

Iodopovidone pleurodesis in the treatment of refractory pleural effusions

Refrakter plevral efüzyon tedavisinde iodopovidon plörodezisi

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Background: In this study, we assessed the efficacy of iodopovidone pleurodesis in patients with refractory pleural effusions.

Methods: Between March 2009 and April 2012, 43 patients (34 males, 9 females; mean age 65.6±9.8 years; range 37 to 79 years) received iodopovidone pleurodesis for the treatment of refractory pleural effusion. Pleural effusion was due to malignancy in 31 and heart failure in 12 patients. Iodopovidone (20 mL 10% plus 80 mL 0.9% NaCl) was delivered through the chest tube. The chest tube was not clamped and raised 60 cm above the chest level. The tube was removed when the amount of drainage reduced to 50 mL/day.

Results: In patients with malignant pleural effusion, iodopovidone irrigation produced significant decrease in daily pleural drainage from 574.9±169.0 mL to 71.7±25.9 mL (p=0.000), and in patients with heart failure daily drainage decreased from 588.9±138.4 mL to 63.5±12.5 mL which was also significant (p<0.001). No clinical side effect related to the procedure was observed.

Conclusion: Iodopovidone was shown to be effective in patients with refractory pleural effusions. The use of this agent without clamping the chest tube is safe, inexpensive and effective.

Key words: Iodopovidone; pleura; pleural effusion; pleurodesis; treatment.

Amaç: Bu çalışmada refrakter plevral efüzyonlu hastalarda iodopovidon plörodezinin etkinliği değerlendirildi.

Çalışma planı: Mart 2009 - Nisan 2012 tarihleri arasında refrakter plevral efüzyonlu 43 hastada (34 erkek, 9 kadın; ort. yaş 65.6±9.8 yıl; dağılım 37-79 yıl) iodopovidon plörodez tedavi amacı ile kullanıldı. Plevral efüzyon nedeni 31 hastada malignite ve 12 hastada kalp yetmezliği idi. İodopovidon (20 mL 10%'luk artı 80 mL %0.9 NaCl) göğüs tüpünden verildi. Tüp klempe edilmeksizin göğüs seviyesinden 60 cm yukarıda tutuldu. Drenaj miktarı 50 ml/güne gerilediğinde tüp çıkarıldı.

Bulgular: İodopovidon irigasyonu ile malign plevral efüzyonlu hastalarda günlük drenaj miktarında 574.9±169.0 ml'den 71.7±25.9 mL'ye anlamlı bir düşüş sağlandı (p=0.000), kalp yetmezliği olan hastalarda da günlük drenaj miktarında 588.9±138.4 mL'den 63.5±12.5 mL'ye anlamlı bir düşüş sağlandı (p<0.001). İşleme ait hiçbir klinik yan etki gözlenmedi.

Sonuç: İnatçı plevral efüzyonu olan hastalarda iodopovidon plörodezinin etkinliği gösterilmiştir. Bu ajanın göğüs tüpünü klempmeden kullanılması güvenli, ucuz ve etkindir.

Anahtar sözcükler: İodopovidon; plevra; plevral efüzyon; plörodez; tedavi.

Pleurodesis is achieved by the intrapleural injection of a sclerosing agent that induces an inflammatory response and the subsequent fibrotic process that leads to fusion of the parietal and visceral pleura, thus obliterating the

pleural space.^[1-3] Several agents have been described and used for chemical pleurodesis, and they have a success rate ranging from 60-94%.^[4] Talc, tetracycline, and doxycycline are the most popular and widely used



Available online at
www.tgkdc.dergisi.org
doi: 10.5606/tgkdc.dergisi.2013.7026
QR (Quick Response) Code

Received: April 26, 2012 Accepted: July 5, 2012

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sclerosing agents, but none of these have solved the problem definitively.^[5]

Iodopovidone has been used for pleurodesis to treat refractory pleural effusions and has been shown to be safe and effective in several studies, whether it was administered at the time of the thoracoscopy or applied through a chest tube.^[1,6] This study was conducted to evaluate the efficacy of iodopovidone pleurodesis in 43 patients with refractory pleural effusions.

PATIENTS AND METHODS

Between March 2009 and April 2012, iodopovidone pleurodesis was used for the treatment of refractory pleural effusions in 43 patients (34 males, 9 females; mean age 65.6 ± 9.8 years; range 37 to 79 years) at the department of internal medicine in multicenter, and written informed consent was obtained from all participants in this study. Thoracentesis was performed several times in all patients to evacuate the massive pleural effusions, which occurred due to malignancy in 31 patients and heart failure in 12. Iodopovidone pleurodesis was used to treat the refractory pleural effusions in the 31 patients with malignant pleural effusions along with 18 patients with non-small cell lung cancer (NSCLC), three with small cell lung cancer (SCLC), five with breast cancer, three with metastatic colon cancer, two with mesothelioma, and 12 with heart failure.

A small bore chest tube was inserted in the patients through the sixth intercostal space along the midaxillary line and was connected to an underwater sealed drainage system. The pleurodesis was performed at each patient's bedside where they received subcutaneous 0.5-0.7 mg/kg pethidine hydrochloride (HCl) (Aldolan[®], Gerot Pharmazeutika GmbH, Vienna, Austria). Previously, an intrapleural instillation of 20 mL bupivacaine (Marcain Polyamp Steripack, AstraZeneca UK Limited, London, England) had also been given. A mixture of 20 ml 10% iodopovidone and 80 ml 0.9% saline solution was then administered into the pleural cavity through the chest tube, which was not clamped, and it was kept at 60 cm above the chest wall to prevent backflow of the iodopovidone. Next, the patient was rotated in the bed to achieve a complete

distribution of the iodopovidone in the cavity. After leaving the chest tube in for two hours, it was returned to its natural position and removed when the pleural drainage decreased to 50 ml/day.

Statistical analysis

Statistical analyses were performed using the Statistical Package for Social Science (SPSS Inc., Chicago, Illinois, USA) version 17.0 software program. Paired samples t-tests were used to compare the mean test scores before and after application. A value of $p < 0.05$ was considered to be statistically significant.

RESULTS

In the patients with malignant pleural effusions, iodopovidone irrigation produced a significant decrease in the daily pleural drainage from 574.9 ± 169.0 mL to 71.7 ± 25.9 mL ($p < 0.001$), and in the patients with heart failure, the daily drainage decreased from 588.9 ± 138.4 mL to 63.5 ± 12.5 mL, which was also significant ($p < 0.001$) (Table 1). All patients had a complete response, and the daily drainage decreased rapidly. Five (11.6%) chest tubes were removed on the first day, 24 (55.9%) on the second day, 10 (23.2%) on the third day, and four (9.3%) were removed on the fourth day after pleurodesis. Four patients (9.3%) suffered from a minimal degree of chest pain. No signs or symptoms of hypothyroidism or hyperthyroidism were observed during the follow-up period, and all patients were discharged uneventfully and followed up for one year.

DISCUSSION

Malignant pleural effusion is a common, recurrent, distressing condition seen at the advanced stage of various malignant diseases and is associated with significant morbidity.^[5,7] Additionally, heart failure can also cause recurrent pleural effusion. The pleural effusion is expected to decline with medical treatment, but if that does not occur, therapeutic thoracentesis is recommended. When pleural effusion persists, pleurodesis is also an appropriate treatment approach.^[8] Pleurodesis is a common palliative treatment method that was first reported at the beginning of the 20th century, and a wide variety of agents have been used

Table 1. Comparison of the amount of drainage before and after iodopovidone irrigation

Etiology	n	Drainage before Ip irrigation (mL/day)	Drainage after Ip irrigation (mL/day)	p
Malignant pleural effusion	31	574.9 ± 169.0	71.7 ± 25.9	0.000
Heart failure	12	588.9 ± 138.4	63.5 ± 12.5	0.000

Ip: Iodopovidone.

for this procedure.^[7] An ideal agent for pleurodesis must be effective, safe, inexpensive, and readily available. It is also necessary for it to have a high molecular weight along with chemical polarity, low regional clearance, rapid systemic clearance, and a steep dose-response curve.^[6,9]

Along with commonly used agents like talc, tetracycline, and doxycycline iodopovidone should be accepted as an alternative sclerosing agent^[1] as it is an inexpensive and readily available agent for chemical pleurodesis.^[10] Previous studies have suggested that the use of iodopovidone has a high success rate. Kelly-Garcia et al.^[11] reported the use of this agent in 14 patients with a 64.2% success rate. Morales-Gómez et al.^[12] performed pleurodesis with iodopovidone in 39 patients with malignant pleural effusions and achieved control of the effusions in 33 patients (91.6%). Furthermore, in the series reported by Olivares-Torres et al.,^[9] complete response was observed in 50 (96.1%) out of 52 patients, with the iodopovidone pleurodesis having been performed through a tube thoracostomy or at the end of a diagnostic thoracoscopy. More recently, a study that included 43 patients with malign pleural effusions showed a success rate of 88%, and small bore catheters and large bore chest tubes were used to administer the iodopovidone into the pleural space in these cases.^[13] Agarwal et al.^[10] reported comparable results in 37 patients who received iodopovidone through a chest tube. There were no reports of any recurrences of the effusions in 32 (86.5%) of their patients. In our series, iodopovidone was used for pleurodesis with a success rate of 100% in 43 patients with either benign or malignant recurrent pleural effusions.

Iodopovidone is an iodine-based topical antiseptic that may be absorbed by the thyroid gland and can appear in saliva, sweat, and milk. It undergoes minimal metabolism and is excreted practically unchanged in the urine.^[9] The exact mechanism that iodopovidone uses to produce pleural symphysis is not known, but it has been suggested that this could be related to the low pH of the iodopovidone solution, which is 2.97.^[14] Additionally, iodine has oxidative and cytotoxic properties that may include a potent inflammatory response to initiate the pleural symphysis.^[14] The rapid reduction of the effusions in all the cases in our series supports this idea.

The main complication observed in the study of Neto et al.^[14] was mild thoracic pain (16%) after iodopovidone instillation, and in the study by Olivares-Torres et al.,^[9] three patients (5.8%) required opioid analgesics for pain

control. Empyema is also a rarely seen complication,^[14] and visual loss after iodopovidone pleurodesis was reported by Wagenfeld et al.^[15] Although it has been reported that topical iodopovidone applications or the use of iodopovidone-based contrast agents may cause transient thyroid dysfunction, especially in infants, the study of Yeginsu et al.^[16] determined that the intrapleural administration of iodopovidone did not affect thyroid hormone levels.^[17] In our study, we did not observe any signs or symptoms of hypothyroidism or hyperthyroidism in the patients during the follow-up period. However, four patients suffered from a minimal degree of transient chest pain.

In conclusion, we recommend the use of iodopovidone for the treatment of refractory pleural effusions since it is a cheap, effective, and safe approach.

Declaration of conflicting interests

The authors declared no conflicts of interest with respect to the authorship and/or publication of this article.

Funding

The authors received no financial support for the research and/or authorship of this article.

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