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Evaluation of Systemic Thrombolytic Treatment in the Emergency Service in Unstable and Resuscitated Patients Due to Massive Pulmonary Embolism

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Abstract

Background: PE accounts for 3% of out-of-hospital cardiac arrest. In this case, treating patients with thrombolysis during resuscitation has been associated with better survival. The aim of this study is to evaluate the use of systemic thrombolytic in unstable and/or resuscitated patients who are evaluated in the red area in emergency service practice and who are diagnosed with massive pulmonary embolism with bedside examinations.

Materials and Methods: This prospective study was designed on 17 patients who were transferred as unstable to the emergency service of a tertiary hospital by Emergency Health Services and/or who needed resuscitation due to non-shockable fatal rhythm disorder on admission and who underwent systemic thrombolysis due to the diagnosis of pulmonary embolism during resuscitation.

Results: Of the 17 patients included in the study, 52.9% were discharged and improvement was detected in unstable vital findings in 47.1% patients after thrombolysis. Of the bedside examinations performed on admission, ECG showed T wave negativity at V1-4 deviations and P-pulmonale in 41.2% patients and ECHO showed right ventricle dilatation indicating right ventricle dysfunction in 82.4% patients. CTPA taken after stabilization showed thrombus at bilateral pulmonary artery in 88.2% patients.

Conclusion: Cardiopulmonary arrest caused by PE is a life-threatening condition that requires urgent systemic thrombolysis. Patients who are evaluated as unstable or in need of resuscitation in the emergency service should be diagnosed quickly as a result of examinations performed at bed-side and thrombolytic treatment should be started.

Keywords: Emergency treatment, pulmonary embolism, massive, thrombolytic treatment

Introduction

Acute Pulmonary Embolism (PE) is a fatal condition caused by venous thromboembolism. Although its prevalence varies between societies, it doubles every ten years after the age of 40[1]. Clinical symptoms and signs are not specific. Most of the time, it presents with symptoms such as dyspnea, chest pain, syncope and hemoptysis. However, it can also present with acute pressure increase in right ventricle dysfunction and arrest which are indicators of decreased hemodynamic reserve and instability as a result of prevention of both circulation and gas exchange[2]. Acute PE should be suspected especially in out-of-hospital cardiac arrests of unknown cause if there is anon-shockable rhythm and in the presence of risk factors for venous thromboembolism[3].

PE accounts for 3% of out-of-hospital cardiac arrest. In such a situation, treating patients with thrombolysis during resuscitation in accordance with the recommendation of American Heart Association has been associated with better survival[4]. Thrombolytic agents form plasmin, which accelerates thromboembolism lysis, by activating plasminogen. Therefore, thrombolytic therapy is used in patients diagnosed with acute PE to rapidly resolve the embolic load and improve cardiovascular hemodynamic. However, since thrombolytic therapy is associated with life-threatening hemorrhage, careful patient selection is critical for the success of this therapy. In this case, it is very important to determine that the cause of the arrest is PE. Screening techniques such as transthoracic echocardiography (TTE), lower extremity Doppler ultrasonography, laboratory tests such as electrocardiography (ECG), troponin-I and D-dimer and risk scorings performed at bedside at resuscitation area in the emergency service will guide the diagnosis[5].

The aim of this study is to evaluate the use of systemic thrombolytic in unstable and/or resuscitated patients who are evaluated in the red area in emergency service practice and who are diagnosed with massive PE with bedside examinations.

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Materials and Methods

Study Population:

The study was designed as a retrospective study on 17 patients who were transferred as unstable to Recep Tayyip Erdoğan University Training and Research Hospital emergency service by Emergency Health Services and/or who needed resuscitation due to non-shockable fatal rhythm disorder on admission and who received systemic thrombolysis due to PE diagnosis during resuscitation between January 2019 and February 2020. The data of the patients were obtained from Hospital Information Management System. The study was evaluated and approved by the ethics committee of the university.

Systemic thrombolysis was applied to patients with thromboembolism risk factors who were transferred unstable to the emergency service due to out-of-hospital sudden cardiac arrest upon detection of right ventricle (RV) dysfunction in bedside transthoracic echocardiography (TTE) in the resuscitation room. Hospital records of all of the patients were reviewed in terms of demographic data, predisposing factors, clinical picture, diagnostic studies, hemodynamic status and the results.

Study Protocol:

To identify patients who received systemic thrombolysis after being diagnosed with PE among unstable patients admitted to the resuscitation area, I26, I26.0 and I26.9 ICD-10 codes used in the application of thrombolytic agents were used.

Patients with a systolic blood pressure of <90 mmHg or a ≥40 mmHg decrease in systolic blood pressure were considered as hemodynamically unstable. Bedside TTE was performed (Esaote Mylab 50 Xvision with a 5 MHz transducer). Echocardiographic criteria of RV dysfunction were evaluated as RV dilatation and/or increased diastolic RV-LV diameter ratio (> 0.9), hypokinesia of the free RV wall, tricuspid regurgitation jet velocity, or a combination of these[2]. Pulmonary hypertension, pulmonary artery systolic pressures were defined as > 40 mmHg. At the same time, electrocardiography (ECG), arterial blood gas, haematological profile, serum troponin I levels, D-dimer and coagulation parameters were requested for the patients. Systemic thrombolysis was achieved by bolus administration of Alteplase (rtPA recombinant DNA technology) 0.6 mg/kg (maximum 50 mg) in 2-15 minutes. D-dimer test was performed by using enzyme-dependent fluorescent method and any value higher than 500 ng / ml was accepted as positive (normal value range 0-500 ng/ml). Troponin I was performed by using electrochemistry luminescence method and values higher than 34.2 pg/ml were considered abnormal (normal value range 0-34.2 ng/ml).

Statistical Analysis:

Data were analysed by using SPSS for Windows version 17 (SPSS, Chicago, IL, United States). All metric and normally distributed variables were reported as mean ± SD. Categorical variables were presented as frequency and percentage.

Results

Patient characteristics: 10 (58.8%) of the 17 patients included in the study were female, male 7 (41.2%) and mean age was 78.05 ± 10.26 (min: 58, max: 95). The most frequent complaint of the patients on admission or in the period before admission was shortness of breath with 64.7% (n=11) and 23.5% (n=4) of the cases were admitted to the emergency service due to syncope. The most frequent clinical finding was low terms oxygen saturation (76.7%, n=13), followed with tachycardia with a rate of 64.7% (n=11) and tachypnea with a rate of 47.1% (n=8). 6 (23.5%) patients were found to have symptoms of deep vein thrombosis (DVT) and it was confirmed with lower extremity Doppler ultrasound imaging. In general, all of the patients were found to have risk factors for PE. The risk factors found were previous surgery/immobilization (41.2%, n=7), hypertension (17.6%, n=3) and malignancy in 3 (17.6%) patients (Table-1). Four of the patients were smokers (23.5%). Serum troponin I and D-dimer levels were above normal in all patients.

ECG Features: On admission, rhythm was asystole in 23.5% (n=4) of the patients. After admission, sinus tachycardia was observed in the ECGs of 41.7% (n=7) of the patients following the necessary stabilization interventions. ECG was found to be normal in 3 (17.6%) patients. The most common ECG anomalies were T inversion in V1-V4 and P-pulmonale in 7 (41.2%) patients. Other findings were RBBB with a rate of 35.3% (n=6), atrial fibrillation with a

Table 1: Demograpic data (n = 17)

Age	78.05 ± 10.26 (min: 58, max: 95)	
Gender	Female	10 (58.8%)
	Male	7 (41.2%)
Risk factors	Immobilization	5 (29.4%)
	Deep vein thrombosis	4 (23.5%)
	Smoking	4 (23.5%)
	Hypertension	3 (17.6%)
	Canser	3 (17.6%)
	Fracture surgery	2 (11.8%)
Pre-incident complaint	Shortness of breath	11 (64.7%)
	Syncope	4 (23.5%)
	Haemoptysis	1 (5.9%)
	Cough	1 (5.9%)

Minimum-Maximum (Mean ±Standard Deviation).

Table 2: Bedside diagnostic tests.

Admission rhythm	Asystole	4 (23.5%)
	Sinus tachycardia	7 (41.2%)
	V1-4 Twave inversion	7 (41.2%)
	P-pulmonale	7 (41.2%)
	Right branch block	6 (35.3%)
	Atrial fibrillation	4 (23.5%)
	S1Q3T3	2 (11.8%)
Risk ECHO	Pulmonary hypertension	15 (88.2%)
	RV dilatation	14 (82.4%)
	D-septum	13 (76.5%)
D-dimer	>500 ng/ml	17 (100%)
Troponin-I	>34.2 pg/ml	17 (100%)

Table 3: Treatment and outcome.

Vital Findings	Pre-treatment	Post-treatment
Systolic blood pressure	67.05 ± 37.37 mmHg	118 ± 23 mmHg
Respiratory rate	18.11 ± 9.91 min.	13 ±8.1 min.
Pulse oxymeter %	72.17% ± 30.97	93% ± 2.01
Response to trombolytic treatment	Post-treatment recovery	8 (47.1%)
	Temporary response to treatment	5 (29.4%
Outcome	No response to treatment	4 (23.5%)
	Discharge	9 (52.9%)
	Death	8 (47.1%)

rate of 23.5% (n=4) and S1Q3T3 changes in 11.8% (n=2) of the patients (Table-2).

ECHO Findings: The most common echocardiography finding was pulmonary hypertension in 15 (88.2%) patients. Other findings were RV dilatation suggesting right ventricle (RV) dysfunction in 82.4% (n=14) of the patients and D-septum finding in 76.5% (n=13) of the patients (Table-2).

Computerized Tomography Pulmonary Angiography (CTPA) Findings: Imaging examinations performed after stabilization of the patients (patients with airway safety, systolic blood pressure >90 mmHg, heart beat that provides peripheral perfusion after it is provided) showed thrombus image in both the right and left pulmonary artery in 88.2% (n=15) of the patients and in only unilateral (right or left) pulmonary artery in 11.8% (n=2) of the patients.

Treatment: After thrombolysis, improvement was detected in unstable vital findings in 47.1% (n=8) of the patients. Systolic blood pressure was found to increase to 118 ± 23mmHg from 67.05 ± 37.37 mmHg. The same improvement was detected in respiratory rate (from 18.11 ± 9.91 min. to 13 ± 8.1 min) and pulse oximeter values (from 72.17 ± 30.97% to 93 ± 2.01%). However, 23.5% (n=4) of the patients did not respond to thrombolytic therapy. 29.4% (n=5) of the patients responded temporarily to the treatment and then they became unstable again.

As a result of the treatment, no major complications such as hemorrhage, blood transfusion, intracranial hemorrhage or fatal hemorrhage developed during the study period. Following the bed-side thrombolytic treatment in the emergency service, the patients were followed in the Intensive Care Unit. Mean follow-up time was 4.76 ± 7.21 days. 52.9% (n=9) of the patients included in the study were discharged after follow-up (Table-3).

Discussion

The present study describes the features and results of 17 patients who were transferred as unstable to the emergency service and who were resuscitated due to non-shockable fatal rhythm disorder and who received systemic thrombolytic treatment after being diagnosed with massive PE with bedside examinations. Massive PE has a high mortality rate and systemic thrombolysis both decreases these rates and increases the quality of life. Guidelines created in line with the studies conducted also suggest the use of thrombolytic[6]. Its fast and effective use during cardiopulmonary resuscitation is an advantage over surgical methods. Especially in patients with unstable findings, systemic thrombolytic therapy that will restore the pulmonary flow as a result of examinations that will provide rapid diagnosis at the bedside will improve diagnosis[7]. In this study, it was found that 76.5% of the patients became stable after systemic thrombolytic therapy, while 38.5% were found to have temporary recovery. It was found that 52.9% of the patients were discharged after follow-up and treatment at the hospital.

While PE accounts for 3% of out-of-hospital cardiac arrests, the presences of non-shockable rhythm and thromboembolism history are the risk factors that lead us to the diagnosis that should be considered at bedside in this group[3]. In this study, 23.5% of the patients were found to have non-shockable rhythm asystole on admission and all of the patients were found to have risk factors of thromboembolism such as cancer, immobilization and deep vein thrombosis. Current rates were the same as other studies[3, 8]. However, while the rhythm of the patients' during admission was asystole in this study, it was found as PEA in literature[9]. We believe that this difference results from the time of transportation to the hospital after the incident. PE is a condition that has the potential of sudden and fatal deterioration and requires urgent diagnosis and effective treatment. However, it is not easy to reach correct diagnosis despite advancing technology. It is important to identify especially unstable patients in the emergency service with bedside diagnostic tools and to apply appropriate treatment methods. Hypotension and deteriorations in right ventricle functions should be defined with ECHO and risk factors should be evaluated with clinical probability scores[10]. Bedside methods were used in the diagnosis of the patients

in this study since they were unstable to be removed from the care area in accordance with the guidelines.

Aggressive methods such as systemic fibrinolysis, pharmaco-mechanical catheter or surgical pulmonary embolectomy are needed in patients with suspected or proven diagnosis of massive PE. Among the treatment methods, fibrinolysis has a practical use since it can be applied quickly and easily and is available in most health institutions. In arrest cases, fibrinolytic therapy combined with chest compressions can increase survival by restoring spontaneous circulation[11]. In studies conducted, mortality rates varying between 22% and 90% have been reported after fibrinolytic therapy[9, 12]. We found that 52.9% of our cases had been discharged after their treatment.

The fact that it causes life-threatening hemorrhage and literature information is based on retrospective analyses, case series and reports has caused concerns and fibrinolytic therapy to be applied less[13-17]. The most important concern is the fact that hemorrhages that may occur after fibrinolytic therapy, which causes injury to the abdomen and thoracic cavity, especially during chest compressions. Despite this, no high fatal hemorrhage risk was found in both the present study and the literature[18].

The tissue plasminogen activator adopted for fibrinolytic therapy is Alteplase[19]. The recommended application regime is 100 mg infusion for two hours. However, 2-hour long Alteplase application during cardio pulmonary resuscitation is not applicable for emergency service practice. For this reason, it has become preferable to apply bolus for 2 to 15 minutes at a dose of 0.6 mg/kg (maximum 50 mg). In studies conducted, the results of stabilization of hemodynamic state, recovery of spontaneous circulation and neurological recovery have been found to be as effective as 2-hour long regime[20-22]. The patient group in the present study was given 0.6 mg/kg dose bolus application and hemodynamic stabilization was obtained in 47.1%. 29.4% of the patients were found to become unstable again after short term recovery. These results are also in parallel with experimental studies which show that reperfusion following fibrinolytic therapy can improve micro circulation[23-25].

Conclusion

As a conclusion, massive PE is a life-threatening condition that requires urgent systemic thrombolysis. Unstable patients or patients in need of resuscitation who are evaluated in the emergency service should be diagnosed quickly and their treatment should be started as a result of bedside examinations. Bolus Alteplase therapy does not increase the risk for major hemorrhage even if chest compression is applied. In addition, bolus therapy was found to be as effective as 2 hour long regime on mortality and survival. The most important limitation of the study was the fact that it was carried out retrospectively in a single center on a small sample without control group. In addition, especially the sensitivity and specificity of ECHO, which is one of the bedside diagnostic methods used, is limited when compared with CTPA.

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