Best evidence topic - Thoracic general

Using non-steroidal anti-inflammatory drugs (NSAIDs) following pleurodesis

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Summary

A best evidence topic in cardiothoracic surgery was written according to a structured protocol. The question addressed was whether non-steroidal anti-inflammatory drugs (NSAIDs) decrease the effect of pleurodesis. Only 17 papers were identified using the search below. Three papers presented the best evidence to answer the clinical question. The author, journal, date and country of publication, patient group studied, study type, relevant outcomes, results, and study weaknesses of the papers are tabulated. We conclude that despite a limited number and type of study, there is some histopathological evidence to support the concern that NSAIDs may reduce effectiveness of pleurodesis. Until further clinical studies with appropriate outcome measures are available, NSAIDs following pleurodesis should be used with caution and probably avoided routinely.

Keywords: Evidence-based medicine; Thoracic surgery; Pleural disease; Pleurodesis; NSAIDs

1. Introduction

A best evidence topic was constructed according to a structured protocol. This protocol is fully described in the ICVTS [1].

2. Clinical scenario

A 25-year-old man with his second spontaneous right-sided pneumothorax has undergone VATS bullectomy and talc pleurodesis this morning. Patient controlled analgesia (PCA) was set up at completion of surgery and oral paracetamol prescribed. You are asked to see him on the ward later that evening because he is in a lot of pain, and his morphine PCA is making him feel very sick. You think the pain is likely to be muscular and aggravated by his chest drain, and you think he would benefit from a NSAID such as diclofenac, but the thoracic surgical nurse looking after him is unhappy to give it. She was told that it may reduce the chances of a successful pleurodesis.

3. Three part question

In [patients undergoing pleurodesis] is the use of [NSAIDs] detrimental in terms of [successful pleurodesis].

4. Search strategy


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### Table 1

Summary of best evidence topics

<table>
<thead>
<tr>
<th>Authors, date, country, Study type (level of evidence)</th>
<th>Patient group</th>
<th>Outcomes</th>
<th>Result</th>
<th>Study weakness/ comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ors Kaya et al. (2005) J Invest Med, Turkey [3] Experimental study (Level 4) 12 male NZ rabbits – given tetracycline pleurodesis 2 groups – 2 mg/kg diclofenac IM for 10/7</td>
<td>After 28 days: Scored for macroscopic pleurodesis (gross inspection)</td>
<td>Mean macroscopic score Dic 2.16 ± 0.40 &amp; Acet 2.83 ± 0.40 (P = 0.027) (Scoring system used ranged from 0 = normal to 4 = complete obliteration of pleural space)</td>
<td>Small animal study with short term outcome</td>
<td>Relies on extrapolation to humans</td>
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<td></td>
<td>–30 mg/kg acetaminophen (Paracetamol) po for 10/7</td>
<td>Scored for microscopic pleurodesis (microscopic evidence of fibrosis, inflammation &amp; collagenization)</td>
<td>Mean microscopic score Dic 2.3 ± 0.63 &amp; Acet 3.5 ± 0.54 (P = 0.045) (Scoring system used ranged from 0 = absent to 4 = severe)</td>
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<tr>
<td>Texeira et al. (2005) Chest, Brazil [4] Experimental study (Level 4) 60 male NZ rabbits 2 groups Silver nitrate pleurodesis vs. talc pleurodesis</td>
<td>After 28 days scored for macroscopic pleurodesis</td>
<td>Macroscopic Pleural adhesions: Silver nitrate 3.2 ± 1.1 &amp; Talc 2.2 ± 0.8 (P = 0.019) In subgroup test Silver nitrate with Pred 3.5 ± 0.5 or Dic 3.3 ± 1.0 Talc with Pred 1.3 ± 0.7 or Dic 1.2 ± 0.7 (0–4 scoring score used ranging from 0 = normal pleural space to 4 = complete obliteration of pleural space by adhesions.)</td>
<td>Animal study with short term outcome</td>
<td>Extrapolation to humans</td>
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<td>Further subgroups: –sclerosing agent alone vs. sclerosing agent + Pred IM vs. sclerosing agent + Dic 1 mg/kg IM</td>
<td></td>
<td></td>
<td>Neither silver nitrate nor prednisolone are part of standard clinical practice</td>
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<tr>
<td></td>
<td>After 28 days scored for microscopic pleurodesis</td>
<td>Microscopic Pleural inflammation: Silver nitrate with Pred 1.3 ± 0.5 or Dic 2.2 ± 1.6 Talc with Pred 0.9 ± 0.3 or Dic 0.7 ± 0.5</td>
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<td>Microscopic Pleural fibrosis: Silver nitrate with Pred 3.4 ± 0.5 or Dic 3.2 ± 1.0 Talc with Pred 1.5 ± 1.0 or Dic 1.4 ± 0.8</td>
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<td>Microscopic process scored using scoring system ranging from 0 = equivocal to 4 = marked changes</td>
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<tr>
<td>Lardinois et al. (2004) Eur J Cardiothorac Surg, Switzerland [2] Experimental study (Level 4) 10 VLS pigs underwent VATS &amp; apical mechanical abrasion: 2 groups postop diclofenac 2 mg/kg po for 3 weeks vs. Control (no NSAIDs)</td>
<td>After 21 days macroscopic pleurodesis scored (5-point pleurodesis score &amp; 4-point obliteration score)</td>
<td>Macroscopic pleurodesis (using 5-point scoring, 0 = normal pleural space no adhesions to 4 = severe dense adhesions): 3.67 ± 1.0 vs. 2.0 ± 2.2 (control) (P = 0.01) Distribution of adhesions comparable</td>
<td>Small animal study with short term outcome</td>
<td>Extrapolation to humans</td>
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<td></td>
<td></td>
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<td>Different scoring systems from 2 other studies</td>
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(Continued on next page)
as talc is used, pleurodesis relies on the generation of inflammation and consequent adhesion between the two layers of pleura to prevent the build of fluid in the pleural cavity. The studies reviewed address whether the use of NSAIDs inhibits pleurodesis. All studies were in animals. In two studies rabbits were used and in one study pigs. Kaya et al. [3] used intrapleural tetracycline and compared macroscopic and microscopic evidence of pleurodesis after 3 weeks in animals on diclofenac or acetaminophen (para-cematol). Following IM administration of diclofenac for 10 days tetracycline pleurodesis was reduced both macroscopically and microscopically, though not significantly. Teixeira et al. [4], using the same animal model, albeit a larger number of animals, concluded that systemic administration of both steroidal and non-steroidal anti-inflammatory agents reduces the degree of pleurodesis with talc but not silver nitrate.

The final animal study involved thorascopic abrasion pleurodesis of pigs and evaluated gross and microscopic evidence of pleurodesis after 21 days in pigs given oral diclofenac or controls (Lardinosis et al. [2]). Macroscopically pleurodesis appeared to be reduced in animals taking NSAIDs but microscopically no statistically significant difference between the two groups was found. However, a trend toward a higher amount of organised collagen fibres suggestive of dense adhesions was observed in the control group. The authors concluded that peri-operative use of NSAIDs affects quality of pleural adhesions obtained after mechanical abrasion in pig models.

In the available animal studies the histopathological influence of NSAIDs on pleurodesis was assessed. The authors suggest that there is a reduction in the quality of pleurodesis achieved at a macroscopic and/or microscopic level. There are no studies which assess clinical outcomes such as recurrence of pneumothorax or pleural effusion. Clinical studies would be very hard to perform because the only realistic means of assessing outcome is to await recurrence; a substantial proportion do not recur in the natural history of the condition and the stapling of the apex may on its own be sufficient to prevent some of the recurrences (Table 1).

7. Clinical bottom line

Best evidence suggests that there is some histopathological evidence derived from animal experiments that the use of NSAIDs may decrease the effect of pleurodesis. Until clinical evidence becomes available, the routine use of NSAIDs following pleurodesis should probably be avoided.

References