Intrapericardial streptokinase in purulent pericarditis

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Abstract

Six consecutive children with proven purulent pericarditis were treated with pericardial irrigation with streptokinase. Mean (SD) 861 (678) ml (range 240–2000) of thick purulent fluid was drained, and five children had complete clearance of the pus within 3–8 days. One child developed intrapericardial haemorrhage with a submural pseudoaneurysm and underwent patch closure of the neck of the aneurysm as well as anterior pericardectomy. Follow up of 13 to 30 months revealed no pericardial constriction. (Arch Dis Child 1999;80:275–277)

Keywords: purulent pericarditis; streptokinase

Purulent pericarditis has conventionally been managed with intravenous antibiotics and pericardial drainage. Although intrapericardial streptokinase instillation to facilitate drainage in purulent pericarditis was reported in a limited number of patients in the early 1950s, these reports failed to generate any enthusiasm for this treatment until recently. We evaluated the role of intrapericardial streptokinase in purulent pericarditis.

Patients and methods

Six consecutive children (aged 8 months to 12 years (mean (SD) 5.95 (4.1) years; weight 6.5 to 25 kg (mean (SD) 13.3 (6.6))) were enrolled in the study. In all patients the diagnosis of purulent pericarditis had been confirmed by pericardial aspirate examination, and pericardiocentesis had led to incomplete fluid removal. Informed consent was obtained from the parents of all the children.

STREPTOKINASE PROTOCOL

Normal coagulation status was documented before the first instillation. Diluted streptokinase (10 000 to 15 000 units/kg) was instilled every 12 hours through an 8 F pigtail catheter into the pericardium. The patient was rotated every 15 minutes and syringe aspiration done every two hours. Patients were clinically monitored for signs and symptoms of anaphylaxis, chest pain, arrhythmias, bleeding, and hypotension. Serial radiographs, haemoglobin measurements, clotting parameters, and echocardiography were carried out. Duration of streptokinase treatment was based on an estimate of pericardial fluid using echocardiography and amount of aspirate.

Intravenous antibiotics were started empirically and modified as per the culture reports and antibiotic treatment. In two children there was a sudden increase in pericardial fluid after streptokinase. Streptokinase could not be given for more than four doses in one child because of intrapericardial haemorrhage and later development of a submural pseudoaneurysm. Streptokinase dosage ranged from 8 000 to 15 000 units/kg for 4 to 8 days. In five patients, fever and systemic symptoms responded to various combinations of antibiotics; however, one child received empiric anti-tubercular treatment because of persistent fever and a positive Mantoux test.

Two patients developed a right atrial mass after starting streptokinase (noted on the 11th and third days of antibiotic treatment, respectively) in the superior vena cava–right atrial junction. Amphotericin was used empirically in one child and the mass resolved over the subsequent three weeks. Spontaneous resolution occurred over three days in the other child.

One 8 year old boy (weight 14 kg) with staphylococcal septicaemia and purulent pericarditis developed a submural pseudoaneurysm during treatment. Intrapericardial streptokinase (150 000 units) was started on the fourth day, and 500 ml of thick pus mixed with blood was aspirated. However, after four doses of streptokinase there was a sudden increase in the fluid with cardiac tamponade; we aspirated 300 ml of frankly haemorrhagic fluid. Clotting
time was 15 minutes (basal 6 minutes). Streptokinase instillation was withheld but restarted (lower doses of 75,000 units) after four days because of continuing fever and evidence of organisation. Although drainage increased to 300 ml over the next two days, a submirtal aneurysm was noted and streptokinase stopped. Review of a retrospective video recording showed a small intramyocardial echoluency in the submirtal area on the second day of starting the first streptokinase course. Vancomycin and cefotaxime rapidly controlled the infection. However, evidence of constriction remained and the submirtal pseudoaneurysm gradually increased in size. At open heart surgery the neck of the aneurysm was closed with a polytetrafluoroethylene patch and anterior pericardectomy was done. Follow up at 13 months revealed complete regression of the pseudoaneurysm.

No patient had systemic bleeding, arrhythmias, or hypotension. There was no instance of infection at the site of pigtail insertion, nor was there any local pain during streptokinase instillation. Mean (SD) follow up of 19.8 (6.7) months (range 13–30) revealed no patient with pericardial constriction.

Discussion

We believe this is the first study to document the efficacy and safety of intrapericardial streptokinase in children with purulent pericarditis. Needle aspiration or catheter drainage alone is not sufficient to remove the infected fluid in most patients, but was attempted initially in all our patients. Intrapericardial streptokinase started as late as two to four weeks after the onset of illness despite the presence of adhesions and thick fluid was effective in draining the fluid. Reduced fibrinolytic activity in purulent pericarditis has been shown to cause extensive fibrin deposition over denuded mesothelial surfaces, and intrapericardial streptokinase helps in dissolving the fibrinous components of these exudates.3

This approach may have several advantages over surgical techniques. Limited procedures like subxiphoid drainage may not prevent acute constriction while more extensive procedures like pericardial window with a pleural drain and partial pericardiectomy both need a thoracotomy, which carries significant morbidity.4 Adequate surgical drainage prevents delayed constriction and even in our patients delayed constrictive pericarditis was not seen. Surgical approaches have a further disadvantage of requiring specialised care, which is scarce and costly in developing countries. In our children the cost of streptokinase was less than Rs4000 (US$120) per patient.

We cannot fully explain the presence of a right atrial mass in two of our patients. A similar case was reported by Rao et al who speculated that decreased cardiac output was responsible for the thrombus.5 We believe this mass may be an infected collection seeping into the thin walled right atrium from the pericardium. Thrombolytic treatment may have influenced its occurrence.

<table>
<thead>
<tr>
<th>Weight (kg)</th>
<th>Organism isolated</th>
<th>Antibiotics</th>
<th>Streptokinase dose (units)/duration</th>
</tr>
</thead>
<tbody>
<tr>
<td>15</td>
<td>Staphylococcus aureus</td>
<td>Cloxacillin, gentamicin (NR)</td>
<td>150,000, 8 days</td>
</tr>
<tr>
<td>10</td>
<td>None</td>
<td>Cloxacillin, amikacin, cefotaxime</td>
<td>150,000, 8 days</td>
</tr>
<tr>
<td>9</td>
<td>S aureus</td>
<td>Cloxacillin, amikacin + ciprofloxacin</td>
<td>75,000, 4 days</td>
</tr>
<tr>
<td>6.5</td>
<td>None</td>
<td>Cloxacillin, amikacin, cefotaxime</td>
<td>75,000, 3 days</td>
</tr>
<tr>
<td>25</td>
<td>S aureus</td>
<td>Cloxacillin, amikacin (NR)</td>
<td>150,000, 2 days</td>
</tr>
<tr>
<td>14</td>
<td>S aureus</td>
<td>Cloxacillin, amikacin, cefotaxime</td>
<td>75,000, 3 doses</td>
</tr>
</tbody>
</table>

NR, no response.
Submitral aneurysm following intrapericardial streptokinase has not been previously reported. Streptokinase stimulates interstitial collagen breakdown and it is possible that high local concentration might have led to the submtral aneurysm. This patient also had intrapericardial haemorrhage associated with deranged clotting time, suggesting systemic fibrinolysis. Berglin et al found no effect on fibrinogen, fibrin degradation products, or thrombin times after intrapleural instillation of streptokinase.

The choice of thrombolytic agent as well as doses and duration of treatment remains open. Winkler et al used urokinase while we preferred streptokinase because of its cost and familiarity.

We conclude that intrapericardial streptokinase is useful in treating purulent pericarditis.

Close clinical, haematological, and echocardiographic monitoring is warranted during its instillation.