

# Can blood seal the deal?

Autologous blood patch pleurodesis vs doxycycline in patients with secondary spontaneous pneumothorax with persistent air leak

# THE CLINICAL QUESTION



Does autologous blood patch pleurodesis (ABPP) have higher success rates in air leak closure than doxycycline pleurodesis in patients with secondary spontaneous pneumothorax (SSP) with persistent air leak?

# STUDY CONCLUSION

ABPP and doxycycline pleurodesis had similar success rates in closure of air leak, though ABPP had earlier closure and greater patient tolerability. ABPP may be used as a safe alternative to doxycycline pleurodesis.

## **BACKGROUND**



- Persistent air leak is a common complication of SSP
- While surgical pleurodesis is preferred due to low recurrence rates, medical pleurodesis is often pursued in non-surgical candidates
- Options for medical pleurodesis include agents such as talc or doxycycline, both of which cause inflammation and scarring to promote pleurodesis in a fully expanded lung

- ABPP is a promising alternative with less side effects with potential to both seal the air leak due to clot formation and induce a pleurodesis reaction
- ABPP has been successful in sealing post-lobectomy air leaks, but role of ABPP in SSP is not well established
- Small studies have shown reduced duration of air leak compared to conservative management in spontaneous pneumothorax, though optimal volume of administration, timing, and frequency of ABPP is unknown
- Comparative studies of ABPP to other agents in medical pleurodesis are lacking

# **CURRENT PRACTICE / GUIDELINES**

- Both British Thoracic Society (BTS) guidelines and American College of Chest Physicians (ACCP) Delphi consensus statement recommend surgical referral for persistent air leak in SSP and consideration of medical pleurodesis in patients who have contraindications to surgery or prefer a less-invasive approach
- No consensus on which agent should be used in medical pleurodesis
- ACCP recommends talc slurry or doxycycline while BTS does not make a specific recommendation; neither comment on ABPP

# **STUDY DESIGN**



**Type of trial:** Prospective, non-blinded, randomized control trial

N: 38

#### Study groups:

- Patients with secondary spontaneous pneumothorax and persistent air leak 72 hours after tube thoracostomy
- Randomized to autologous blood patch pleurodesis (study group) or doxycycline pleurodesis (control group, standard of care at institution)

Settings: Single center, tertiary care hospital in India

Enrollment: September 2020 to May 2021

Treatment period: N/A

Follow up: 28-days post-procedure

**Primary/secondary outcome:** Not defined by the authors; based on the chronology of results reported, we assume the primary end-point was successful closure of air leak at 7 days, and the secondary end-points were median time to leak closure, complication rates and 28-day recurrence rates

# **POPULATION**

#### **Inclusion criteria:**

- Age >18
- Patients with secondary spontaneous pneumothorax and persistent air leak grade 1-2

#### **Exclusion criteria:**

- Prior pleurodesis
- Traumatic spontaneous pneumothorax
- Underlying hematological disorders or coagulopathy
- Hypotension or other cardiopulmonary diseases
- Known doxycycline allergy
- Active pulmonary infection

#### **Baseline Characteristics:**

- 38 total patients, 19 in each group
- Male predominance (75%)
- Mean age: 48 years
- · Most patients had chest pain, dyspnea, and cough
- Median air leak grade of 2 in ABPP vs 1 in doxycycline group

#### **Underlying lung conditions:**

- COPD most common (n=8 ABPP vs 12 doxycycline)
- Malignancy second most common (n=3 ABPP vs 7 doxycycline)
- Interstitial lung disease in 18% patients (n=1 ABPP vs 6 doxycycline)



### INTERVENTIONS

Patients with secondary spontaneous pneumothorax with persistent air leak at 72 hours were randomized to the following groups:

#### Autologous blood patch pleurodesis

- 50ml venous blood drawn from patient and injected into pleural cavity through intercostal tube without anticoagulation
- Subjects turned and changed position in bed every 15 minutes for 2 hours to evenly distribute the blood throughout the pleural cavity

#### **Doxycycline pleurodesis**

- 200mg of 2% lignocaine instilled in pleural cavity followed by doxycycline 500mg mixed with 50ml normal saline 15 minutes later
- Subjects turned and changed position in bed every 15 minutes for 2 hours to evenly distribute the drug throughout the pleural cavity

# **OUTCOMES**

#### **Primary outcome:**

 Success rate at 7 days: 94.7% ABPP vs 84.2% doxycycline (p=0.6)

#### Secondary outcomes:

- Median time to closure: 24 hours (IQR 12,24) ABPP vs 36 hours (IQR 24,72) doxycycline
- Recurrence rate at 28 days: Same in both groups (n=1)

#### **Complication rates:**

- Pain: 16% ABPP vs 74% doxycycline (p <0.01)</li>
- Fever: 11% ABPP vs 37% doxycycline (p=0.019)
- No infections reported in either group

## **FUNDING**



# **ARTICLE CRITIQUE**

#### **Study Strengths:**

- First study to compare doxycycline to ABPP in patients with SSP
- Participants had similar baseline characteristics to other studies



#### **Study Limitations:**

- Single-center study in a community in India which may limit generalizability
- Trend toward better success rate in ABPP, however study may have been underpowered to achieve statistical significance
- Only grade 1-2 air leaks were studied, thus applicability cannot be extended to higher grade air leaks
- More subjects in the doxycycline group had chronic lung diseases (8 vs 12 COPD, 3 vs 7 malignancy, 2 vs 4 COPD + malignancy, 1 vs 6 ILD) compared to the ABPP despite randomization, which may have been inadvertently caused by the non-blinded nature of randomization here; eventually, both the trend towards higher pleurodesis rates and shorter duration of air leak may have favored ABPP due to these differences in baseline patient characteristics
- Prior studies have required repeat administrations of ABPP with longer time to air leak seals as compared to this study (5 days vs 24 hours)
- Only ABPP to doxycycline were compared, as doxycycline was the standard of care at the study site.
   Many institutions use talc as the preferred agent, so a larger, multicenter comparison study is required

# TAKE HOME MESSAGE

Evidence supporting an "agent of choice" in medical pleurodesis for patients with SSP and persistent air leak is lacking. ABPP may be considered as an alternative agent to doxycycline with better patient tolerability, but larger studies comparing doxycycline, talc, and ABPP are required



to assess the true pleurodesis success rates and the time to cessation of air leak of these interventions individually.

## **ARTICLE CITATION**

Narenchandra V, Vishnukanth G, Dwivedi DP, et al. Comparison of efficacy of autologous blood patch pleurodesis versus doxycycline pleurodesis in the management of persistent air leak in patients with secondary spontaneous pneumothorax. A randomized control trial. Monaldi Arch Chest Dis. Doi: 10.4081/monaldi.2022.2036



## SUGGESTED READING



- 1. MacDuff A., Arnold A., Harvey J.
  Management of spontaneous
  pneumothorax: British Thoracic Society
  pleural disease guideline 2010. Thorax.
  2010;65((Suppl. 2)):ii18-ii31. doi:
  10.1136/thx.2010.136986.
- 2. Baumann M.H., Strange C., Heffner J.E., Light R., Kirby T.J., Klein J., Luketich J.D., Panacek E.A., Sahn S.A. Management of spontaneous pneumothorax: An American College of Chest Physicians Delphi consensus statement. Chest. 2001;119:590-602. doi: 10.1378/chest.119.2.590.
- 3. Nava GW, Walker SP. Management of the Secondary Spontaneous Pneumothorax: Current Guidance, Controversies, and Recent Advances. J Clin Med. 2022 Feb 22;11(5):1173. doi: 10.3390/jcm11051173. PMID: 35268264; PMCID: PMC8911306.
- 4. Ibrahim IM, Elaziz MEA, El-Hag-Aly MA. Early Autologous Blood-Patch Pleurodesis versus Conservative Management for Treatment of Secondary Spontaneous Pneumothorax. Thorac Cardiovasc Surg. 2019 Apr;67(3):222-226. doi: 10.1055/s-0038-1642028. Epub 2018 Apr 19. PMID: 29672817.
- 5. Hallifax RJ, Yousuf A, Jones HE, Corcoran JP, Psallidas I, Rahman NM. Effectiveness of chemical pleurodesis in spontaneous pneumothorax recurrence prevention: a systematic review. Thorax. 2017 Dec;72(12):1121-1131. doi: 10.1136/thoraxjnl-2015-207967. Epub 2016 Nov 1. PMID: 27803156; PMCID: PMC5738542.

- 6. Shackcloth MJ, Poullis M, Jackson M, Soorae A, Page RD. Intrapleural instillation of autologous blood in the treatment of prolonged air leak after lobectomy: a prospective randomized controlled trial. Ann Thorac Surg. 2006 Sep;82(3):1052-6. doi: 10.1016/j.athoracsur.2006.04.015. PMID: 16928534.
- 7. Park EH, Kim JH, Yee J, Chung JE, Seong JM, La HO, Gwak HS. Comparisons of doxycycline solution with talc slurry for chemical pleurodesis and risk factors for recurrence in South Korean patients with spontaneous pneumothorax. Eur J Hosp Pharm. 2019 Sep;26(5):275-279. doi: 10.1136/ejhpharm-2017-001465. Epub 2018 Apr 18. PMID: 31656615; PMCID: PMC6788261.

## **CONTRIBUTORS**



# **AUTHOR**

Stephanie Hampton

Emory University Atlanta, GA <u>stephanie.faye.hampton@emory.edu</u>

# **REVIEWERS**

Abesh Niroula, MD Emory University @aniroulaMD



#### Abhishek Kumar. MD

Kirk Kerkorian School of Medicine, University of Nevada, Las Vegas <u>@medshek</u>



If you would like to become a reviewer for the "AABIP Journal Club,"
Please contact Christian Ghattas at christian.ghattas@osumc.edu