**CASE REPORT**

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

O Brissaud, L Desfrere, R Mohsen, M Fayon, J L Demarques

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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. Cytotype 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. Cytotype 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...
Intrapleural instillation of Betadine

Table 1

<table>
<thead>
<tr>
<th>Case No</th>
<th>Diagnosis</th>
<th>Number and time of instillations</th>
<th>Volume (ml) of Betadine, chest tube occlusion</th>
<th>Duration of post-instillation chest tube occlusion</th>
<th>Adverse effect</th>
<th>Adverse effect</th>
<th>Maximal analgesia</th>
<th>Outcome (chest tube removal)</th>
<th>Advanced diagnosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Yes</td>
<td>OC Scrub R: 1 (day 65)</td>
<td>10,000</td>
<td>4</td>
<td>None</td>
<td>Rare nausea</td>
<td>Fentanyl (10)</td>
<td>Successful (10 days)</td>
<td>ND</td>
</tr>
<tr>
<td>2</td>
<td>Yes</td>
<td>OC Scrub L: 1 (day 11)</td>
<td>2000</td>
<td>3</td>
<td>Sufentanyl (0.8)</td>
<td>Failure</td>
<td>Increase in contralateral pleural effusion</td>
<td>ND</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>Yes</td>
<td>Dermique R: 1 (day 59)</td>
<td>3000</td>
<td>3</td>
<td>Fentanyl (10)</td>
<td>Failure</td>
<td>Increase in contralateral pleural effusion</td>
<td>ND</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>Yes</td>
<td>Dermique + 3 ml saline</td>
<td>3000</td>
<td>3</td>
<td>Fentanyl (10)</td>
<td>Failure</td>
<td>Increase in contralateral pleural effusion</td>
<td>ND</td>
<td></td>
</tr>
</tbody>
</table>

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-naloxone (fentanyl or sufentanyl), as Betadine injection causes pain, and sedation with intravenous midazolam (Hypnovel). 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. 1, 15

Evacuation of pleural fluid can be controlled by either a conservative or a surgical approach. 1–6 10–12 14 Because of its high success rate (75–80%), 1–6 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. 11 In addition, Selles et al. 14 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 abnormalities. A chromosome analysis was normal. At birth, bilateral chest tube pleurodesis was performed during the first 6 days of life followed by repeated left thoracocenteses every three days. Because of persistent effusion, a chest tube was inserted again on day 16 on the left side and day 22 on the right side. The daily effusion volume at that time was about 300–350 ml, and the total volume was 2600 ml. On day 22, chemical pleurodesis with povidone-iodine (Betadine 4% Scrub) through the left chest tube was carried out. The left sided pleural effusion resolved over 48 hours, but a parallel increase in the right sided pleural effusion was observed. Further intrapleural instillations of povidone-iodine (right side on day 25 and left side on day 26) were unsuccessful. The infant developed renal failure, with bilateral candida related thrombosis of the renal veins. He died from end stage renal failure, oliguria, hydrops, and refractory hypotension. An autopsy showed diffuse lymphatic abnormalities with congenital pulmonary lymphangectasia.

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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 t alc, 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 lymphocele s\textsuperscript{15}–\textsuperscript{16} and pleural lavage of empyema in adults.\textsuperscript{17} A 100% success rate has been reported when this agent was administered to 15 adult patients with a malignant pleural effusion.\textsuperscript{14}

The mechanism of action of povidone-iodine appears to be related to enhanced sclerosis,\textsuperscript{17} although the precise mode of action remains unclear. Iodine has strong oxidative and cytotoxic properties, which induce a potent inflammatory action.\textsuperscript{18} Moreover, povidone-iodine may have antitumour properties related to the chelation of proteins.\textsuperscript{19}

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.\textsuperscript{20}

The only adverse effect that we considered to be possibly related to the treatment was generalised oedema, which occurred 24 hours after povidone-iodine instillation in case 3. This may have been of allergic origin, although other manifestations of an allergic reaction were not present. Hydrazine (Atarax) was given because of allergy (asthma, skin allergy) in the parents. No cases of anaphylaxis were observed. The contralateral increase in pleural effusion may simply be due to the transfer of fluid through collateral lymphatic vessels in the chest. It 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 after 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\textsuperscript{17}). 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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**REFERENCES**