Thrombolysis in Angiographically Proved Intermediate to High Risk Pulmonary Embolism

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Abstract

Purpose of study: Pulmonary embolism is a common emergency in the hospital setting. Main line of treatment is anticoagulant therapy. However, patients with right ventricular dysfunction are the subgroup with increased mortality and may have better outcome with initial treatment with thrombolytic therapy. The study was done to see the outcome of thrombolytic therapy in angiographically proved patients of pulmonary embolism

Methods: We performed systemic workup of patients suspected of pulmonary embolism(PE). Diagnosis of PE was ruled out in patients with low probability of PE, as defined by Wells score and negative d dimer asssay. All patients were subjected to echocardiography. Those showing findings suggestive of PE, with right ventricular dysfunction, with or without hypotension, were subjected to pulmonary arteriography. Patients having evidence of PE were subjected to thrombolysis. Repeat angiography was done after the thrombolysis to see the effect of thrombolysis and fall in pulmonary artery pressures.

Introduction

Pulmonary embolism remains a major cause of morbidity and mortality in the general community, with an estimated incidence of 0.5 per 1000 people[1] and a case-fatality rate of 15% at 3 months.[2] Mortality is even higher for patients with "major" pulmonary embolism; registry data indicate in-hospital mortality of up to 30% in patients with acute pulmonary

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Results: 27 consecutive patients with angiographically proved PE were thrombolized. Mean age was 45.8±15.2 years. 18 were male and 9 were female. Average systolic and mean pulmonary artery pressure before thrombolysis was 71.2±14.4 and 47.5±10.5 mm Hg. Angiographic success was seen in 22 patients (81.5%). Average systolic and mean pulmonary pressure after thrombolysis was 47.1 ±21.7 and 29.4±16.5 mm Hg. Three patients with unsuccessful thrombolysis were successfully subjected to trans catheter thrombus extraction. One patient died during thrombolysis. None of the patients had major bleeding complications.

Conclusion: Thrombolysis is effective in majority of patients with pulmonary embolism with right ventricular dysfunction. The bleeding risk is low.

embolism who are hemodynamically unstable at presentation.[3,4] The study was conducted to see the effectiveness of thrombolytic therapy (TLT) in patients with angiographically proved pulmonary embolism(PE).

Material and Methods

Patients coming to our hospital with symptoms suggestive of PE were subjected to detailed examination. ECG was done in all patients. Patients with low probability of PE on the basis of wells score and negative d dimer essay were excluded. All subjected were subjected to detailed echocardiography. Patients showing high risk features such as hypotension, dilatation of right atrium(RA) and right ventricle(RV), evidence of tricuspid regurgitation(TR) with TR velocity 3M/s and evidence of right ventricular free wall hypokinesia were included in the study. When study was started, our hospital did not have facilities of 64 slice CT. Patients having contraindication to TLT were excluded. All patients were subjected to pulmonary arteriography with Pig tail catheter, through femoral vein puncture. Pulmonary artery pressures (PAP) were recorded. Patients showing evidence of occlusion or filling defect of proximal part of either pulmonary were subjected to TLT, through the same venous sheath. Most of the patients received streptokinsae (STK). Dose used was 2.5 lac units in 30 minutes and then infusion of one lac units/hour for 12-24 hours. Echocardiographic evaluation was done 6 hourly. Pulmonary angiography was repeated after 24 hours. PAP was again measured. Those showing partial recanalization were subjected to further infusion of STK for 12-24 hours and again angiography was repeated.

Table 1: Patient characteristics and presentation

Total patients	27
Male	18
Female	09
Mean age (yrs.)	45.8±15.2
Symptoms / Signs :	
Dyspnoea	24(88.8%)
Syncope	02 (7.4%)
Swelling feet	02 (7.4%)
Hemoptysis	01(3.7%)
Sweating	01(3.7%)
Suffocation on exertion	01(3.7%)
Chest pain	01(3.7%)
BP< 90mm Hg	06(22.2%)
ECG findings:	
Sinus tachycardia	27(100%)
T inversion in V1-V4	11(40.7%)
S1,Q3,T3 pattern	7(25.9%)
ST elevation in V1-V4	1(3.7%)
RVH with right axis deviation	1(3.7%)
Normal (except tachycardia)	4(14.8%)

Results

27 consecutive patients who had evidence of PE on pulmonary arteriography with RV dysfunction on echocardiography were included in the study. Table 1 show patient characteristics. 18 were male and 9 were female. Mean age was 45.8±15.2 years. Breathlessness was most common presenting symptom, seen in 24 patients (88.8%). Table 2 shows ECG findings. Commonest ECK finding was T wave inversion in V1-V4, seen in 11 patients (44.7%), followed by S1Q3T3 pattern seen in 7 patients (25.9%. ST elevation was seen in V1-V4 in one patient. 4 patients had normal ECG.) 13 patients had predisposing factors for PE, 3 of these had post partum state, 4 had long bone fracture in the past, one had past history of PE.25 patients received STK. One patient had anaphylactic reaction to STK, and was given tenecteplase (TNK). Another patient with treated carcinoma of bladder received TNK. Average systolic and mean pulmonary artery pressure before thrombolysis was 71.2±14.4 and 47.5±10.5 mm Hg respectively. Main pulmonary artery was involved in one patient, right pulmonary artery in 12 patients and left pulmonary artery in 5 patients and both pulmonary arteries in 9 patients. 21 patients had complete resolution of thrombus, 3 of these required TLT for 48 hours. Out of 5 patients, who did not achieve successful thrombolysis, 3 had successful transcatheter thrombus extraction. One patient was subjected to surgical embolectomy outside the state. One patient died during thrombolysis due to cardiogenic shock. No patient had major bleeding.

Table 2: Angiographic findings and result of thrombolysis

Total patients	27	
Angiographic findings: Filling defect in:		
RPA	12 (44.4%)	
LPA	05 (18.5%)	
Both LPA and RPA	09 (33.3%)	
MPA	01 (3.7%)	
Angiographically successful thrombolysis	22 (81.48%)	
Thrombus extraction	03	
Surgical embolectomy	01(3,7%)	
Mortality	01(3.7%)	
Mean PA pressures (mm Hg)	**Before thrombolysis**	**After thrombolysis**
Systolic	71.16±14.4	47.12±21.68
Mean	47.46±10.52	29.36±16.5

Discussion

Pulmonary embolism should be suspected in all patients who present with new or worsening dyspnea, chest pain, or sustained hypotension without an alternative obvious cause. However, the diagnosis is confirmed by objective testing in only about 20% of patients[5]. Depending on the clinical presentation, the case fatality rate for acute pulmonary embolism ranges from about 60% to less than 1%[2]. To guide the management of acute PE, the European Society of Cardiology[5] and the American Heart Association have proposed a three-level risk stratification scheme based on haemodynamic status and the presence of right ventricular dysfunction (RVD) or myocardial injury.[6] High-risk (or massive) PE is defined as an acute PE with sustained systemic arterial hypotension. Intermediate-risk (or

submassive) PE is defined by the presence of RVD or injury in the absence of arterial hypotension. Finally, low-risk PE is defined by the absence of hypotension and of markers of RVD or injury.

In 1970, the first randomized trial comparing urokinase with heparin for patients with PE was published [7]and 7 years later streptokinase was approved by the US Food and Drug Administration (FDA) for the treatment of high-risk PE. The preferred fibrinolytic agent is alteplase as a 100-mg continuous 2-hour infusion. Alteplase is the only contemporary fibrinolytic drug approved by the Food and Drug Administration for massive PE.

Although systemic fibrinolysis is not worth the risk in all patients with acute PE,[8] it is recommended as standard, first-line treatment in patients with massive PE.[9] In an overview of the 5 randomized controlled trials that included patients with massive PE, fibrinolysis reduced the risk of death or recurrent PE by 55%.[8]

Although thrombolytics are accepted as the standard of care for patients with hemodynamic instability, a great deal of controversy remains about the benefits of thrombolytic therapy for patients who present with acute PE, are hemodynamically stable, but have echocardiographic or other evidence of RV failure or strain. Registry data from the International Cooperative Pulmonary Embolism Registry[2] indicated that patients with RV hypokinesis on echocardiography even in the presence of a normal systemic arterial BP were at a twofold increased risk of death compared to those patients who had normal RV wall motion. Another series[10] of 162 consecutive patients presenting with acute PE reported that 31% had concomitant RV dysfunction that was associated with a 5% mortality rate compared to a 0% mortality rate in those with preserved RV function. Based on early data suggesting that patients with RV dysfunction are at an increased risk of PE-associated death, Konstantinides and colleagues[11] designed a study that enrolled 256 hemodynamically stable patients (systolic BP > 90 mm Hg) with proven acute PE and evidence of RV dysfunction or pulmonary hypertension. Patients were randomized to receive rt-PA plus heparin or placebo plus heparin with a follow-up period of 30 days. The main outcome measure was a combined end point that included in-hospital death and clinical deterioration requiring escalation of care. The study results indicated that patients who received rt-PA were significantly less likely to deteriorate clinically and reach the combined clinical end point than those who received placebo (11% vs 25%, respectively; relative risk reduction, 55%; 95% CI, 21 to 75%; number needed to treat, eight). However, the groups did not differ in all-cause mortality with a 3.4% mortality rate in the rt-PA group compared to 2.2% in the placebo group (relative risk increase, 56%; 95% CI, 60 to 513%).The study has been criticized because it allowed treating physicians to break protocol and administer "rescue" thrombolysis if they judged that a patient's clinical condition was deteriorating. The high rate of rescue thrombolysis may have driven the composite end point to statistical significance.

We thrombolized all patients with intermediate to high risk pulmonary embolism, with streptokinase, and got good results, though currently FDA has approved alteplase. This was done due to low cost of streptokinase and easy availability. In fact, STK is available free of cost in our hospital. Moreover, there are no conclusive findings from studies comparing different thrombolytic regimens in patients with acute pulmonary embolism. Short infusion times (2 hours or less) are recommended over prolonged infusion times, since they achieve more rapid thrombolysis and are probably associated with less bleeding.[12]

Conclusion

Commonest presentation of PE is breathlessness. Most common ECG finding is T inversion in leads V1-V4. Thrombolysis with STK can be done in intermediate to high risk patients, with good results. There are no major bleeding complications. The patients not responding to TLT, can be subjected to mechanical thrombus extraction.

Limitations

It was not a randomized control trial and did not compare the results of TLT with heparin.

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