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Original Research Article

Efficacy of Streptokinase and Urokinase as Thrombolytic Agent for Thrombosed Arterio-Venous Fistula and Tunnelled Cuffed Catheter

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Abstract:

Arterio-Venous Fistula or tunnelled cuffed catheter or Central Venous Catheter (CVC) is considered to be the lifeline for the patients on Maintenance Hemodialysis. One of the most common complications for AVF or CVC is thrombosis. Studies have shown Endo-vascular procedures are effective in managing thrombosed AVF which requires catheterisation laboratory. For CVC thrombosis intraluminal administration of thrombolytic agent is an effective way, but to diagnose intramural versus extramural obstruction catheter angiography is required which again requires catheterisation laboratory. In a resource constrain country availability of catheterisation laboratory is not always there and procedures are costly. This study tries to evaluate the efficacy of thrombolytic agent for both thrombosed AVF and CVC rather than going for Angiography. Patients with history of recent and sudden onset AVF thrombosis and tunneled cuffed CVC flow problem have been taken for intervention. Injection Streptokinase or Urokinase have been administered for both, for maximum 2 occasions 24 hours apart and flow is assessed after 24 hours of each injection. If flow is not established even after 2 dosages, it is considered to be treatment failure. Out of 17 patients having AVF, 12 have received Streptokinase, out of that 3 (25%) has immediate restoration of flow and in 2 (17%) that flow lasted at 3 months. 5 patients have received Urokinase, out of that 2 (40%) have immediate restoration of flow and in 2 (40%) that flow lasted at 3 months. Out of 38 patients having CVC, 15 have received Streptokinase, out of that 9 (60%) has immediate restoration of flow and in 4 (27%) that flow lasted at 3 months. 23 patients have received Urokinase, out of that 15 (65%) have immediate restoration of flow and in 9 (39%) that flow lasted at 3 months. So, from this study it has been concluded that Thrombolysis success rate is low for AVF thrombosis, though it still can be tried in resource constraint situations and for CVC thrombosis bed side Thrombolysis is an effective way to restore the flow and outcomes are also good at 3 months follow-up.

Keywords: Streptokinase, Urokinase, Thrombolytic-Agent, Arterio-Venous Fistula, Tunnelled Cuffed Catheter

Introduction

Arterio-Venous Fistula (AVF) is the permanent and ideal access for maintenance hemodialysis (HD). The most important complications of AVF for HD are lymphedema, infection, aneurysm, stenosis, congestive heart failure, steal syndrome, ischemic neuropathy and thrombosis. Thrombosis is the second most common (17 – 25%) complication of AVF after stenosis (14 – 42%). [1] Studies have shown Catheter-Directed Thrombolysis is effective for AVF thrombosis [2,3] and KDOQI Clinical Practice Guideline For Vascular Access: 2019 [4] suggests that Angioplasty with or without Stenting being the First line strategy for thrombosed AV access.

Both of these procedures require catheterization laboratory, but in a resource constrained country availability of a catheterization laboratory for Catheter-Directed Thrombolysis is not always there, and even if it is there, the cost of it often prohibits the patients undergoing the procedure. Even if the patient bears the cost, the success rate of these procedures are not sent percent. So often patients find creating a new AVF more convenient and cost effective rather than going for these Endo-vascular procedures for old thrombosed AVF, but this costs them permanent loss of one AVF site.

In this category of patients, local thrombolysis using Streptokinase or Urokinase can be an alternate cost-effective option. On the other hand, a significant proportion of patients are dependent on tunnelled cuffed catheter or Central Venous Catheter (CVC) for maintenance hemodialysis. Thrombosis related catheter malfunction and infection are common complications of tunnelled

cuffed catheter. [5] Obstruction may be intra mural due to thrombosis or extra mural due to fibrin sheath formation. KDOQI Clinical Practice Guideline for Vascular Access: 2019 [4] supports the use of intra luminal thrombolytic agents for intra luminal thrombosis and CVC exchange and fibrin sheath disruption is required for extra mural obstruction. The diagnosis of intra or extra mural fibrin sheath requires catheter angiography and catheterisation laboratory is required for that, which is again costly for the same reason. Intra luminal use of thrombolytic agents like Streptokinase or Urokinase can be tried even before going for catheter angiography, though resistant cases require catheter removal.

This study has been planned to see the efficacy of Streptokinase and Urokinase as thrombolytic agent for recently thrombosed AVF, (less than 24 hrs) which has a history of good flow on immediate previous Hemodialysis (HD) session. Cases having gradually progressive slowing of flow followed by complete absence of flow are excluded as they suggest stenosis and are poor candidates for thrombolysis.

Similarly, the efficacy of Streptokinase and Urokinase as thrombolytic agent for recently occluded (less than 24 hrs) CVC have been assessed, even before going for catheter angiography.

The choice of Streptokinase or Urokinase is based on patient's financial ability and the prior use Streptokinase for any reason, as second use can cause anaphylaxis.

Materials and Method

The study has been conducted at the Dialysis unit of Medica Super-specialty hospital, Kolkata, West Bengal, India. Patients with history of recent and sudden onset AVF thrombosis and tunneled cuffed CVC flow problem have been taken for intervention. In 1 year study duration after excluding 2 patients with recent history of black stool and 1 for stroke, 17 patients have been included in thrombosed AVF group and 38 in occluded tunneled cuffed CVC group.

The location of thrombosed area in AVF has been identified by Doppler USG. Out of 17 patients in AVF group 12 have received injection Streptokinase and 5 have received injection Urokinase.

Injection Streptokinase 15 lakh IU have been diluted with 100 ml of NS and out of that 3 ml is taken which contains 45000 IU. That 3 ml have been diluted with 7 ml NS to make it total 10 ml. Skin over thrombosed area has been marked with a skin marking pencil and a torniquet has been applied downstream to the thrombosed area to prevent systemic dissemination of the thrombolytic agent. In a 10 ml syringe 10 ml of diluted 45000 IU Streptokinase has been taken and injected facing the needle (21G) towards the thrombosis. The torniquet has been kept for 30 minutes and then released.

Injection Urokinase 5 lakh IU have been diluted with 10 ml. of NS and out of that 1 ml is taken which contains 50000 IU. That 1 ml have been diluted with 9 ml NS to make it total 10 ml. This 10 ml containing 50000 IU Urokinase has been injected in similar way as described above for Streptokinase.

The flow in AVF has been assessed 24 hours after first injection by doppler USG. If flow is not established, second dose of Streptokinase or Urokinase have been administered at 24 hours interval and flow is again reassessed after 24 hours. Maximum 2 doses have been administered and even after that if AVF had no flow, it is considered to be treatment failure.

Similarly, 38 patients with history of recent and sudden onset CVC dysfunction have been taken and 15 have been administered Streptokinase and 23 of Urokinase.

Injection Streptokinase 15 lakh IU have been diluted with 100 ml of NS and out of that 4 ml is taken and 2 ml is injected in each Arterial and Venous port that is 30000 in each port.

Injection Urokinase 5 lakh IU is diluted with 10 ml of NS and out of that 2 ml is taken and that 2 ml is further diluted with 2 ml NS to make it 4 ml. out of that 4 ml, 2 ml is injected in each Arterial and Venous port, that is 50000 IU in each port.

The flow in CVC has been assessed 24 hours after first injection by aspiration by 10 ml syringe. Initially 2 ml of blood from both Arterial and Venous ports have been aspirated and discarded to prevent embolism by intra-luminal clots, subsequently rapid saline flushing has been done, followed by Heparin lock as per unit protocol. If flow is not established, second dose of Streptokinase or Urokinase have been administered at 24 hours interval and flow is again reassessed after 24 hours. Maximum 2 doses have been administered and even after that if CVC had no flow, it is considered to be treatment failure.

Results

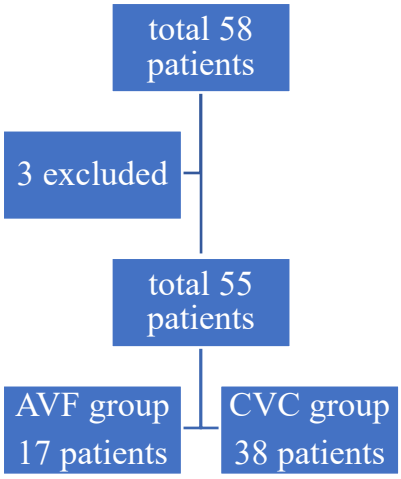

Figure 1:

AVF group: In AVF group out of 17 patients 12 (71%) have received injection Streptokinase and 5 (29%) have received injection Urokinase.

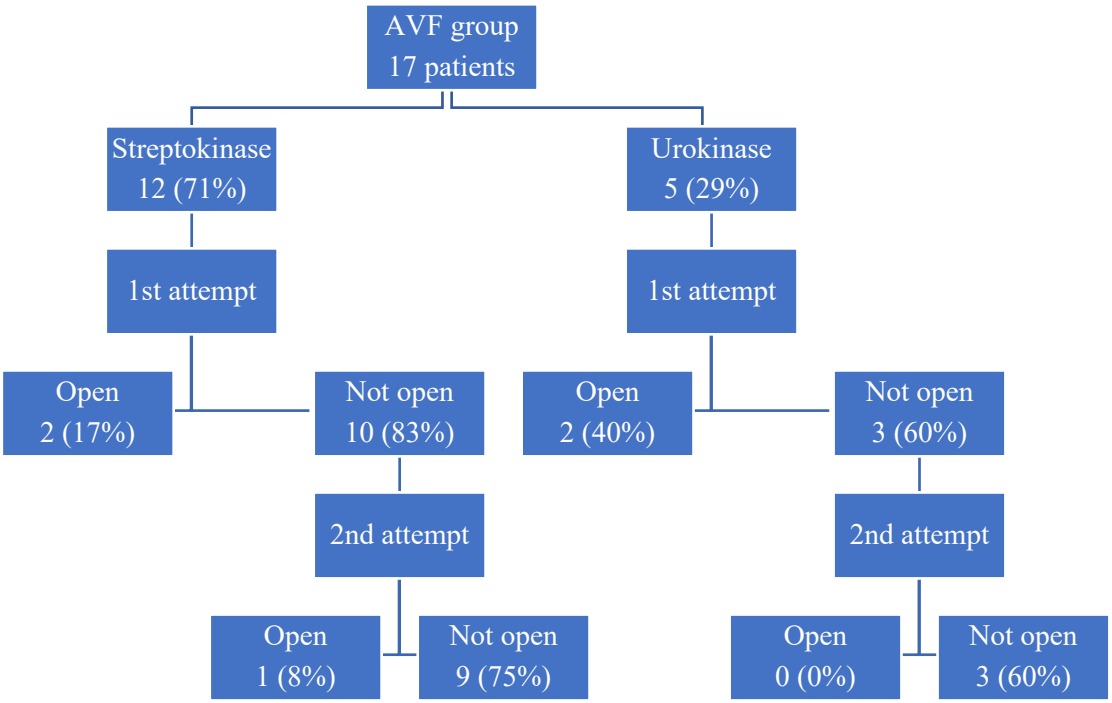

Figure 2:

In Streptokinase group on first attempt out of 12 patients 2 (17%) have shown evidence of effective flow and 10 (83%) have not shown effective flow. Out of those 10 patients, on second attempt 1 (8%) has shown effective flow and 9 (75%) have not shown effective flow. So, in total, in Streptokinase group out of 12 patients 3 (25%) have shown adequate flow and 9 (75%) have not.

In Urokinase group, on first attempt out of 5 patients 2 (40%) have shown evidence of effective flow and 3 (60%) have not shown effective flow. Out of those 3 patients, on second attempt 0 (0%) has shown effective flow and 3 (60%) have not shown effective flow.

So, in total, in Urokinase group out of 5 patients 2 (40%) have shown adequate flow and 3 (60%) have not.

CVC group

In CVC group out of 38 patients 15 (39%) have received injection Streptokinase and 23 (61%) have received injection Urokinase.

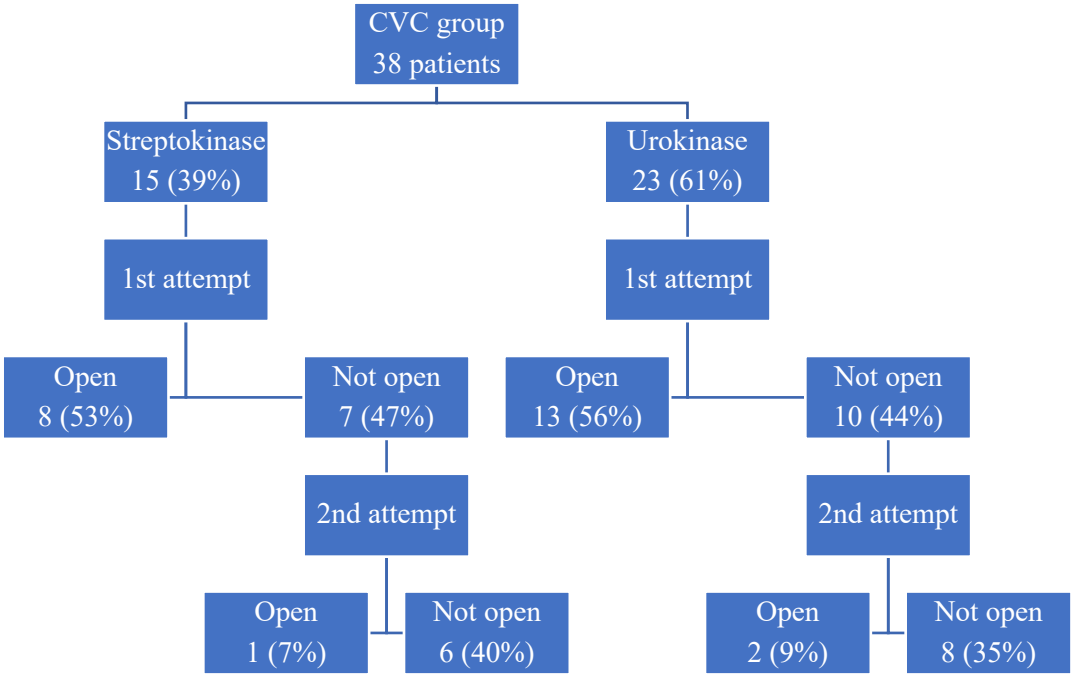

Figure 3:

In Streptokinase group on first attempt out of 15 patients 8 (53%) have shown evidence of effective flow and 7 (47%) have not shown effective flow. Out of those 7 patients, on second attempt 1 (7%) has shown effective flow and 6 (40%) have not shown effective flow. So, in total, in Streptokinase group 9 (60%) out of 15 patients have shown adequate flow and 6 (40%) have not. In Urokinase group, on first attempt out of 23 patients 13 (56%) have shown evidence of effective flow and 10 (44%) have not shown effective flow. Out of those 10 patients, on second attempt 2 (9%) have shown effective flow and 8 (35%) have not shown effective flow. So, in total, in Urokinase group 15 (65%) out of 23 patients have shown adequate flow and 8 (35%) have not.

3 months follow-up

In patients having AVF, in Streptokinase group 3 (25%) out of 12 patients had successful revascularization, out of that 3 patients on 3 months follow up 2 (17%) have adequate flow and 1 has expired of LRTI. In Urokinase group 2 (40%) out of 5 patients had successful revascularization, out of that 2 patients on 3 months follow up both 2 (40%) have adequate flow.

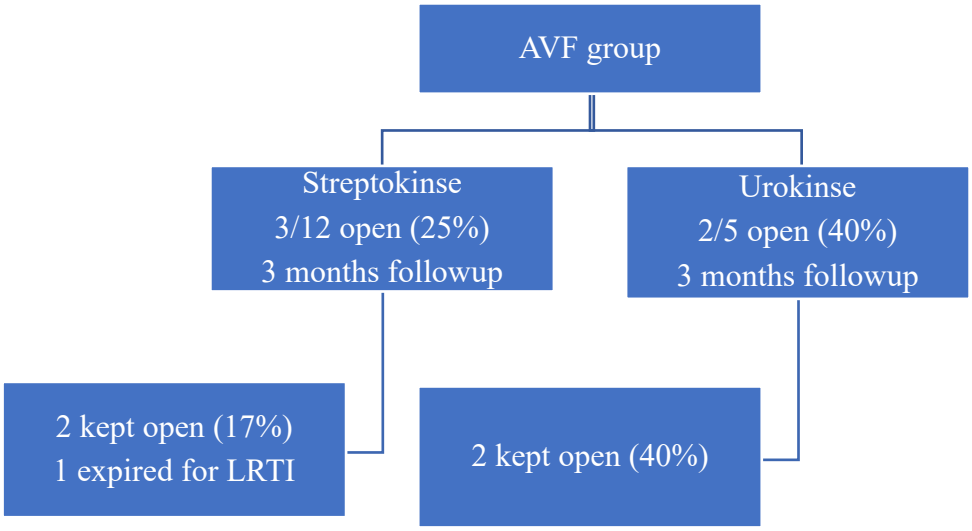

Figure 4:

In patients having CVC, in Streptokinase group 9 (60%) out of 15 patients had successful recanalization, out of that 9 patients on 3 months follow up 4 (27%) have adequate flow, 2 (13%) have got occluded, 2 have been lost

to follow up and 1 has expired of sepsis. In Urokinase group 15 (65%) out of 23 patients had successful re-canalization, out of that 15 patients on 3 months follow up 9 (39%) have adequate flow, 2 (9%) have got occluded, 1 has been lost to follow up, 2 had catheter removal for CRBSI and 1 has expired of LRTI.

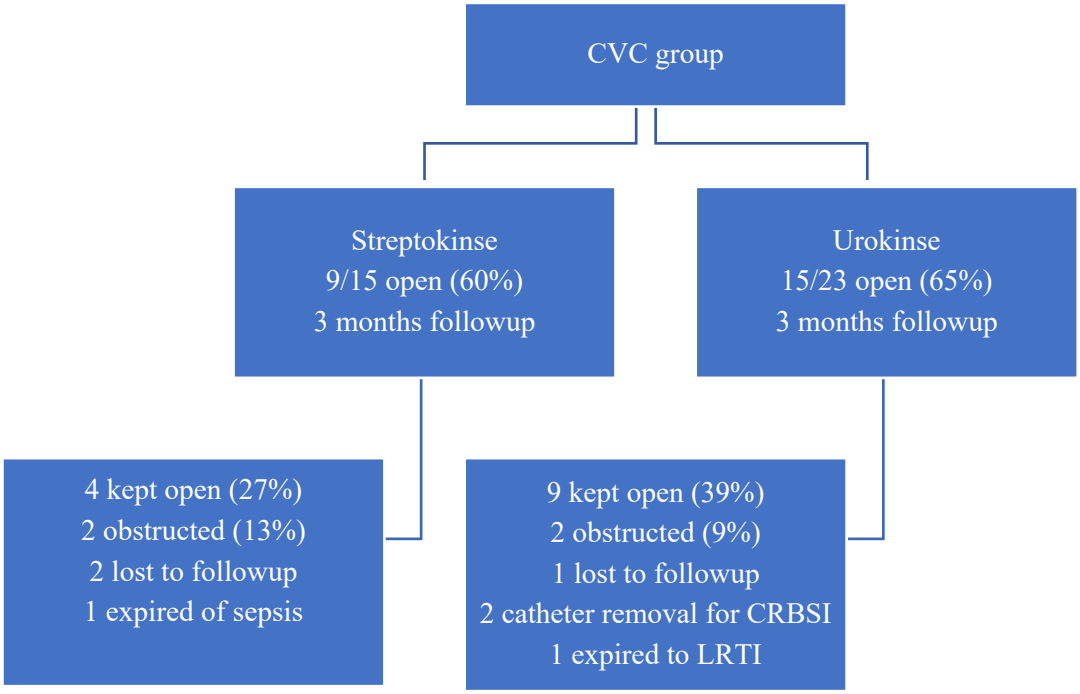

Figure 5:

Discussion and Conclusion

KDOQI Clinical Practice Guideline for Vascular Access: 2019 [4] suggests that Angioplasty with or without Stenting being the First line strategy for thrombosed AV access. Thrombolysis success rate being low, with reported rates of 25%-50% at 6 months and 10%-20% at 1 year and Open surgical repair is generally reserved for recurrent lesions, those not amenable to endovascular treatment and those for which the outcomes associated with the endovascular approach are poor.

Similar findings have been found in this study also. In cases of AVF, in total, in Streptokinase group out of 12 patients 3 (25%) have shown adequate flow and 9 (75%) have not and on 3 months follow up, 2 (17%) have adequate flow and 1 has expired of LRTI. In Urokinase group out of 5 patients 2 (40%) have shown adequate flow and 3 (60%) have not and on 3 months follow up out of that 2 patients both 2 (40%) have adequate flow. For CVC, KDOQI Clinical Practice Guideline for Vascular Access: 2019 [4] recommends intraluminal administration of thrombolytic agent in each catheter port to restore function of dysfunctional hemodialysis catheters due to thrombosis as first choice.

It recommends the use of Alteplase or Urokinase plus citrate 4% per limb for restoring intraluminal catheter blood flow in an occluded hemodialysis catheter. If it fails, KDOQI considers it reasonable to perform fibrin sheath disruption during CVC exchange for CVC dysfunction and it reasonable that CVC removal followed by replacement at a different site should be the last resort after conservative, medical, and other mechanical (e.g. angioplasty, CVC exchange) strategies have all failed to treat CVC dysfunction. Similarly in this study also Thrombolysis for CVC dysfunction shows good efficacy. In total, in Streptokinase group 9 (60%) out of 15 patients have shown adequate flow and 6 (40%) have not and out of that 9 patients on 3 months follow up 4 (27%) have adequate flow, 2 (13%) have got occluded. In Urokinase group 15 (65%) out of 23 patients have shown adequate flow and 8 (35%) have not and out of that 15 patients on 3 months follow up 9 (39%) have adequate flow, 2 (9%) have got occluded.

So, from this study it has been concluded that Thrombolysis success rate is low for AVF thrombosis, though it still can be tried in resource constraint situations and for CVC thrombosis bed side Thrombolysis is an effective way to restore the flow and outcomes are also good at 3 months follow-up.

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