that all other causes of blockage of the catheter have been ruled out, 100 patients were finally recruited for the study from whom data could be collected and analyzed. of 100 CKD patients with blocked or malfunctioning catheters due to thrombus formation studied in the given period, 91 (91%) had achieved successful thrombolysis. In contrast, 09 (9%) did not achieve successful thrombolysis, and the catheter remained blocked with a flow rate of <200 ml/min. The mean age of the study participants was 44.63 ± 3.782 years, and the mean duration of CKD was2.19 ± 6.814 years. Table showed the distribution of the parameters studied during the study and the application of the chi-square test to establish the correlation. Streptokinase emerged as a better agent for thrombolysis in blocked catheters as compared to Urokinase.

Table: Outcome of various variables studied in the analysis.

Factors Studied	Successful thrombolysis	Unsuccessful Thrombolysis	*p*-value
Age			
<35 years	40 (43.9%)	03 (33.3%)	0.534
>35 years	51 (56.1%)	06 (66.7%)	
Gender			
Male	49 (53.8%)	05 (55.5%)	0.922
Female	42 (46.2%)	04 (44.5%)	
Thrombolytic Agent	55 (60.4%)	02 (22.2%)	0.026
Streptokinase	36 (39.6%)	07 (77.8%)	
Urokinase			

DISCUSSION

Patients suffering from CKD pass through many phases as the stages of CKD advance. Medical treatment, dialysis and transplant are the modes of treatment, which could cater for many aspects of this debilitating illness. However, many aspects remain unaddressed, and the quality of life of the CKD patient remains compromised in one way or another. Hill *et al,* and Crews *et al,* in their studies published in 2016 and 2019, respectively, have highlighted the facts regarding the epidemiology of CKD that it has been equally prevalent in Asian and developing countries as it is in the West. The developed countries.[15,16] In 2019, Shafique *et al,* and Hyder *et al,* published studies in our setup regarding the long term use and complications of using tunnel catheters for hemodialysis.[17,18] Thrmobosis and blocking of the catheter were the commonly encountered complications in this regard.[17,18] Studying the data generated by their studies and considering it a common complication in our setup, we deigned this study to compare the efficacy of Streptokinase and Urokinase for thrombolysis in blocked thrombolysis tunnel cuffed catheter among the patients with Chronic renal failure undergoing hemodialysis.

Bahardoust *et al,* published a study in 2017 highlighting the use of Streptokinase as a low-cost, safe and effective option for restoring patency to hemodialysis central venous catheters.[7] Our findings were consistent in this regard and supported the results generated by Bahardoust *et al,* Though, in current practice, Streptokinase is not preferred that much, and other agents are used in routine but seeing its cost-effectiveness and minor nature of side effects, it may be a suitable option especially for developing country like ours where cost has a significant role in determining the suitable treatment for the patients.

Clase *et al,* in 2001 published a systematic review on this subject and summed up their findings as 1-2 mg/lumen tissue plasminogen antigen (tPA) is a suitable dose for catheter installation and likely to be more effective than 5000 units/lumen Urokinase. Systemic analysis with 5-10 mg tPA is likely to be safe and effective in suitably selected patients.[8] tPA can be a good option and could be made part of future trials. However, the cost factor matters a lot, especially for a country like ours. Moreover, using a higher dose of Urokinase is quite effective in our analysis. Though it may be less efficacious than Streptokinase, the overall response rate and successful thrombolysis in most of the patients in this study show that both the agents could be used for this purpose.

The lack of data, especially comparative studies for Streptokinase, makes our study important. Individual studies have been published in this regard,[7] but very limited data is available regarding its comparison with Urokinase or other agents. Statistically significant results generated by our study analysis on this topic may be taken as a baseline by future researchers and generate more data to establish the local guidelines for thrombolysis of blocked tunnel catheters among CKD patients undergoing hemodialysis.

LIMITATIONS OF STUDY

Selection of study ample from the patients of one hospital was a significant limitation of our study. It should have been a population-based study recruiting patients from multiple centres. Secondary endpoints as complications faced by the patients in both groups were not considered to establish the protocols in this regard, and we require data both on efficacy and tolerability.

CONCLUSION

This study concluded that most the catheters regain the proper functioning after thrombolysis with either Urokinase or Streptokinase. However, Streptokinase emerged as a better agent for this purpose in our study.

Conflict of Interest: None.

Authors' Contribution

TT: Article design, Acquisition of data, KMR: Article conception, MNA: Data analysis, ARA: Article drafting, AWM:, S: Interpretation of data.

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