Low dose thrombolysis in submassive pulmonary embolism at the extremes of age

Dr Lorna Neill, Dr William Nevin, Dr Hannah Skene
Acute Assessment Unit, Chelsea and Westminster NHS Foundation Trust

Introduction

Thrombolysis as a treatment for massive pulmonary embolism is well established; however, the management of submassive pulmonary embolism (PE without hypotension but with RV dysfunction or myocardial ischaemia) is controversial. The clinician must balance the substantial risk of bleeding against variably significantly improved outcomes. As our patient population changes and we treat an older demographic, current evidence for the optimal treatment is lacking, and risk vs benefit of thrombolysis must be considered individually.

Case report

97 year old female presented with collapse and shortness of breath.

PMHx: Hypertension

Drug Hx: Bendroflumethiazide 2.5mg OM Losartan 25mg OD

Allergy Status: Penicillin - Rash

Social Hx: Fully independent, no mobility aids, no carers

On examination:

Profoundly hypoxic (saturations of 78% despite 15L via NRBM) 

T1RF with a pO2 of 4.6kbP and pCO2 of 4.6kbP, Lac 1.9, BE -1.0

HR - 100bmp. BP - 120/80mmHg

Respiratory rate - 40. Temperature - 35.0°C

HS 1 x 1-0

Chest auscultation: crepitations and bronchial breathing at right base

Abdomen: soft and non tender

Calves: no evidence of DVT

Investigations:

ECG by ambulance service - ST elevation V1-V3 ST depression V4-V6

ECG in department - less ischaemic change

CRP - 123mg/l

WCC - 20x10

U&Es - K - 2.9mmol/l Ur 28mmol/l Cr 200mmol/l

Bedside ECHO/fast scan - no RV strain

Events:

- Initially covered for both CAP and ACS with antibiotics and ACS protocol (fondaparinux, aspirin and clopidogrel) in ED.
- Patient remained very unstable, and her oxygen saturations remained low despite non-invasive ventilation (saturations of 86% on CPAP 10cm H2O/FiO2 1.0).
- Repeat echocardiogram by sonographer showed a normal LV size and function, but dilated RV size with moderately reduced function, raised pulmonary pressures, PAP 42 - 47 mmhg.
- Differential of submassive PE raised; however her AKI and oxygen requirements made CTPA impossible.
- She was empirically treated for a submassive PE with low dose alteplase (50mg/ 1hour). A reduced dose was chosen due to AKI, previous ACS treatment and concerns regarding bleeding risk.
- Despite minor complications, her oxygen requirements dramatically decreased, and within 5 hours she was maintaining saturations of 99% on nasal high flow (40ml/min FiO2 1.0).
- CTPA several days later confirmed right pulmonary artery embolus extending into the upper and lower lobe arteries.
- She was successfully discharged and continues to live independently.

Discussion

NICE guidelines state that systemic thrombolysis is contraindicated for PE with haemodynamic stability with or without RV dysfunction and therefore contraindicated in our case; but the patient’s oxygenation requirements led our team to trial thrombolysis.

Several recent trials have looked at whether patients with submassive PE would benefit from receiving thrombolytic therapy. Those trials did show a lower risk of haemodynamic deterioration in comparison to low molecular heparin but with a risk of bleeding.

Dosing or agent for thrombolysis is ambiguous – NICE does not provide guidance; the British Thoracic Society in 2003 suggests 100mg/90min in patients with massive PE. The latest BNF edition advises a 10mg bolus of alteplase followed by an infusion of 90mg over 2 hours. Our team chose 50mg alteplase/1 hour after discussion with several consultants and the pharmacy team due to concerns that our patient was at a much higher risk of bleeding.

It has been suggested that a low dose of thrombotic agent could be a way of safely giving thrombolysis to patients with submassive PE, based on the theory that as the lungs alone receive the whole cardiac output, a reduced systemic dose can be given effectively for PE.

A recent study concluded that low dose alteplase (50mg) was effective in non-massive PE at reducing pulmonary artery systolic pressure, with risk of no bleeding but no significant difference in reducing the risk of death.

The risk of major bleeding, especially intracranial bleeding when giving thrombolysis, is reported as 9.24% -9.9% for major bleeding, with a significantly increased risk in the over 65s. The potential benefit of thrombolysis must be weighed against the risk of doing actual harm to the patient. For our case, at extremely high risk of an intracranial or gastrointestinal bleed due to her advanced age, the risk led us to treat with low dose thrombolysis of 50mg alteplase as a bolus. Although some bleeding occurred, it was minor, and her oxygen requirements markedly reduced after receiving thrombolytic therapy.

Conclusion

Thrombolysis for a 97 year old – a potentially lifesaving treatment with the threat of disastrous consequences. Would you do it? Thrombolysis is only recommended by NICE for patients with massive PE; and there is no consistent guidance on dosing. Using thrombolysis in submassive PE is contentious; however several recent trials have postulated that using a lower dose of thrombolysis can be effective and safe. In giving thrombolysis, the consequences can be catastrophic if the patient suffers haemorrhagic stroke or major haemorrhage. As our patient population is now becoming older, with multiple co-morbidities, decisions regarding high risk treatments are becoming more complex, and often patients do not meet the criteria set by national guidelines. In these situations, an MDT approach becomes more important and a decision must be made on a clinical and individual basis.

Here we present a patient, who despite advanced age, was successfully treated with low dose alteplase for a presumed submassive PE.

References


