

# IDOPOVIDONE PLEURODESIS FOR FIRST PRESENTATION OF PRIMARY SPONTANEOUS PNEUMOTHORAX

By

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## ABSTRACT

**Background:** The optimal initial management of primary spontaneous pneumothorax (PSP) remains controversial.

**Aim of the work:** Evaluation of the safety and efficacy of intrapleural iodopovidone following intercostal tube drainage for initial treatment of PSP.

**Patients and Methods:** Between June 2010 and June 2014, 64 patients with documented first time primary spontaneous pneumothorax were enrolled in this study after obtaining informed consents. They were divided into two groups; Group 1 (control group) were 24 patients have PSP first time and managed by intercostal tube drain without pleurodesis, and group 2 were 40 patients have PSP first time and managed by intercostal tube drain with iodopovidone pleurodesis (20mL of 10% iodopovidone hydrochloride).

**Results:** There was no significant difference between the two groups in terms of demographic data. Also, hospitalization rates and mean hospital stays had no significant difference between both groups. Patients in the iodopovidone group had higher doses of pethidine injection. After a mean follow-up of 9 months (range 6-12 months), recurrence was noted in one patient (2.5%) of the iodopovidone group and 7 patients in the control group (29.2%).

**Conclusion:** Intrapleural iodopovidone following intercostal tube drain is a simple, safe and convenient initial treatment for PSP that reduce the rates of ipsilateral recurrence but associated with significant controllable chest pain.

## INTRODUCTION

Spontaneous pneumothorax can be classified as either primary or secondary. Primary spontaneous pneumothorax (PSP), which is defined as a pneumothorax without underlying lung disease, predominantly occurs in young, thin males. It is usually caused by ruptured pleural blebs or bullae (*Chen et al., 2008*). Primary spontaneous pneumothorax (PSP) most commonly occurs in young, tall, lean

males. The estimated recurrence rate is 23–50% after the first episode (*Tschopp et al., 2006*). Secondary spontaneous pneumothorax (SSP) usually occurs in older people with underlying pulmonary disease, such as emphysema or asthma, acute or chronic infections, lung cancer, and congenital diseases including cystic fibrosis, catamenial pneumothorax, or lymphangiomyomatosis (LAM) (*Luh, 2010*).

First episode of primary spontaneous pneumothorax can be managed conservatively and there is no consensus on optimal treatment of patients presenting with spontaneous pneumothorax. Regardless of the chosen therapeutic modality, the treatment goals of spontaneous pneumothorax consist of elimination of the pleural air and also prevention of future recurrence. Therapeutic options include bed rest, oxygen supplementation, manual aspiration, chest tube drainage, thoracoscopic and surgical interventions. Till present, there are nonprospective randomized comparative studies between various treatment strategies but only few between various therapeutic techniques are available (*Chen et al., 2008 and How & Chen, 2015*).

Chest tube drainage can be effective in about 85% to 90% of patients on the first episode of PSPs. However, probabilities of recurrent PSPs can be increased up to 50% after the first recurrence and 85% after the second recurrence (*Qureshi et al., 2005*).

Chemical pleurodesis is a procedure which uses sclerosing agents to cause adhesion between the two layers of the pleura. It has been recommended if the patient is unwilling or unable to undergo surgery. Several prospective randomized trials have shown that additional chemical pleurodesis following simple aspiration or chest tube drainage is a safe and more effective initial treatment for PSP than simple aspiration and drainage alone, and significantly reduces pneumothorax recurrence and subsequent thoracic surgery (*How and Chen, 2015*).

The aim of this work was to evaluate the safety and the effectiveness of chemical pleurodesis using iodopovidone via intercostal tube drain management of first time primary spontaneous pneumothorax.

## SUBJECTS AND METHODS

This study included 64 patients with documented first time primary spontaneous pneumothorax (PSP), admitted to the Chest Department, AL-Hussein University Hospital, Al-Azhar University, during the period from June 2010 to June 2014 after obtaining informed consents. They were divided into two groups: group 1 (control group) were 24 patients have first time PSP and managed by intercostal tube drain without pleurodesis, and group 2 were 40 patients have first time PSP and managed by intercostal tube drain with iodopovidone pleurodesis.

### Exclusion criteria:

- 1- Patients with recurrent or secondary spontaneous pneumothorax.
- 2- Patient managed by successful aspiration.
- 3- Patient with PSP first time managed by intercostal tube drain but lung failed to re-expand or leak still persist for more than 7 days and shifted to surgical intervention.

All patients were subjected to the following:

- Full history taking including age, sex, smoking index and history of other diseases.
- Thorough clinical examination including general examination and local chest examination.

- Laboratory investigations including prothrombin activity and INR.
- Plain X-ray chest postero-anterior and lateral views.
- High resolution computed tomographic (CT) scan of the chest after lung re-expansion after insertion of intercostal tube with focus made on the detection of emphysema like changes (blebs or bullae) and to detect other abnormalities to exclude secondary spontaneous pneumothorax.

Between June 2010 and June 2014, 64 patients with a first episode of PSP were treated by small intercostal chest tube 20 French. The control group consisted of the first 24 patients of the series who had successfully undergone intercostal tube drainage alone in the period from June 2010 to June 2012. From June 2012, 40 patients with PSP first time were managed by intercostal tube drain, and pleurodesis was done by 20 mL iodopovidone hydrochloride (10%) post lung expansion, instilled through the tube into the pleural space (iodopovidone group).

**Pleurodesis technique: (iodopovidone group):** A chest tube (20 F) was inserted into the mid-axillary line through the fifth inter-costal space and connected to water-sealed drainage system to achieve complete drainage of the air and lung re-expansion. Re-expansion was verified radiographically. As soon as the air was completely drained and the lung fully expanded, and was no air leak, pleurodesis was performed at the bedside.

With proper antiseptic technique, fifty milliliters of normal saline solution containing 2 mg/kg lidocaine were infused through the chest tube. After 15 minutes, a

pleurodesis solution containing a mixture of 20 mL of iodopovidone hydrochloride (10%) and 80 mL normal saline solution was infused into the pleural cavity, after which the tube was clamped for 2 hours, and then the tube was unclamped. The thoracostomy tube was removed as soon as the chest radiograph showed total lung re-expansion and no residual pleural air. As soon as this was achieved, the subject was discharged and observed as an outpatient. Follow up plain X-rays chest PA view were performed 30 and 90 days after the procedure to assess initial, early and late success of pleurodesis. The success of iodopovidone pleurodesis was denoted by the absence of air during follow-up for 1 month. Any re-accumulation was considered to be a failure or recurrence.

Statistical analysis was carried out using the SPSS computer package version 17.0 (SPSS Inc., Chicago, IL, USA). The mean  $\pm$  SD were used for quantitative variables, while number and % were used for qualitative variables. In order to assess the differences in frequency of qualitative variables Chi-Square and Fischer's exact test were applied. In order to assess differences in means of quantitative variables, independent samples t-test was applied. The statistical methods were verified, assuming a significance level of  $p < 0.05$ .

## **RESULTS**

**Table (1)** demonstrated comparison between the two studied groups according to demographic data, symptoms and radiological findings. Comparing demographic data, symptoms and radiological findings in both groups; no statistical significant differences were found

between both groups regarding age, gender, symptoms and side of lesion. It was noticed that dyspnea and chest pain

were found in all patients of the two studied groups.

**Table (1):** Comparison between different variables of control and iodopovidone groups.

Variables		Control group (n= 24)	Iodopovidone group (n= 40)	P-value
Age (ys) <sup>1</sup>		25.6 ± 4.5	25.4 ± 4.0	0.838
Days before diagnosis <sup>1</sup>		2.9 ± 2.1	2.8 ± 1.8	0.881
Gender <sup>2</sup>	Males	21 (87.5%)	36 (90.0%)	1.000
	Females	3 (12.5%)	4 (10.0%)	
Smoking habit <sup>2</sup>	Smoker	21 (87.5%)	35 (87.5%)	1.000
	Non-smoker	3 (12.5%)	5 (12.5%)	
Symptoms <sup>2</sup>	Chest pain	24 (100.0%)	40 (100.0%)	1.000
	Dyspnea	24 (100.0%)	40 (100.0%)	
Side of lesion <sup>2</sup>	Rt	19 (79.2%)	30 (75.0%)	0.769
	Lt	5 (20.8%)	10 (25.0%)	

- <sup>1</sup>Values presented as mean ± SD analyzed by Independent samples t-test.

- <sup>2</sup>Values presented as number &% and analyzed by Fisher's exact test.

Emphysema like changes (blebs and/or bullae) was present in 21 cases (87.5%) of control group and in 34 cases (85%) in

iodopovidone group with no significant difference (**Table 2**).

**Table (2):** Comparison between control and iodopovidone groups regarding emphysema-like changes in HRCT.

HRCT		Control group (n=24)		Iodopovidone group (n=40)		P-value
		N	%	N	%	
Emphysema-like changes	Yes	21	87.5	34	85.0	1.000
	No	3	12.5	6	15.0	

- Values presented as number and % and analyzed by Fisher's exact test.

No procedure-related complications were observed in either group. Chest pain was a common complaint after iodopovidone instillation, with severe pain that required immediate pethidine injection occurring in 5 patients (12.5%) in the iodopovidone group but only one patient (4.1%) of the controls (p=

0.003). After a mean follow-up of 9 months (range 6–12 months), recurrent ipsilateral pneumothorax was noted in one patient in iodopovidone group (2.5%), and 7 controls (29.2%) (p=0.003) indicating that patients in the iodopovidone group had a significant lower rate of recurrence and greater efficacy (**Table 3**).

**Table (3):** Comparison between control and iodopovidone groups regarding complications.

Complications	Control group (n=24)		Iodopovidone group (n=40)		P-value
	N	%	N	%	
<b>Pain</b>	1	4.1	5	12.5	0.003*
<b>No</b>	16	66.7	34	85.0	
<b>Recurrence</b>	7	29.2	1	2.5	

Values presented as number and % and analyzed by Chi-Square test.

No significant difference was found between both groups as regard days of hospital stay (**Table 4**).

**Table (4):** Comparison between control group and iodopovidone group regarding days of hospital stay.

Groups	Control group (n=24)	Iodopovidone group (n=40)	P-value
<b>Hospital stay</b>			
<b>Duration (Days)</b>	3.4± 1.1	3.5±1.2	0.697

Values presented as mean ± SD analyzed by Independent samples t test.

**DISCUSSION**

The initial management of PSP has been a subject of controversy. Choice of initial treatment includes observation, simple aspiration, chest tube drainage, chest tube drainage with sclerosis, medical

thoracoscopy, and video-assisted thoracoscopic surgery (VATS). Among the published methods, prevention of recurrence can only be obtained by chest tube drainage with sclerosis, medical thoracoscopy, or VATS. However, VATS

is not suggested as the initial treatment for PSP by most physicians because it results in 70% of patients undergoing unnecessary operations (*Chen et al., 2008 and British Thoracic Society, 2010*).

There is a general agreement to recommend intervention to prevent pneumothorax recurrence after the first occurrence because of the potential lethality of secondary pneumothorax. However, some authors still suggest performing an intervention only after the second episode of spontaneous pneumothorax. To prevent recurrence, the diseased site should be resected and pleural space obliterated. Chemical pleurodesis with sclerosing agents is another accepted treatment option and talcage is regarded as the best conservative technique in achieving pleurodesis (*Morimoto et al., 2002; Henry et al., 2003; Al-Qudah, 2006 and Andrés et al., 2008*).

This study demonstrated that iodopovidone pleurodesis following intercostal tube drain provided a safe easy minimally-invasive, and convenient initial treatment for PSP that may reduce the rates of recurrence.

CT can provide more detailed information to assist in the subsequent management. Findings which can be noted include the number, size, and location of bullae/ blebs (ipsi- or contra-laterally), as well the possibilities of pleural adhesion, pleural fluid accumulation, and possible underlying pulmonary diseases. In this study, radiological changes of emphysema were detected in HRCT after lung inflation in 85- 87.5%. *Luh and Tsao (2007)* found more than 90% of patients with PSP had pathological lung changes in

HR CT chest. The most common type is few and small blebs, followed by mixed blebs and bullae. *Chena and Co-workers (2008)* found over 85% of patients with visible bullae during VATS could be detected pre-operatively by CT scan.

The success rate of pleurodesis in this study was 97.5% by iodopovidone. *Estrada and Coworkers (2003)* found the efficacy of iodopovidone pleurodesis (90.6%) almost similar to the efficacy of talc pleurodesis (93%), and other inexpensive agents used for chemical pleurodesis. The efficacy of iodopovidone was regardless of the etiology (pleural effusion vs. pneumothorax) or the technique (tube thoracostomy vs. thoracoscopy) used for performing pleurodesis.

This result agreed with the result of *Mahmodlou and Coworkers (2011)* that use diodopovidone pleurodesis for first presentation of spontaneous pneumothorax and found complete response with no recurrence in 27 (93% percent) patients. Also, *Mohamed and Abd Alla (2013)* found that the success rate of iodopovidone pleurodesis was 92.3% after 1 month. *Agarwal and Coworkers (2012)* performed a systematic review and meta-analysis of patients with either malignant pleural effusions or pneumothorax who had received iodopovidone for pleurodesis. They found that success was not affected by the method of delivery or whether the procedure was performed for malignant pleural effusion or pneumothorax.

The efficacy of pleurodesis with iodopovidone without any significant adverse effects was 91.6% in a study conducted by *Morales-Gomez et al. (1993)* and 64.2% in

a study conducted by *Kelly-Garcia et al., (1997)*. Pleurodesis with iodopovidone can be performed under local anesthesia with excellent tolerance and acceptability (*Maskell et al., 2003*).

Chest pain was the most common complaint associated with iodopovidone pleurodesis (8%). Although an intrapleural dose of 2 mg/kg of lidocaine had been administered before iodopovidone instillation, our results showed that pethidine was immediately required in 4% of the patients. In general, iodopovidone instillation proved safe in our sample, with no pleural effusions or infections noted. Iodopovidone pleurodesis can be easily and safely applied after successful intercostal drain for PSP without increasing hospital stay (days of hospital stay was  $3.4 \pm 1.1$  for control group, and  $3.5 \pm 1.2$  for iodopovidone group) or complication rates.

*Estrada & Coworkers (2003) and Mohamed & Abd Alla (2013)* reported iodopovidone is not only inexpensive, but is also associated with minimal side effects. *Light (2013) and How & Chen (2015)* found iodopovidone, which is cheap and easily available, used for pleurodesis and demonstrated low morbidity with good results similar to talcum powder. *Mahmodlou and Coworkers (2011)* found five (13%) patients experienced chest pain with visual scale measurement 1 to 5. No hypotension, allergic reaction and visual impairment were observed.

## CONCLUSION

Intrapleural iodopovidone following intercostal tube drain is a simple, safe and convenient initial treatment for PSP that reduce the rates of ipsilateral recurrence

but associated with significant controllable chest pain.

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**خلفية البحث:** العلاج الأمثل للإسترواح الصدري التلقائي الأولي ما زال مختلفا عليه.

**الهدف من الدراسة:** تقييم أمان وكفاءة إستخدام الأيودوفيدون بعد تركيب أنبوب صدري كعلاج أولي للإسترواح الصدري التلقائي الأولي.

**طريقة البحث:** شملت الدراسة أربعاً وستين مريضاً يعانون من إسترواح صدري تلقائي أولي في الفترة من يونيو 2010 إلى يونيو 2014 بقسم الصدر فى مستشفى الحسين الجامعى وبعد الحصول على موافقة المريض على إجراء البحث تم تقسيم الحالات إلى مجموعتين المجموعة الأولى وتشمل 24 مريضاً يعانون من الإسترواح الصدري التلقائي الأولي تم علاجهم عن طريق تركيب أنبوب صدري بدون إلتصاق والمجموعة الثانية وتشمل 40 مريضاً يعانون من الإسترواح الصدري التلقائي الأولي تم علاجهم عن طريق تركيب أنبوب صدري وتم عمل إلتصاق بلوري من خلال الأنبوب الصدري عن طريق استخدام الأيدوفيدون (20مل أيدوفيدون هيدروكلوريد 10%) .

**النتائج:** أظهرت النتائج أنه لا يوجد إختلاف بين المجموعتين بالنسبة للبيانات الديموغرافية وعدد مرات الحجز فى المستشفى، وفترات الإقامة. وقد أستخدمت جرعات أكثر من دواء البتيدين المسكن لمرضى مجموعة الأيودوفيدون وقد تم متابعة المرضى لفترة من 6 إلى 12 شهر، ووجد أن معدل تكرار المرض فى مجموعة الأيودوفيدون كان مريضاً واحداً (2.5%) و 7 مريضاً (29.2%) فى المجموعة الأخرى.

**الإستنتاج:** إستخدام الأيودوفيدون لعمل التصاق بلوري بعد تركيب الأنبوبة الصدرية يعتبر علاج بسيط وآمن وكفاء كعلاج مبدئى لحالات الإسترواح الصدري التلقائي الأولي عند حدوثه لأول مرة ويمنع حدوث تكرار الإسترواح الهوائي، ولكن يوجد بعض الآلام البسيطة أثناء العلاج بتلك الطريقة.