AABIP JOURNAL CLUB

Dual-agent intrapleural fibrinolytic therapy (IPFT) for complicated pleural space infections (CPSI), does it compare to surgery?

BACKGROUND & OVERVIEW

THE CLINICAL QUESTION

Does fibrinolytic therapy have comparable outcomes to surgery as the primary management for CPSIs?

STUDY CONCLUSION

In patients who are surgical candidates, operative management may offer more benefits and should be considered early in the management of complicated pleural space infections.

STUDY BACKGROUND

Complicated pleural space infections are common and challenging to treat, typically affecting ~65,000 patients in the U.S. annually. Management can be morbid and costly with prolonged hospital stays. Surgery has remained the mainstay of treatment when antibiotics and drainage of pleural space fail to resolve the infection. In the past, the MIST-II study showed that IPFT can be an effective treatment strategy. Intrapleural fibrinolytic therapy offers a less invasive option to treatment. There is limited data that compares the two management strategies.

CURRENT PRACTICE

When antibiotics and drainage of pleural space are ineffective in the management of complicated pleural space infections, current guidelines recommend surgery as the primary management strategy. However, more recent data from the second Multicenter Intrapleural Sepsis Trial (MIST II) demonstrates that dual-agent IPFT with alteplase and DNase can be an effective treatment strategy. There is little high quality evidence directly comparing surgical drainage vs. dual-agent IPFT.

METHODS & RESULTS

STUDY DESIGN

Type of trial: Retrospective

Patients analyzed: 566 patients identified

Study groups: Adults with CPSI managed with surgery or fibrinolytics

Settings: Providence-Swedish Healthcare System which includes 18 hospitals spanning five states (Alaska, California, Montana, Oregon, and Washington)

Enrollment: Patients identified through pharmacy database for dornase alpha administration, surgical intervention identified through billing database for surgical decortication.

Treatment Period: 01/01/2015-03/31/2018

Follow up: 90-day

Primary Outcomes: Treatment failure (evidence of ongoing infection or persistent pleural collection requiring additional treatments) and crossover (receiving any dose of IPFT after surgery or receiving surgery after IPFT).

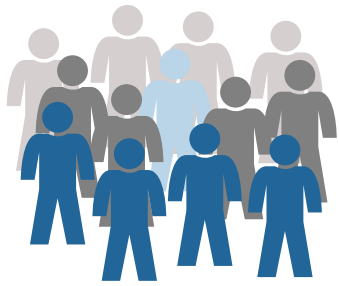
POPULATION

Inclusion Criteria:

- Adult patients with CPSIs
  - Complicated pleural space infections were defined as clinical suspicion of a pleural infection as well as pleural fluid analysis of positive Gram stain/culture, purulence, lactate dehydrogenase >1000 units/L, glucose <60mg/dL or pH<7.2
- Receiving surgical management or intrapleural fibrinolytic therapy

Exclusion Criteria:

- Prior chest surgery
- Malignant/paramalignant pleural effusion
- Hemothorax
- Incomplete medical records
- Esophageal perforation
- Indwelling pleural catheter in situ



Baseline Characteristics:

- Age, median (IQR) years: 58 (46-88) in overall cohort, 57 (46-67) in surgery group vs 58 (46-68) in IPFT group
- Gender, male (%): 67% in overall cohort, 68% in surgery group vs 64% in IPFT group
- BMI, median (IQR): 27 in overall cohort, 27 (23-31) in surgery group vs 26 (23-30) in IPFT group
- RAPID score, median (IQR): 3 in overall cohort, 3 (2-4) in surgery group vs 3 (2-4) in IPFT group
- Presence of purulent pleural fluid, %: 45% in overall cohort, 50% in surgery group vs 39% in IPFT group
- Community-acquired infection source, %: 88% in overall cohort, 87% in surgery group vs 87% in IPFT group
- Hospital Acquired infection, %: 12% in overall cohort, 13% in surgery group vs 11% in IPFT group

INTERVENTIONS

Initial surgical management (decortication including thoracotomy and thoracoscopy) or initial IPFT management with any dose/schedule of dual-agent IPFT, including MIST II dosing of 10mg alteplase and 5mg dornase BID for 5-6 doses

OUTCOMES

Primary outcome:

- Treatment failures 7% in surgery group vs 29% IPFT group, p<0.001
- Crossovers 6% in surgery group vs 20% in IPFT group, p<0.001

Secondary outcomes:

- Time to initiation of management was longer in the surgery group (3 days vs 2 days, p=0.002)
- Overall hospital length of stay was shorter for the surgery group (10 days vs 12 days, p<0.001)
- Intensive care unit length of stay was longer in surgery group (1 day vs 0, p=0.001)
- Chest tube duration was shorter in surgery group (5 days vs 7 days, p<0.001)
- No difference in in-hospital mortality, 30- and 90-day mortality between groups

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- Less re-admissions in the surgery group (5% vs 12%, p=0.004)

Adverse Events:
- No difference in rates of minor and major complications

FUNDING

FUNDING

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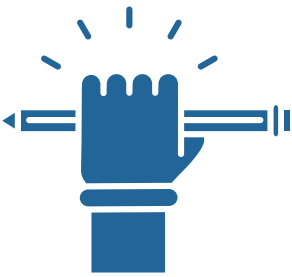
ARTICLE CRITIQUE

STUDY STRENGTHS



- Data derived from a large multicenter healthcare system allows some degree of generalizability
- Similar baseline demographics and clinical characteristics between the two groups

STUDY LIMITATIONS & POTENTIAL FOR BIAS

- Retrospective study which makes it difficult to clearly ascertain true treatment failures
- Patients in IPFT group had higher proportion of co-morbidities
- Unable to account for non-surgical candidates in IPFT group
- No standardized dose or schedule of IPFTs
- Only 13/18 hospitals had thoracic surgery services available, 15% of patients were managed at hospitals without thoracic surgery support

RESEARCH QUESTION

Is dual IPFT comparable to surgery in the initial management of CPSIs?

TAKE HOME MESSAGE

In patients with complicated pleural space infections, who are deemed to be surgical candidates, operative management might offer more benefits than fibrinolytic therapy: less readmission rates, treatment failure, additional interventions, and cross over. This in addition to shorter length of hospital stay and chest tube duration, with similar complication rates and mortality at 30 and 90-days. Thus, surgical intervention should be considered early in the management of CPSI.

This observation is based on retrospective data which carries significant limitations. Prospective, randomized trials are needed to explore this question further.

REFERENCES

ARTICLE CITATION

Wilshire CL, Jackson AS, Meggyesy AM, Buehler KE, Chang SC, Horslen LC, Rayburn JR, Fuller CC, Farivar AS, Bograd AJ, Louie BE, Vallières E, Aye RW, Gilbert CR, Gorden JA. Comparing Initial Surgery versus Fibrinolytics for Pleural Space Infections: A Retrospective Multicenter Cohort Study. Ann Am Thorac Soc. 2022 Nov;19(11):1827-1833.

SUGGESTED READING

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