Intrapericardial streptokinase in purulent pericarditis

Rajnish Juneja, Shyam S Kothari, Anita Saxena, Rajesh Sharma, Anuradha Joshi

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 submitial pseudoaneurysm and underwent patch closure of the neck of the aneurysm as well as anterior pericardietomy. Follow up of 13 to 30 months revealed no pericardial constriction. (Arch Dis Child 1999;80:275–277)

Keywords: purulent pericarditis; streptokinase

Intravenous antibiotics were started empirically and modified as per the culture reports and amount of aspirate. At follow up, we evaluated patients clinically and by echocardiography for evidence of persistent infection and pericardial constriction.

Results
Four patients had had symptoms suggesting acute pericardial collection for almost two weeks and had been feverish for nearly four weeks (mean (SD) 22 (7.6) days). There was evidence of an extracardiac infection in two patients (arthritis, osteomyelitis, and parietal abscesses). Staphylococcus aureus was isolated in blood or pericardial fluid cultures in four patients, but no organism was isolated in the other two.

Echocardiograms in five children showed an echodense collection suggestive of thick pus (fig 1) while one had an echolucent collection with no organisation. Pericardial aspirates were negligible in three patients while in the remaining three, 200–500 ml of fluid was drained over 1–4 days before starting streptokinase. Mean (SD) pretreatment drainage volume was 178 (200) ml (range 15–540). In all patients, a large volume of thick purulent fluid was removed over the 3–8 days of streptokinase instillation (861 (678) ml, range 240–2000) (fig 2). Table 1 summarises streptokinase doses and duration, 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 submitial 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 antitubercular 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 submitial 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 submitral aneurysm was noted and streptokinase stopped. Review of a retrospective video recording showed a small intramyocardial echolucency in the submitral 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 submitral pseudoneurysm gradually increased in size. At open heart surgery the neck of the aneurysm was closed with a polytetrafluoroethylene patch and anterior pericardiectomy was done. Follow up at 13 months revealed complete regression of the pseudoneurysm.

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 (fig 1) 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 1 Streptokinase and antibiotic regimens

<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>150000, 8 days</td>
</tr>
<tr>
<td>10</td>
<td>None</td>
<td>Cloxacillin, gentamicin (NR)</td>
<td>150000, 8 days</td>
</tr>
<tr>
<td>9</td>
<td>S aureus</td>
<td>Cloxacillin, amikacin, ciprofloxacin</td>
<td>75000, 4 days</td>
</tr>
<tr>
<td>6.5</td>
<td>None</td>
<td>Cloxacillin, amikacin, cefotaxime</td>
<td>75000, 3 days</td>
</tr>
<tr>
<td>25</td>
<td>S aureus</td>
<td>Cloxacillin, amikacin</td>
<td>250000, 6 days</td>
</tr>
<tr>
<td>14</td>
<td>S aureus</td>
<td>Cloxacillin, amikacin (NR)</td>
<td>150000, 2 days</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Vancomycin, cefotaxime</td>
<td>75000, 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 submitral 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.

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