CASE REPORT

Congenital idiopathic chylothorax in neonates: chemical pleurodesis with povidone-iodine (Betadine)
O Brissaud, L Desfere, R Mohsen, M Fayon, J L Demarquez

Chylothorax is defined as an accumulation of chyle in the pleural space. This condition usually occurs after an operation, the congenital idiopathic form being rare (1/15,000 births). Recovery is observed within four to six weeks of diagnosis in most cases. Treatment is either conservative or surgical. Four cases are reported of congenital chylothorax (three idiopathic, one accompanied by diffuse lymphangectasia) managed by chemical pleurodesis (intrapleural injection of povidone-iodine). Tolerance was satisfactory: unaltered thyroid function in the three cases explored; one case of transient generalised oedema. Treatment was deemed successful in three of the four cases. One child died from renal failure (unrelated to the chemical pleurodesis). Pleurodesis by povidone-iodine appears to be well tolerated and may represent a good alternative to mechanical abrasion or surgery for congenital idiopathic chylothorax. Its use for refractory chylothorax may also decrease the morbidity related to prolonged hospital stay.

Congenital idiopathic chylothorax is the most common cause of pleural effusion in the neonatal period. Its prevalence is about 1/15,000 births, and accounts for 8% of chylothoraces in children. The outcome is characterised by a perinatal mortality of 15–57%. If chylothorax is associated with hydrops fetalis, mortality can reach 98%. Antenatal management consists of thoracocenteses or pleuroamniotic shunts to prevent secondary pulmonary hypoplasia. In the postnatal period, the classical management of the pleural effusion (in addition to the symptomatic treatment of the respiratory distress) can be either conservative or surgical (see the box). Another recent conservative treatment is the use of a continuous infusion of somatostatin. Morbidity related to the management of congenital idiopathic chylothorax is high because there is a risk of nosocomial infections (low serum immunoglobulins, malnutrition, lymphopenia, long term central venous catheters, and chest tube drainage). It is important to develop methods than can decrease this morbidity and reduce hospital stay. Pleurodesis with a chemical agent in children has previously been described, but never with povidone-iodine (Betadine). We report on four cases of congenital chylothorax treated by a simple method—that is, povidone-iodine pleurodesis. All patients were recruited over a period of six months during the year 2000. Informed consent to perform the procedure was obtained from the children’s parents.

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Table 1 gives the basic details of the four cases.

Case 1
A bilateral chylothorax was diagnosed in a female fetus during pregnancy. Bilateral pleuroamniotic tubes were inserted at 30 weeks because of compressive hydrothorax and maintained until birth at 31 weeks gestation. Her parents were unrelated, and chromosome analysis was normal. After birth, the chest tubes were removed with a good initial outcome. However, a right pleural effusion reappeared rapidly, requiring 26 pleural thoracocenteses up to day 53 (total volume 1250 ml), initially one a week, then two a week despite total parenteral nutrition. At day 53, a chest tube was inserted. Because of loculations, a larger tube was surgically inserted on day 65 when an intrapleural instillation of povidone-iodine (Betadine 4% scrub) was performed. The chest tube was finally removed on day 81 after complete recovery. The infant is healthy, without recurrence of the pleural effusion. Thyroid function tests were normal before and after treatment.

Case 2
A 2300 g, 35 week gestation female infant was born after a tocolysis failure. The parents were first cousins. Fetal hydrops was diagnosed at 34 weeks, and bilateral pleuroamniotic tubes were then inserted. Caryotype was normal. Soon after birth, she presented with respiratory distress. Repeated bilateral thoracocenteses were performed during the first 11 days with an increasing volume extracted (total volume 1100 ml). A left sided chest tube was then inserted in order to instil povidone-iodine (Betadine 4% scrub). The pleural effusion resolved within 48 hours, but increased on the right side. On day 13, a right sided chest tube was therefore inserted and povidone-iodine was instilled. The chylothorax had resolved completely on day 20. Thyroid function tests were normal before and after this treatment. The infant is at present healthy.

Case 3
Macrosomy and hydramnios were observed at 32 weeks in a female fetus. Caryotype was normal. At 36 weeks, a right compressive pleural effusion was noted, and caesarean section was performed immediately. At birth, the first thoracocentesis revealed chylothorax. Initial management consisted of repeated bilateral thoracocenteses. After three weeks, the left pleural effusion had disappeared. However, because of a residual right sided effusion, a chest tube was inserted for six weeks. The maximal daily pleural effusion volume reached 300 ml. On day 59, povidone-iodine (Betadine 10% dermique) was instilled through the chest tube. A rapid recovery was noted six days later, and the chest tube was removed. Blood and urinary iodine levels and thyroid function tests were normal before and after treatment. The infant is alive and well 22 months later.

Case 4
At 32 weeks gestation, an antenatal diagnosis of left chylothorax was made. It was well tolerated until the appearance of a right effusion at 35 weeks. At 36 weeks, in utero effusion puncture was performed because of heart rate...
Table 1 Intrapleural instillation of Betadine

<table>
<thead>
<tr>
<th>Case No</th>
<th>Antenatal diagnosis</th>
<th>Diagnosis</th>
<th>Type of Betadine</th>
<th>Number and time of instillations</th>
<th>Volume (ml) of Betadine, child's weight (g)</th>
<th>Duration of post-instillation chest tube occlusion (h)</th>
<th>Maximal analgesia (g/kg/h)</th>
<th>Outcome (chest tube removal)</th>
<th>Adverse effect</th>
<th>Thyroid function</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Yes</td>
<td>OC</td>
<td>Scrub</td>
<td>R: 1 (day 65)</td>
<td>10,&lt;&lt;&gt;</td>
<td>4</td>
<td>Fentanyl (10)</td>
<td>Successful (16 days)</td>
<td>None</td>
<td>Normal before and 19 days after instillation</td>
</tr>
<tr>
<td>2</td>
<td>Yes</td>
<td>OC</td>
<td>Scrub</td>
<td>R: 1 (day 11)&lt;&lt;&gt;</td>
<td>2500 5 per instillation,&lt;&lt;&gt;</td>
<td>Right side: 2&lt;&lt;&gt;</td>
<td>Fentanyl (10)</td>
<td>Successful (10 days)</td>
<td>Increase in contralateral pleural effusion after the first instillation of Betadine</td>
<td>Normal before and 16 days after instillation</td>
</tr>
<tr>
<td>3</td>
<td>Yes</td>
<td>OC</td>
<td>Dermique</td>
<td>L: 1 (day 13)</td>
<td>2200 3,&lt;&lt;&gt;</td>
<td>Left side: 3</td>
<td>Sufentanyl (0.8)</td>
<td>Successful (6 days)</td>
<td>Generalised oedema (spontaneous resolution)</td>
<td>Normal before and 30 days after instillation</td>
</tr>
<tr>
<td>4</td>
<td>Yes</td>
<td>Diffuse lymphangectasia</td>
<td>Scrub</td>
<td>L: 2 (days 22 and 26)&lt;&lt;&gt;</td>
<td>3000 5 per instillation,&lt;&lt;&gt;</td>
<td>Fentanyl (10)</td>
<td>Failure</td>
<td>Increase in contralateral pleural effusion after the first instillation of Betadine</td>
<td>ND</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>R: 1 (day 25)</td>
<td>3100</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

ND, Not done; L, left; R, right; OC, congenital idiopathic chylothorax.

In an attempt to decrease the morbidity usually associated with the classical management of congenital chylothorax (infections, thrombosis, defects in intestinal nutrition, complications of mechanical ventilation), we treated four neonates by intrapleural instillation of povidone-iodine through a chest tube. This procedure was effective in three of the four cases and appeared to be well tolerated. Systemic analgesia was achieved with a combination of fentanyl and lidocaine. The infant developed renal failure related to the renal venous thrombosis. He died from end stage renal failure, oliguria, hyperkalemia, and refractory hypertension.

**DISCUSSION**

In an attempt to decrease the morbidity usually associated with the classical management of congenital chylothorax (infections, thrombosis, defects in intestinal nutrition, complications of mechanical ventilation), we treated four neonates by intrapleural instillation of povidone-iodine through a chest tube. This procedure was effective in three of the four cases and appeared to be well tolerated. Systemic analgesia was achieved with a combination of fentanyl and lidocaine. The infant developed renal failure related to the renal venous thrombosis. He died from end stage renal failure, oliguria, hyperkalemia, and refractory hypertension.

An autopsy showed diffuse lymphatic abnormalities with congenital pulmonary hypoplasia.

A chromosome analysis was normal. At birth, bilateral chest tube pleurodesis was normal. At birth, bilateral chest tube pleurodesis was normal. The infant developed renal failure, oliguria, hyperkalemia, and refractory hypertension. The infant developed renal failure, oliguria, hyperkalemia, and refractory hypertension. The infant developed renal failure, oliguria, hyperkalemia, and refractory hypertension.
Neonatal chylothorax and Betadine response in the wall of any fluid containing structure. A 100% success rate has been reported in chylothorax. However, to our knowledge, the intrapleural injection of povidone-iodine as a chemical agent for pleurodesis in congenital chylothorax has never been reported. This agent has previously been used for the sclerosis of postoperative pelvic lymphoces15-16 and pleural lavage of empyema in adults. A 100% success rate has been reported when this agent was administered to 15 adult patients with a malignant pleural effusion.14

The mechanism of action of povidone-iodine appears to be related to enhanced sclerosis, although the precise mode of action remains unclear. Iodine has strong oxidative and cytotoxic properties, which induce a potent inflammatory response in the wall of any fluid containing structure. Moreover, povidone-iodine may have antitoxic properties related to the chelation of proteins.15

As this treatment was new to our unit, we paid careful attention to any adverse effects. The frequent use of topical cutaneous povidone-iodine in neonates can induce allergic sensitisation and impairment of thyroid function. Local cytotoxic mucosal and skin lesions have been described.19

The only adverse effect that we considered to be possibly related to the treatment was generalised oedema, which led us to suggest that a bilateral procedure should be performed if the chylothorax involves both pleural spaces. The risk of hypothyroidism is theoretically greater with the intrapleural instillation of iodine than after its application to the skin. In the three cases investigated (1, 2, and 3), thyroid function tests before and after the procedure remained unchanged. Of note, the infant who did not respond to the treatment (case 4) had serious renal involvement before the procedure. Povidone-iodine may have worsened his oligoanuria and end stage renal failure. Necropsy revealed diffuse lymphangectasia involving the lungs and abdomen.

Conclusion
This report illustrates the feasibility of intrapleural injection of povidone-iodine for the treatment of congenital idiopathic chylothorax. This treatment was administered when the classical management of the disease (nil by mouth, parenteral nutrition, pleural punctures, chest tube drainage) failed in an attempt to avoid more invasive surgical procedures. Adverse effects were minor (allergic oedema?). A recent study confirms the effectiveness of this treatment for recurrent pleural effusion in adults. Used early, this method has the potential to reduce the morbidity related to prolonged hospital stay. Use of adequate analgesia is a priority. The present results are not sufficient to assert that the therapeutic regimen proposed is efficacious, and a prospective randomised study in newborns treated with intrapleural povidone-iodine is required.

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Accepted 14 October 2002

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