Povidone-Iodine Pleurodesis for Refractory Congenital Chylothorax: A Review of Literature

Pleurodèse à la Povidone Iodée dans le traitement du Chylothorax Congénital: Revue de la littérature.

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RÉSUMÉ

Introduction: La pleurodèse à la Povidone iodée (PVI) est largement utilisée chez l'adulte. Cependant, l'utilisation de cette procédure chez le nouveau-né est non consensuelle.

Objectif : Nous rapportons un nouveau cas de chylothorax congénital (CTC) réfractaire traité par pleurodèse à la PVI ; avec une revue des cas publiés sur PubMed.

Méthodes : Nous avons étudié les caractéristiques cliniques, les modalités thérapeutiques et le devenir de nouveau-nés traités par cette procédure.

Résultats : Il s'agissait d'un nouveau-né à terme avec CTC réfractaire au traitement conservateur ayant bénéficié d'une pleurodèse à la PVI par une seule instillation intrapleurale de 5 ml de PVI avec arrêt rapide et durable de l'épanchement et sans effet indésirable. L'analyse des 18 cas similaires publiés sur Pubmed et de notre observation nous a permis de conclure aux données suivantes : cette procédure a été utilisée avec succès et sans effets indésirables dans 11/19 cas. Des effets indésirables sévères ont été rapportés uniquement chez 4 patients qui avaient un terrain à risque avant la réalisation de la procédure.

Conclusion : La pleurodèse à la PVI semble être un moyen thérapeutique efficace et inoffensif dans la prise en charge du CTC. Elle peut représenter une alternative moins invasive que la chirurgie. Cependant, des études randomisées chez de larges populations sont nécessaires pour préciser: les risques et les bénéfices de cette procédure, le temps exacte et les modalités de sa réalisation (dosage et dilution de la PVI, durée de l'intervention) selon les caractéristiques du nouveau-né (âge gestationnel, poids et morbidité associée).

Mots-clés

Pleurodèse, Povidone iodée, chylothorax congénital

SUMMARY

Background: Povidone iodine (PVI) pleurodesis is commonly used in adult. However, this procedure is still nonconsensual in newborns.

Aims: This article aimed to report a new case of refractory congenital chylothorax (CCT) managed with PVI pleurodesis with a review of previous reported cases.

Methods: a systematic review of similar cases published in PubMed. Clinical patterns, therapeutic modalities and outcome variables were reported.

Result: In a full term neonate presenting refractory CCT, PVI pleurodesis was performed at day 16 of life by one intrapleural instillation of PVI 4% with rapid success and no side effects. Renal function and thyroid tests stilled normal before and after instillation. The analysis of 18 cases reported in Medeline and our observation provided the following data: this procedure was successful without side effects in 11/19 cases. Severe side effects were reported in four patients with high risks before procedure.

Conclusion: PVI pleurodesis seems to be effective and inoffensive in the management of refractory CCT. It may be a good alternative to surgery. Nevertheless, randomized studies on large neonatal population are required to precise: the risks and benefits of this procedure, the timing and the modalities of its realization (duration of intervention, dilution and dosage of PVI) according to the patient`s field (gestational age, weight and associated morbidity).

Key-words

Chemical pleurodesis, Povidone iodine, congenital chylothorax

Obliteration of the pleural space, either chemically or surgically is one of procedures used to manage refractory chylothorax. Povidone iodine (PVI) has been shown to be safe and effective for chemical pleurodesis in several studies in adult (1). Nevertheless, in neonates, the use of PVI to perform chemical pleurodesis for refractory congenital chylothorax (CCT) was reported in only eight previous studies in PubMed (2-9) and still nonconsensual. The aim of this study was to report a new case of CCT successfully managed with PVI pleurodesis with a systematic review of reported cases published in peer-reviewed journals.

METHODS

A new case of refractory CCT managed with PVI pleurodesis was reported. An extensive electronic search of the relevant literature from January first, 1990 to March 31st, 2016 was carried out using Medline database. Key words used were “Povidone iodine”, “Chylothorax, Congenital” and “Pleurodesis. We retained only the articles reporting one or several neonatal cases. All types of articles were considered. Clinical patterns, therapeutic modalities and outcome variables were reported. A descriptive analysis of the collected sample including our case was performed.

RESULTS

Case Report:

A 3050 g, female neonate, was delivered at term via elective cesarean without complication. At birth, she presented moderate respiratory distress. Chest radiography showed right abundant pleural fluid effusion (figure 1). Thoracentesis brought 130 ml of straw-colored liquid (figure2).

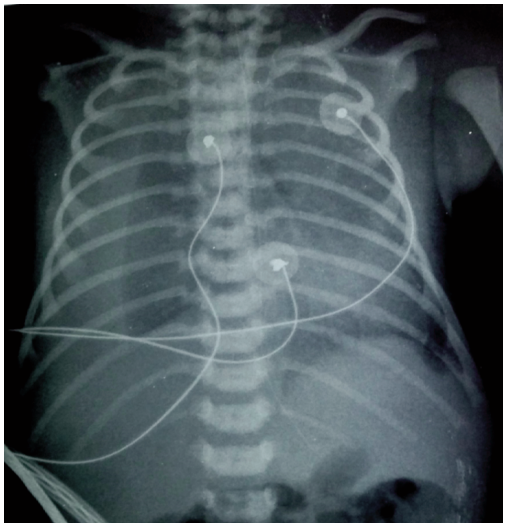

Figure 1: Eight hours of life Chest x-ray showing right sided pleural effusion with underlying collapse and deviation of the mediastinum to the left.

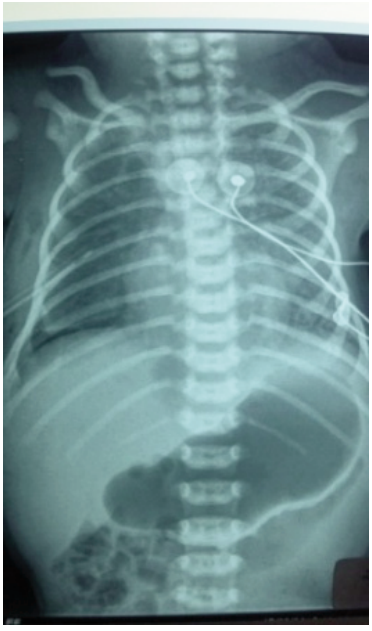

Figure 2: Pleural fluid from the first thoracentesis at 45 hours of life: straw-colored liquid

Diagnosis of CCT was confirmed by pleural fluid analysis. A right chest tube was performed and kept for 4 days. Daily effusion volume was 49 ml/kg/day under medium-chain triglyceride enriched formula. Recurrence of effusion happened 48 hours after removal of the drain requiring the use of a second thoracentesis at 14 days of life. Nosocomial infection was clinically, suspected and treated at day 15 of life.

At 16 days, chemical pleurodesis was performed after obtaining informed parental consent. Intrapleural instillation of 5ml PVI 4% was carried out through the chest tube under systemic anesthesia (Fentanyl). We cleared the chest tube with 10 ml of physiologic serum and we clamped it for 5 hours, then we remove the clamp. No ventilation support was necessary during the hospitalization.

The total amount of extracted liquid was 830 ml before pleurodesis (45 ml/kg/day). Impressive reduction of the daily flow (10 ml/Kg/day) was noted during the following 48 hours (total of 65 ml) then pleural liquid effusion was completely and definitively dried (figure 3). The chest tube was kept for right moderate pneumothorax, which occurred 24 hours after the procedure and completely resolved 5 days later. No other complication was noted, spatially respiratory distress or any allergic manifestation. The chest tube was, definitively removed 7 days after the procedure. She remained clinically and radiologically asymptomatic 9 months after pleurodesis. Biologic functions spatially renal, thyroid tests stilled normal before and after instillation.

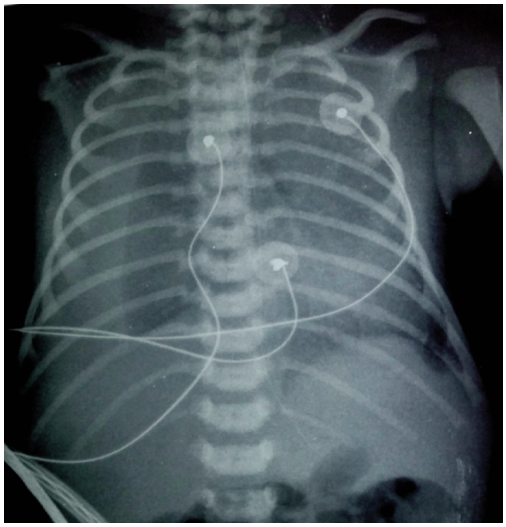

Figure 3: Chest x-ray 24 hours after pleurodesis: moderate pneumothorax and no effusion recurrence.

Descriptive analysis of the eighteen cases reported with our case

We collected 18 neonatal cases of CCT managed with PVI pleurodesis in eight previous studies in Medline (2-9). Table 1 summarizes clinical features, PVI pleurodesis modalities and outcome of the 18 newborns and our case. Procedure was achieved under systemic anesthesia (Fentanyl/Sufentanyl®) in three of the five studies in which it was specified (2) at the dose maximal dose of 10 µg/kg/h. The concentration of eiæther 4% or 10% was used: Betadine 10% dermique was used diluted with normal saline (3 ml Betadine 10% dermique +7 ml saline) by 3 studies (2, 4, 7) and not diluted in two studies (3, 8). It was indicated to clear chest tube after the injection with 10–15 ml normal saline just before chest tube occlusion (2). The duration of chest tube clamping varied from 2 to 6 hours. Infant position changing during the drain clamping was recommended (2).

The procedure was effective without severe sides effects in 11/19 patients. In one patient with bilateral chylothorax, a single PVI infusion in the right hemi thorax was effective to treat both sides (7). Treatment protocol of pleurodesis was not clearly described by La Nue et al (5) and failure was reported in the four cases (Cases 7 to 10). Case 7 presented respiratory distress and needed re-intubation after the procedure. Case 8 died from respiratory distress and hemodynamic failure after instillation.

Apart from this study, significant adverse effects after PVI pleurodesis were reported in four cases (cases 4, 5, 15 and 17). Case 4 (2) did not respond to PVI instillation and he died from end stage renal failure, oliguria, hydrops, and refractory hypotension after three instillations.

In case 5 (3), and even chyle flow resolved within 24 hours, shock and acute renal failure occurred within 12 hours after instillation. Severe chronic failure was persist 6 months later. Case 15 (7) has developed progressive multiple organ failure after the procedure. Finally, the preterm infant (Case 17) died at the age of 6 weeks due to multiorgan failure after the procedure, even the amount of pleural fluid decreased significantly within 48 hours.

The others adverse effects following pleurodesis were type of transient acute respiratory distress noted in three of the five cases reported by Scottoni F et al (7) and transient generalized edema occurring 24 hours after PVI instillation with spontaneous resolution (case 3) (2).

Table 1: Reported studies about Povidone-Iodine pleurodesis for refractory chylothorax in newborn infants.

Ref year	Case	Gest. (weeks)	Weight (gr)	Diagnosis	Site-Age at instill (days)	Volume / instill (ml)	Type of Betadine®	Clamping duration (h)	Result** Delay of resolution (day)	Severe adverse effects of PVI	Outcome
(2) 2003	1		2500	B, CIC	R(65)	10	Scrub 4%	4	Success (16)	None	Survival
	2	31	2200	CIC	R(11)	5	Scrub 4%	4	Success (10)	None	Survival
	3	35	3000	B, CIC	R(13) L(59)	3	Dermique10%	2	Success(6)	None	Survival
	4	36	3100	Diffuse lymphangiectasis/ CPL	L (22,26)	5	diluted to 4%	3/3	Failure	Yes	Death
	5	40	N/A	B,Lymphangiectasis?	R (25)	5	Scrub 4%	N/A	Success (1)	Yes	Survival
	6		3880	B, CIC	L (35)	10		5	Success(N/A)	None	Survival
	7	35	N/A	B, CIC	B (30, 32)	N/A	Dermique 10%	N/A	Failure	Yes	Survival
	8	40	N/A	B, CCT Noonan?	B	N/A	Dermique10%	N/A	Failure	Yes	Death
(3) 2006	9	35	N/A	B, CCT	N/A	N/A	diluted to 4%	N/A	Failure	None	Survival
(4) 2010	10	35	N/A	B, CCT	N/A	N/A	N/A	N/A	Failure	None	Survival
[5] 2010	11	33	N/A	CIC	N/A	5	N/A	6	Success (1)	None	Survival
	12	33	2650	B CIC	R (18)	2ml/kg	N/A	4	Success (***)	None	Survival
	13	36	2830	Acquired, R	(67)	2ml/kg	N/A	4	Success (***)	None	Survival
	14	40	3670	Acquired, L	(34)	2ml/kg	Scrub 4%	4	Success (***)	None	Survival
(6) 2014	15	35	726	Acquired, B/ SVC thrombosis	(34)	2ml/kg	Dermique 10%	4	Failure	Yes	
(7) 2015		41	2970	Acquired, B/CDH	R(36)		diluted to 4%	4	Success(N/A)	None	Death
	16	28	1530	B CIC, CPL	L (42)	2ml/kg		1	Success (2)	Yes	Survival
	17		2970	CIC R	(27)			N/A	Success (1)	None	Death
	18	39	3050	CIC R	B (37)			5	Success (2)	None	Survival
	19			-	R (13)			2-6	13/19(13/15)*	Yes: 4/15*	Survival
	19	29			R (15)		10%				15/19
(8) 2015		40					4%				
(9) 2016		39			-	5	Dermique 10%				
Our case						5	diluted to 4%				
Total		-				5	-				
						-					

DISCUSSION

If the first-line treatment of CCT is clear, a standardized approach for refractory CCT is still controversial concerning timing when conservative management should been considered failed and the ideal second-line treatment. Failure of conservative management occurs in different not consensual conditions according to the authors. Habitually two parameters are taken into account: daily chyle flow and duration of effusion. A volume exceed 10 ml/kg/day (4) or prolonged more than 2-4 weeks of nonsurgical management (4, 7) are considered as failure. In addition to these conditions, important recurrence of effusion and infectious complication were, also taken into account in our case.

In these non-responders, the best second-line treatment proposed is also controversial. In addition to somatostatine or his analogue, different surgical options have been proposed. None of these approaches have been shown to be superior to other in terms of resolution rate and safety (4).

Chemical pleurodesis is a less invasive alternative to obtain pleural adhesion stopping chylous leaks than surgery (4).

Failure of the treatment in the four patients reported by La Nue et al (5) may be due to differences in procedures which were not clearly described. In the other studies, failure and/or significant harms after this procedure were reported in only complicated cases before the procedure. Case 4 (2) died from end stage renal failure after three instillations. However, this patient had serious renal involvement before the procedure. Further, diffuse lymphangectasia involving the lungs and abdomen revealed by his autopsy may favorite iodine absorption and could explain the worsening of oligoanuria and precipitation of renal failure. Mitanchez et al (3) have postulated that the pulmonary lymphangectasia would have favored the massive iodine absorption and thus intoxication in both cases (case 4 and case 5). The only adverse effect that O.Brissaud et al (2) considered to be possibly related to the PVI was generalised oedema, in case 3.

Case 15 (7) was an extremely low birth weight and premature infant with extensive deep central veins thrombosis, abnormal renal function before treatment.

Case 17 (8) combined three risk factors for developing severe side effects after PVI. First, he was premature and low birth weight newborn. Second, he has a pulmonary lymphangiectasia who already has been jagged as a factor favoring systemic absorption and thus intoxication by the product. Third, he received a high concentration of PVI (10%), as case 5, which could also explain the amplification of the risk of major adverse.

In our opinion, all these hard situations are likely to be either unresponsive to treatment or predictive of major side effects and should been excluded.

In the other hand, transient acute respiratory distress following pleurodesis, reported by Scottoni F et al (7) was probably related to pain and transitory lung atelectasis due to local inflammatory response. Transient generalized edema reported in case 3 may have allergic origin possibly related to the treatment (2).

Risk of hypothyroidism is theoretically greater after the intrapleural instillation of iodine than after its application to the skin. Thyroid function tests remained unchanged before and after the procedure in the 9 cases investigated in different studies. In our patients, neither renal function nor thyroid function were impaired before and after the procedure, may be because absence of associated anomalies and the use of a lower concentration of PVI.

To further reduce the risk and severity of side effects, 2% PVI may be used, as it was experimentally shown that it is as effective as 4% concentration (10).

CONCLUSION

In summary, PVI pleurodesis seems to be an effective and inoffensive means for management of refractory CCT and may represent a good alternative to surgery. Nevertheless, current data are insufficient to draw firm conclusions. Limitations of overall studies include the small series and the lack of control group. Further, we draw attention to the risk of severe adverse effects after this procedure in hard situations that should been excluded (extremely low birth weight infants, premature, pulmonary lymphangiectasis, veins thrombosis, and renal abnormalities before treatment). Randomized studies on large neonatal population are required to precise: the risks and benefits of this procedure, the timing and the modalities of its realization (duration of intervention, dilution and dosage of PVI) according to the patient`s field (gestational age, weight and associated morbidity).

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