Correspondence

Thrombolysis for acute pulmonary embolism in Chinese patients

Sir,

Acute pulmonary embolism is potentially fatal unless treated early. Thrombolytic therapy is beneficial for patients with acute pulmonary embolism who are hypotensive and have arterial hypoxaemia, and those who are clinically stable but with echocardiographic evidence of right heart failure. However, in the Pulmonary Embolism Registry, the rate of major bleeding was higher in patients receiving thrombolytic therapy (21%) than in those on anticoagulation treatment (7.8%). In one study examining risk factors associated with bleeding in patients receiving thrombolysis for pulmonary embolism, the relative risk of bleeding was 3.9 among patients aged >70 years compared with those aged <50 years. With age as a continuous variable, the risk of bleeding increased by 4% for each additional year. The Food and Drug Association (FDA)-approved regimen of recombinant tissue plasminogen activator (rtPA) for treatment of acute pulmonary embolism is 100 mg as a continuous peripheral intravenous infusion over 2 h.

In our centre, we try to give a lower dose of rtPA for treatment of acute massive pulmonary embolism in the elderly.

We assume that the dosage of 100 mg rtPA is based on a 70 kg adult, and our recommended dosage is 80% of the dose, adjusted for patient’s body weight. For example, for a 50 kg patient, dosage will be \(100 \times \frac{50}{70} \times 80\% \approx 60\) mg. A cut-off age of 60 years as elderly is arbitrarily chosen.

From October 1997 to March 1998, we had four elderly patients who suffered from acute massive pulmonary embolism warranting thrombolytic therapy. Their characteristics and outcomes were summarized in Tables 1 and 2.

Our patient 1 presented with pleuritic chest pain and shortness of breath. Emergency spiral CT scan of the thorax showed major pulmonary embolism. She was given weight-adjusted rtPA. Patient 2 presented with of shortness of breath. Emergency spiral CT scan of the thorax revealed major pulmonary emboli. Weight-adjusted rtPA was given. Patient 3 presented with confusion and shortness of breath. Emergency spiral CT of thorax revealed major pulmonary emboli, weight-adjusted thrombolytic therapy was given. Patient 4 presented with syncope and shortness of breath. Electrocardiogram revealed an S_1O_2T_3 pattern, and echocardiogram showed dilated right heart. Emergency spiral CT scan of thorax revealed pulmonary embolism in the right main pulmonary artery and distal branches. Weight-adjusted rtPA was given.

In our centre, as emergency spiral CT is more readily available than ventilation perfusion scanning, and is therefore used for diagnosing emergency cases.

Our four patients all had high clinical probability of pulmonary embolism. All had echocardiographic evidence of right heart dysfunction and arterial hypoxaemia. The prompt improvement in oxygen saturation and haemodynamic parameters of these patients reflected the efficacy of the reduced dosage of thrombolytic therapy in resolving the pulmonary emboli. Repeat spiral CT scans further supported the effectiveness of the treatment.

Despite the reduced dosage there were still bleeding complications in two of our patients. Our first patient had abdominal pain after thrombolytic treatment. Emergency CT scan of the abdomen revealed a retroperitoneal hematoma around the right psoas muscle. The dimension of the blood clot was about 7 cm x 8 cm. She was treated conservatively, but had a significant drop in haemoglobin level, and four units of blood transfusion were required. Our second patient suffered from bleeding around an arterial puncture site. Crepe bandaging of the hematoma site was performed and there was no significant drop in haemoglobin.

In one study by Kanter et al. examining intracranial haemorrhage and associated risk factors in patients with pulmonary embolism receiving thrombolytic therapy, a retrospective analysis involving 312 patients from different centres, the incidence of intracranial haemorrhage was 1.9% (six patients). Two of these six died. They identified increased diastolic blood pressure as a risk factor for intracranial haemorrhage (90.3 ± 15.1 mmHg vs. 77.6 ± 10.9 mmHg, \(p = 0.04\)).

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Table 1  Patient characteristics at presentation

<table>
<thead>
<tr>
<th>Patient</th>
<th>Sex/Age</th>
<th>Clinical features</th>
<th>Initial BP/P</th>
<th>Initial $S_aO_2$ (O$_2$ supplement)</th>
<th>Spiral CT before thrombolysis</th>
</tr>
</thead>
</table>
| 1       | F/71    | Chest pain, shortness of breath  
ECG: normal  
Echocardiogram: dilated RA and RV | 115/75      | 93 (100% O$_2$) | Thrombi in left and right main pulmonary artery, extending into both upper and lower lobe arteries. |
| 2       | F/61    | Shortness of breath  
ECG: $S_1Q_3T_3$, right axis deviation  
Echocardiogram: dilated RV | 125/65      | 90 (50% O$_2$) | Thrombi in left and right main pulmonary artery. |
| 3       | F/82    | Shortness of breath, confused  
ECG: partial RBBB, $S_1Q_3T_3$  
Echocardiogram: dilated RA and RV | 93/59       | 96 (100% O$_2$) | Thrombi in left and right main pulmonary artery. |
| 4       | M/61    | Syncope  
ECG: $S_1Q_3T_3$  
Echocardiogram: dilated RA and RV | 117/78      | 92 (100% O$_2$) | Thrombi in right main pulmonary artery. Segmental branches of both upper lobes, right middle lobe and both lower lobes. |

Table 2  Outcome of treatment

<table>
<thead>
<tr>
<th>Patient</th>
<th>BP/P*</th>
<th>$S_aO_2$* (O$_2$ Supplement)</th>
<th>Repeat spiral CT after thrombolysis</th>
<th>Complications</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>135/85</td>
<td>98 (50% O$_2$)</td>
<td>Thrombi resolved in main pulmonary arteries, upper lobe arteries. Decreased size of lower lobe arteries thrombi</td>
<td>Retroperitoneal haematoma (treated conservatively)</td>
<td>Follow-up in clinic</td>
</tr>
<tr>
<td>2</td>
<td>105/65</td>
<td>100 (50% O$_2$)</td>
<td>Resolved thrombi</td>
<td>Arterial puncture site haematoma (treated conservatively)</td>
<td>Follow-up in clinic</td>
</tr>
<tr>
<td>3</td>
<td>130/85</td>
<td>100 (50% O$_2$)</td>
<td>Small residual thrombus in lateral aspect of right main pulmonary artery</td>
<td>Nil</td>
<td>Follow-up in clinic</td>
</tr>
<tr>
<td>4</td>
<td>115/85</td>
<td>98 (50% O$_2$)</td>
<td>Decrease in size of the thrombi</td>
<td>Nil</td>
<td>Follow-up in clinic</td>
</tr>
</tbody>
</table>

* 4 h after thrombolytic therapy.
We have arbitrarily chosen our recommended reduced dosage of thrombolytic therapy as few studies address this issue. The largest study was by Goldhaber et al.\textsuperscript{6} comparing reduced rtPA bolus (0.6 mg/kg/15 min, maximum 50 mg) and rtPA infusion (100 mg over 2 h) in 87 patients, a double-blind randomized multicentre controlled trial. All patients had baseline, 20-h and 28-h follow-up nuclear scans. Some patients in centres with angiography services had baseline and 2-h pulmonary angiography, and some patients had baseline, 3-h, 20-h and 28-h echocardiogram. There was no significant difference between the two regimens with respect to bleeding complications, adverse clinical events, mortality and imaging studies outcome. In a substudy in 48 patients, there was less fibrinogenolysis in the bolus group.

Another study compared rtPA and Streptokinase in 66 patients with acute massive pulmonary embolism.\textsuperscript{7} There was a more rapid improvement in total pulmonary resistance at 1 h in the rtPA group compared with the streptokinase group, but a similar haemodynamic efficacy at 2 h when both thrombolytic regimens were completed. One-year event-free survival was similar in both groups and there was no significant difference in bleeding complications.

Because of the small sample size of our study group, and lack of matched controls, we can draw no definite conclusion about the efficacy and safety of our reduced dosage of thrombolytic therapy for acute massive pulmonary embolism in Chinese elderly patients. However, we believe that the weight-adjusted reduced dosage is appropriate for this group of patients in whom the bleeding complications will be higher. A large multicentre trial is needed to address this issue.

References


