CASE REPORT

Congenital idiopathic chylothorax in neonates: chemical pleurodesis with povidone-iodine (Betadine)

O Brissaud, L Desfriere, R Mohsen, M Fayon, J L Demarquez

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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.1–4 Its prevalence is about 1/15,000 births, and accounts for 8% of chylothoraces in children.5 The outcome is characterised by a perinatal mortality of 15–57%.1,4,6,7 If chylothorax is associated with hydrops fetalis, mortality can reach 98%.2 Antenatal management consists of thoracocenteses or pleuroamniotic shunts1,4,7 to prevent secondary pulmonary hypoplasia.1,4,6,7 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).1,4,6,7,10–12 Another recent conservative treatment is the use of a continuous infusion of somatostatin.8 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 thus important to develop methods than can decrease this morbidity and reduce hospital stay. Pleurodesis with a chemical agent in children has previously been described,9 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.

CASE REPORTS

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 hydramnios 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 treatment. This 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

<table>
<thead>
<tr>
<th>Case No</th>
<th>Diagnosis</th>
<th>Type of Betadine</th>
<th>Number and time of instillations</th>
<th>Volume (ml)</th>
<th>Duration of post-instillation chest tube occlusion (h)</th>
<th>Adverse effect</th>
<th>Outcome (chest tube removal)</th>
<th>Thyroid function</th>
<th>Adverse effect</th>
<th>Thyroid function</th>
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<tbody>
<tr>
<td>1</td>
<td>Yes</td>
<td>OC</td>
<td>R: 1 (day 65)</td>
<td>10, &lt;, &lt;</td>
<td>6--10</td>
<td>None</td>
<td>Successful</td>
<td>Normally before and after</td>
<td>Normal before and after</td>
<td></td>
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<tr>
<td>2</td>
<td>Yes</td>
<td>OC</td>
<td>R: 1 (day 11), &lt;</td>
<td>2000</td>
<td>5--10</td>
<td>None</td>
<td>Failure</td>
<td>Increase in contralateral pleural effusion</td>
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<td></td>
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<td>3</td>
<td>Yes</td>
<td>Dermique</td>
<td>R: 1 (day 59)</td>
<td>3</td>
<td>3--6</td>
<td>None</td>
<td>Normal before and after</td>
<td>N</td>
<td></td>
<td></td>
</tr>
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<td>4</td>
<td>Yes</td>
<td>Diffuse lymphangectasia</td>
<td>L: 2 (day 22 and 28)</td>
<td>5</td>
<td>5--10</td>
<td>Fentanyl (10)</td>
<td>Failure</td>
<td>Increase in contralateral pleural effusion</td>
<td></td>
<td></td>
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<tr>
<td>ND</td>
<td>No done</td>
<td>L, R, right, OC, congenital idiopathic chylothorax</td>
<td>R: 1 (day 25)</td>
<td>3100</td>
<td>ND</td>
<td>N</td>
<td></td>
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**DISCUSSION**

In an attempt to decrease the morbidity usually associated with the classical management of congenital chylothorax (infections, thrombosis, deficit in lymphocytes, deficit in proteins and immunoglobulins, complications of total parenteral nutrition, complications of mechanical ventilation), we treated four neonates by intrapleural instillation of povidone-iodine through a chest tube. This procedure was successful in three of the four cases and appeared to be well tolerated. Systemic analgesia was achieved with a morphine-nominemetic (fentanyl or sufentanyl), as Betadine injection causes pain, and sedation with intravenous midazolam (Hynoviel). No local anaesthesia (such as intrapleural lidocaine) was required. Pain monitoring using the Objective pain scale showed that the systemic analgesia was effective. Breathing was supported by artificial ventilation in all the babies because of respiratory distress.

We used two different versions of the product: Betadine 4% scrub and Betadine 10% dermique. This was because the procedures were carried out in two different neonatal intensive care units. Betadine 10% dermique (used in case 3) was diluted with normal saline (3 ml Betadine 10% dermique + 7 ml saline). Betadine 4% scrub was used without dilution. With both products, the chest tube was cleared after the injection with 10–15 ml normal saline, just before chest tube occlusion. The duration of chest tube occlusion was empirical; it was supposed to be three to five hours.

Improvement occurred progressively, and the tube was removed 6–16 days after the procedure. The most impressive recovery was observed in case 3, in which the procedure was successful within six days, contrasting with the failure of two months of conservative treatment. However, it may be the natural evolution of this pathology. In fact, from our experiences it is difficult to determine the effectiveness of Betadine in the treatment of congenital idiopathic chylothorax. Usually, the condition resolves in the first few weeks (two to six) with conservative treatment.

Evacuation of pleural fluid can be controlled by either a conservative or a surgical approach. Because of its high success rate (75–80%), it is widely accepted that conservative treatment should be the first option. The point at which conservative treatment should be considered to have failed is not well defined. Some investigators have recommended that surgical treatment should be performed no longer than four weeks after the diagnosis. In addition, Selles et al. recommend surgery rather than conservative treatment whenever the daily output of chylous fluid is in excess of 1500 ml in adults or 100 ml per year of age in children for more than five days, or a persistent flow of chyle for two weeks. We decided to administer intrapleural...
Néonatal management of congenital chylothorax

Conservative approach
- Management of underlying disease
- Repeated thoracocenteses
- Continuous drainage
- Dietary modifications (medium chain triacylglycerol diet or total parenteral nutrition)
- Chest tube pleurodesis
- Chemical or mechanical pleurodesis
- High positive end expiratory pressure during mechanical ventilation

Surgical approach
- Thoracoscopic pleurodesis
- Pleureperitoneal pump
- Surgical abrasion
- Ligation of the thoracic duct (by thoracoscopy or thoracotomy)
- Thoracic duct to azygos vein anastomosis and lung transplantation

povidone-iodine when surgical abrasion of the pleura was being considered. The latter method is fairly invasive, requires general anaesthesia, and increases the risk of adverse effects such as blood loss and pain. In the past, chemical pleurodesis with talc, bleomycin, or tetracycline has been performed 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 lymphocoeles 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.

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 antixudative properties related to the chelation of proteins.

As this treatment was new to our unit, we paid careful attention to any adverse effects. At the usual dose of 4000 mg, the frequency of adverse effects was minor (allergic oedema?). 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.

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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