What have we learnt from recent RCTs in Pleural Disease?

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Overview

Trials in Malignant Effusion Mx
Trials in Pleural Infection Mx
Outcomes and assumptions

What have we learnt?

“It's what we know for sure that just ain't so”

What are our assumptions in the treatment of MPE?

Assumptions

1. CXR is the best outcome in MPE
2. Pleurodesis success rate is ~90%
The TIME trials

Therapeutic Interventions in Malignant Pleural Effusion

Purpose
- Answer clinically meaningful question in MPE management
- Randomised controlled trials with real life comparators

The TIME2 randomised controlled trial

Effect of an indwelling pleural catheter vs chest tube and talc pleurodesis for relieving dyspnea in patients with malignant pleural effusion

Davies et al, JAMA 2012 Jun 13;307(22):2383-9

What’s wrong with talc?
- 30-40% failure rate
- Median hospital stay 5 days
- 15% with trapped lung
- Side effects – systemic and local
IPC complications

<table>
<thead>
<tr>
<th>Complication</th>
<th>Frequency</th>
</tr>
</thead>
<tbody>
<tr>
<td>Failed/displaced insertion</td>
<td>4.0%</td>
</tr>
<tr>
<td>Symptomatic loculation</td>
<td>8.4%</td>
</tr>
<tr>
<td>Asymptomatic loculation</td>
<td>4.0%</td>
</tr>
<tr>
<td>Empyema</td>
<td>3.2%</td>
</tr>
<tr>
<td>Air in pleural space</td>
<td>2.4%</td>
</tr>
<tr>
<td>Infection</td>
<td>1.6%</td>
</tr>
<tr>
<td>Dislodged</td>
<td>1.2%</td>
</tr>
<tr>
<td>Bleeding</td>
<td>0.8%</td>
</tr>
<tr>
<td>Tumour seeding</td>
<td>0.4%</td>
</tr>
<tr>
<td>Pain requiring removal</td>
<td>0.4%</td>
</tr>
</tbody>
</table>

Tremblay and Michaud et al. Chest 2006; 129: 362-8

BTS Guidelines 2010

Multiple case series suggesting utility

No Randomised Controlled Comparisons of talc and IPC

What outcomes?

What is the purpose of Rx?
- CXR improvement?
- “Failed pleurodesis”?
- Survival?

- Improve quality of life:
  - Breathlessness
  - Time in Hospital
  - Need for further invasive procedures
T.I.M.E. 2
MPE requiring pleurodesis

Randomisation
Indwelling pleural catheter n=106
12F tube and pleurodesis

Daily visual analogue score (dyspnea)
Days 1 to 42
Follow up to 26 weeks

Assumptions...
1. IPCs are “better”
2. Talc is much more painful than an IPC
3. IPCs will get patients out of hospital earlier and improve quality of life

Primary Outcome:
• Mean daily dyspnea VAS
• Over first 42 days post-randomisation

Primary Outcome
Mean over 42 days
Talc (n=54) IPC (n=52)

Dyspnea
Secondary Outcomes

Comparison (IPC versus Talc)  Comparator  Statistical Significance
Hospital stay (days)  -3.5 days  p=0.001  95% CI: -4.8 to -1.5
Days in hospital over 12 months  -3.5 days  p=0.001
Requirement for further pleural procedures  OR 0.21  p=0.03  95% CI: 0.04 to 0.86

Adverse Events  OR 4.70  p=0.002  95% CI: 1.75 to 12.60

No significant difference in quality of life
What have we learnt?

1. IPCs are not superior to talc pleurodesis in relieving breathlessness

2. Both IPCs and talc:
   - Improve breathlessness
   - Improve quality of life
   - Reduce chest pain

3. IPCs associated with:
   - Reduced hospital stay (2 days)
   - Reduced further pleural procedures
   - Increased adverse events

Do IPCs truly “reduce pleural procedures”?

“Number of further procedures required”
- TIME2 OR=0.21, p=0.03
- AMPLE1 OR=0.18, p=0.009

IPCs are therefore clearly better…
- Is this the correct outcome?
The IPC journey

Median number of home drainages = 96

33.7% require further review

Where next for IPC vs Talc?

Studies to address

• Patient priorities
• Disease specific quality of life

The TIME1 randomised controlled trial

What constitutes optimal (best outcome, least pain) pleurodesis in MPE?