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Comparative Study Between Streptokinase And Alteplase As Fibrinolytic Agents In Management Of Covid 19 Patients With Acute Pulmonary Embolism : A Retrospective Study

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Abstract

Objectives-This study is sought to compare the efficacy of alteplase versus streptokinase in acute massive pulmonary embolism and asses mortality at 24, 72 hours of diagnosis , resolution, adverse effects of the fibrinolytic agents

Background- Several thrombolytic regimens have been compared for the past 10 years in randomized studies, showing streptokinase versus alteplase which lead to faster hemodynamic improvement in when used alteplase. Many trials have focused on immediate hemodynamic and angiographic outcomes, but none has addressed efficacy in terms of resolution of pulmonary embolism, adverse effects and mortality outcomes at 24, 72 hours.

Methods- its a retrospective comparative study conducted at MGM hospital, Navi Mumbai during the covid pandemic.

Results- Out of 44 study subjects, 26 were thrombolysed with alteplase, 18 were thrombolysed with streptokinase .18 (40.9%) had mortality within 24 hours and 14 (31.8%) had mortality within 72 hours. Out of 44 study subjects, 20 (45.5%) had no bleeding
event, 6 (13.6%) had major bleeding events and 18 (40.9%) had minor bleeding event.

Conclusions- there is significant difference among the alteplase group and streptokinase group when compared with adverse effects and mortality but both groups had similar outcome when compared with pre and post therapy hemodynamics and efficacy in resolution of PE.

Keywords: NIL

Introduction

Since the emergence of coronavirus disease-2019 (COVID-19) as a result of infection with Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2), there has been a rising trend of patients presenting with thrombotic complications including deep vein thrombosis, pulmonary embolism (PE), myocardial infarction, stroke, and disseminated intravascular coagulation, acute limb ischemia and peripheral vascular diseases.

These complications have now been studied to arise from following mechanisms:

1. direct action of viral binding to the ACE receptors, especially within the kidneys, heart, and lungs.
2. micro-angiopathy triggered by hypoxic insult to pulmonary vasculature
3. Endothelial cell damage leads to thrombosis, which can be a defense mechanism that compartmentalizes infection and prevents further dissemination.

The presence of this transient hypercoagulable state due to COVID-19 was confirmed by the presence of elevated biochemical markers of thrombolysis in a

study by Han et al, demonstrating higher levels of D dimer, fibrinogen, fibrinogen degradation products, prolonged prothrombin time (PT), international normalized ratio (INR), and thrombin time (TT). The study also noted a correlation of these abnormalities with higher mortality and long term morbidity in patients infected with SARS-CoV-2.

Rationale of the study

1. As a tertiary care centre, MGM Medical College and Hospital was declared as a COVID Care Center with ICU facility and catered to the most critically ill patients. Among the patients diagnosed with pulmonary embolism as a complication of COVID-19, several patients were found to be eligible for thrombolytic therapy.
2. The choice of fibrinolytic agent was made based on several factors including clinical criteria, affordability of the agent, overall prognosis of the patient's condition.
3. Our study aimed to analyse the difference in outcomes for patients thrombolysed with streptokinase versus alteplase.

Aims And Objectives

Aim: This study sought to compare the efficacy of 2 hour regimens of Alteplase and Streptokinase in acute massive pulmonary embolism.

Objectives:

Primary Outcome: Mortality at 24 and 72 hours

Secondary Outcomes:

Efficacy: Resolution of the pulmonary embolism

Safety: Comparison of incidence rates of bleeding manifestations, and sICH

Materials and Methods

Study design: Retrospective record based comparative study.

Study location: MGM Medical College and Hospital, Kamothe

Study duration: March 2020 to March 2022

Sampling: Convenient sampling as per inclusion and exclusion criteria

Sample size: All critically ill COVID-19 patients diagnosed as acute pulmonary embolism and those who underwent fibrinolytic therapy.

Study conduct: After approval from the institutional ethics committee, hospital records shall be accessed and patient details for all patients fulfilling eligibility criteria shall be recorded as per the study proforma.

Inclusion And Exclusion Criteria

Inclusion Criteria:

1. Age >18 years
2. Severe COVID-19 (as per MOHFW guidelines)
3. Diagnosis of Acute Pulmonary embolism (as per biochemical and radiological criteria)
4. Patients who received fibrinolytic therapy

Exclusion Criteria:

1. Age <18 years
2. Mild and moderate COVID-19
3. Patients diagnosed as acute pulmonary embolism but did not receive fibrinolytic therapy

Statistical Techniques Used

The data was entered into MS-Excel worksheet and analysed using IBM SPSS Statistics 26.0 software. The categorical variables were presented using frequency and percentage. Further analysis was done using paired sample t-test. The level of significance was set at 5%. All p-values less than 0.05 were treated as significant.

Results

Table 1 indicates distribution of study subjects according to the age, gender, and agent used. Out of 44 study subjects, 2 (4.55%) were in the age group 21-30 years, 8 (18.18%) were in the age group 31-40 years, 9 (20.45%) were in the age group 41-50 years, 14 (31.82%) were in the age group 51-60 years, 5 (11.36%) were in the age group 61-70 years and 6 (13.64%) were over 70 years of age. Out of 44 study subjects, 35)79.55%) were males and 9 (20.45%) were females. Streptokinase was used among 26 (59.09%) study subjects and Alteplase was used among 18 (40.91%) study subjects.

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Table 1. Descriptive statistics

Variable	Frequency	Percentage
Age		
21-30	2	4.55%
31-40	8	18.18%
41-50	9	20.45%
51-60	14	31.82%
61-70	5	11.36%
>70	6	13.64%
Mean age = 52.80 ± 13.64, min = 26 yrs, max = 77 yrs		
Gender		
Male	35	79.55%
Female	9	20.45%
Agent used		
Streptokinase	26	59.09%
Alteplase	18	40.91%

Table 2 indicates descriptive statistics for various parameters used in the study. The average Wells score was 10.17±0.63, the average Troponin I was 268.80±253.06, the average D Dimer value was 5.68 ± 1.88, the average BNP was 1295.45 ± 1499.94 and the average PESI score was 230.30 ± 12.94.

Table 2. Descriptive Statistics for quantitative parameters in study

Parameter	N	Min	Max	Mean	SD
Wells score	44	9.00	11.00	10.17	0.63
Troponin I	44	44.00	900.00	268.80	253.06
D Dimer	44	1.80	9.20	5.68	1.88
BNP	44	130.00	5684.00	1295.45	1499.94
PESI Score	44	206.00	257.00	230.30	12.94

Table 3 indicates pre-post comparison of HR, SPO2, RR, SBP and DBP. The average Heart rate prior to diagnose PE was 126.91 ± 6.99 and the average heart rate after therapy was 122.64. no significant difference in the pre and post heart rate was observed (t=1.54, p = 0.132). The average SPO2 prior to diagnose PE and after

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therapy was 77.5 ± 7.85 and 81.07 ± 9.09 respectively. No significant difference was observed in the average SPO2 prior to diagnose PE and after therapy (t=-1.99, p=0.053). The average Respiratory rate prior to diagnose PE was 39.68 ±4.11 and after therapy it was 38.18 ± 6.9. no significant difference was observed in the v=average Respiratory rate prior to diagnose PE and after therapy (t=1.33, p = 0.189). The average systolic blood pressure prior to diagnose PE was 90.23 ± 3.93 and after therapy it was 94.5 ± 12.86. Significant difference was observed in the mean SBP prior to diagnose PE and after therapy (t=-2.06, p=0.046). The average diastolic blood pressure prior to diagnose PE was 56.41 ± 5.67 and after therapy it was 59.27 ± 14.12. No significant difference was observed in the mean diastolic blood pressure prior to diagnose PE and after therapy (t=-1.13, p = 0.266).

Table 3. Pre-post comparison of study parameters

Parameter		Mean	SD	SEM	t-stat	p-value
HR	Prior to diagnose PE	126.91	6.99	1.05	1.54	0.132
	After therapy	122.64	18.6	2.8		
SPO2	Prior to diagnose PE	77.5	7.85	1.18	-1.99	0.053
	After therapy	81.07	9.09	1.37		
RR	Prior to diagnose PE	39.68	4.11	0.62	1.33	0.189
	After therapy	38.18	6.9	1.04		
SBP	Prior to diagnose PE	90.23	3.93	0.59	-2.06	0.046
	After therapy	94.5	12.86	1.94		
DBP	Prior to diagnose PE	56.41	5.67	0.85	-1.13	0.266
	After therapy	59.27	14.12	2.13		

Table 4 indicates distribution according to the mortality and bleeding event. Out of 44 study subjects, 18 (40.9%) had mortality within 24 hours and 14 (31.8%) had mortality within 72 hours. Out of 44 study subjects, 20 (45.5%) had no bleeding event, 6 (13.6%) had major bleeding events and 18 (40.9%) had minor bleeding event. The results were also shown in the figure 1 and figure 2.

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Table 4. Distribution according to mortality and bleeding event

	Frequency	Percent
Mortality		
within 24 hours	18	40.9%
within 72 hours	14	31.8%
Bleeding event		
No bleeding event	20	45.5%
major bleeding event	6	13.6%
minor bleeding event	18	40.9%

Figure 1. Mortality

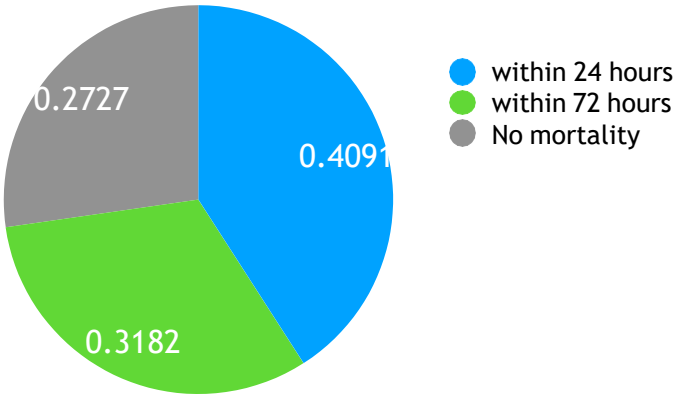
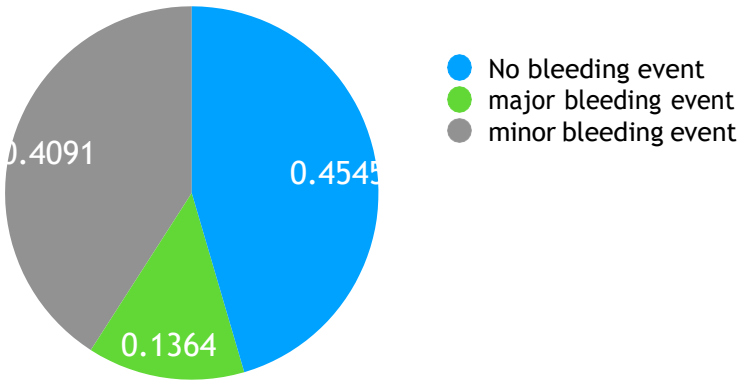


Figure 2. Bleeding event



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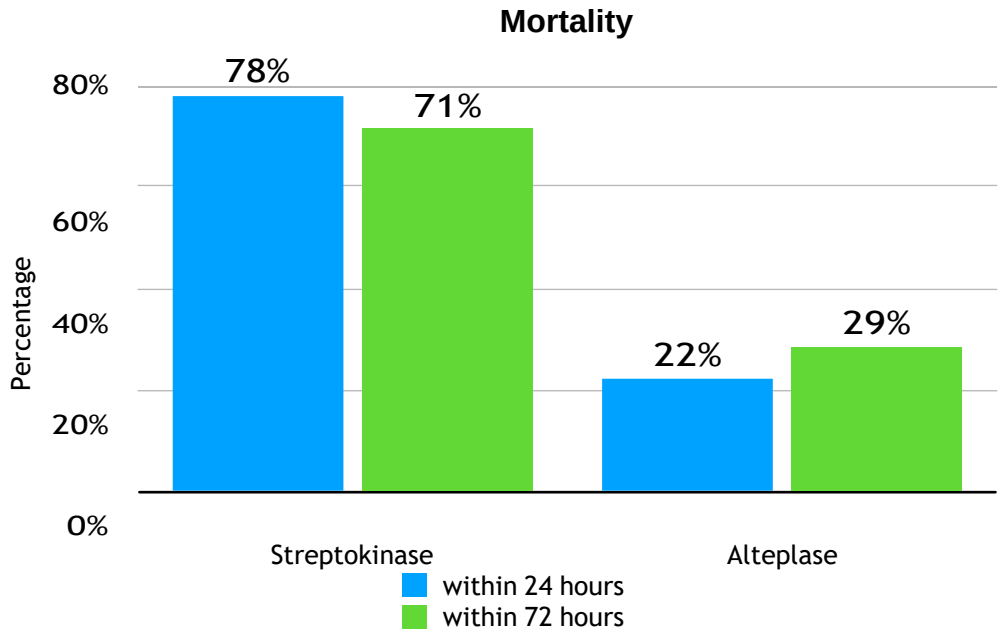

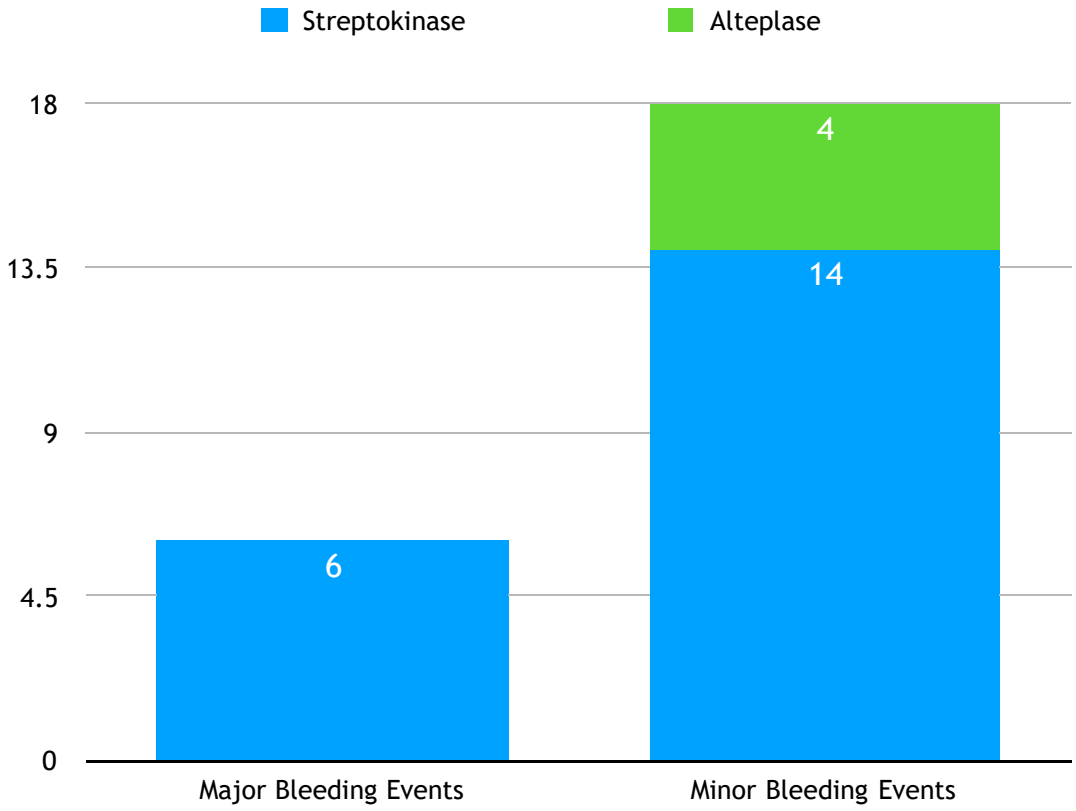

Conclusion

1. There is significant difference among the alteplase group and streptokinase group when compared with adverse effects (major bleeding events) and mortality (both 24 hours, 72 hours)
2. Both groups had similar outcome when compared with pre and post therapy hemodynamics and efficacy in resolution of PE.
3. Significant difference was observed in the mean SBP prior to diagnose PE and after therapy (t=-2.06, p=0.046).

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Limitations of the study

1. We couldn't asses mortality secondary to other causes like sepsis, Acute respiratory distress syndrome due to SARS Covid infection
2. Single centred and self reported study
3. Small sample Size

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