The effect of manual therapy and exercise on mild chronic obstructive pulmonary disease: a randomised controlled trial

by

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Conflict of interest

No conflicts of interest to declare
Chronic obstructive pulmonary disease (COPD)*

A preventable and treatable disease with significant extra-pulmonary effects that contribute to the severity in individual patients

Characterised by:
- Declining lung function
- Decreasing exercise capacity

Clinical presentation:
- Chronic Bronchitis
- Emphysema
- Chronic Asthma

Exercise capacity is a prognostic indicator for long-term survival

* COPDX Guidelines 2.56 (December 2018)
**COPD: Main symptoms**

- Increasing breathlessness (dyspnoea) on exertion
- Cough & sputum production
- **Chest tightness (decrease in thoracic compliance)**
- Wheezing
- Airway irritability
- Frequent chest infections
**COPD**: Classification*

Classified by lung function (spirometry)

Ability to forcibly blow air out (forced expiration)

- Forced expiratory volume in 1st second (FEV$_1$)
- Forced vital capacity (FVC)
- Ratio FEV$_1$ / FVC < 0.70 diagnostic

**Stages**

<table>
<thead>
<tr>
<th>FEV$_1$ % predicted</th>
<th>Severity</th>
<th>Daily activities</th>
</tr>
</thead>
<tbody>
<tr>
<td>≈ 60-80%</td>
<td>Mild</td>
<td>Little or no effect</td>
</tr>
<tr>
<td>≈ 40-59%</td>
<td>Moderate</td>
<td>Increasing limitation</td>
</tr>
<tr>
<td>&lt; 40%</td>
<td>Severe</td>
<td>Severely curtailed</td>
</tr>
</tbody>
</table>

* COPDX Guidelines 2.56 (December 2018)
Goals of treatment

Different for various stages of COPD (Chee & Sin 2008)

- Moderate to severe
  - Prevent respiratory complications such as exacerbations
  - Prevent mortality

- Mild
  - Symptom relief
  - Slowing disease progression
  - Mitigating risk of comorbidities such as cardiovascular disease

- Systematic review on exercise for mild COPD
  (Jacome & Marques 2014)
  - Benefits in short-term but medium to long-term uncertain
### Current evidence for the use of MT for COPD

12 studies over the past 40 years: N = 216

<table>
<thead>
<tr>
<th>Study</th>
<th>Design</th>
<th>COPD stage</th>
<th>MT intervention</th>
<th>Size (n)</th>
<th>Risk of Bias</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Miller 1975</td>
<td>RCT</td>
<td>Moderate</td>
<td>OMT</td>
<td>23</td>
<td>High</td>
<td>Lung function improved&lt;br&gt;Subjective improvements</td>
</tr>
<tr>
<td>Howell <em>et al</em> 1975</td>
<td>Pre-post</td>
<td>Moderate</td>
<td>OMT</td>
<td>17</td>
<td>High</td>
<td>Symptom severity score reduced</td>
</tr>
<tr>
<td>Witt &amp; MacKinnon 1986</td>
<td>RCT</td>
<td>Moderate</td>
<td>Spinal Mobilisation</td>
<td>12</td>
<td>High</td>
<td>Lung function improved&lt;br&gt;Subjective improvements</td>
</tr>
<tr>
<td>Masarsky &amp; Weber 1988</td>
<td>Case study</td>
<td>Moderate</td>
<td>CMT</td>
<td>1</td>
<td>High</td>
<td>Increase in lung function&lt;br&gt;Subjective improvements</td>
</tr>
<tr>
<td>Beeken <em>et al</em> 1998</td>
<td>Pre-post</td>
<td>Moderate</td>
<td>NMRT</td>
<td>5</td>
<td>High</td>
<td>Lung function decreased&lt;br&gt;Subjective improvements</td>
</tr>
<tr>
<td>Noll <em>et al</em> 2008</td>
<td>RCT</td>
<td>Severe</td>
<td>OMT (7 techniques)</td>
<td>35</td>
<td>High</td>
<td>Lung function decreased&lt;br&gt;Subjective improvements</td>
</tr>
<tr>
<td>Putt <em>et al</em> 2008</td>
<td>RCT</td>
<td>Moderate</td>
<td>Muscle stretching</td>
<td>14</td>
<td>High</td>
<td>Lung function improved&lt;br&gt;Short-term increase in FEV&lt;sub&gt;1&lt;/sub&gt;&lt;br&gt;Not sustained at 4 weeks post-intervention</td>
</tr>
<tr>
<td>Dougherty <em>et al</em> 2011</td>
<td>Case series</td>
<td>Severe</td>
<td>CMT</td>
<td>6</td>
<td>High</td>
<td>Short-term increase in FEV&lt;sub&gt;1&lt;/sub&gt;&lt;br&gt;Not sustained at 4 weeks post-intervention</td>
</tr>
<tr>
<td>Noll <em>et al</em> 2009</td>
<td>RCT</td>
<td>Severe</td>
<td>OMT (4 techniques)</td>
<td>25</td>
<td>Low</td>
<td>No change in lung function&lt;br&gt;Only immediate subjective improvements</td>
</tr>
<tr>
<td>Zanotti <em>et al</em> 2012</td>
<td>RCT</td>
<td>Severe</td>
<td>OMT + Exercise</td>
<td>20</td>
<td>Low</td>
<td>Reduction in RV&lt;br&gt;Increase in exercise performance</td>
</tr>
<tr>
<td>Engel <em>et al</em> 2013</td>
<td>RCT</td>
<td>Moderate</td>
<td>OMT + Exercise</td>
<td>15</td>
<td>Low</td>
<td>Increase in FVC &amp; exercise performance&lt;br&gt;Decrease in dyspnoea</td>
</tr>
<tr>
<td>Engel <em>et al</em> 2016</td>
<td>RCT</td>
<td>Moderate/Severe</td>
<td>OMT + Exercise</td>
<td>33</td>
<td>Low</td>
<td>Increase in FVC sustained at 24 weeks&lt;br&gt;Increase in exercise capacity</td>
</tr>
</tbody>
</table>
Underlying mechanism

MANUAL THERAPY PROTOCOL - MTP (2 components)

Soft tissue therapy (STW): Decreases muscle tension
+
Spinal manual therapy (SMT): Increases joint mobility

Increases muscle length

MTP produces short-term decrease in chest tightness

Increase in thoracic compliance

Delayed onset of exercise-limiting dyspnoea

Increase in exercise performance

Over time, increase in exercise capacity
Research questions?

1. Does exercise deliver benefits in mild COPD over the medium to long-term?
2. Does adding MT to exercise increase those benefits in mild COPD?
Trial design

Randomised Controlled Trial (Phase III)

NSW public hospital – outpatients with mild COPD

50 to 65 years

2 groups: Exercise

SMT + Exercise

Outcome measures at 0, 4, 8, 16, 24, 32 & 48 weeks

Lung function (FVC, FEV₁)

Quality of Life (SGRQ; HAD)

Exercise capacity (6MWT)

Interventions (SMT & Ex)

16 weeks of exercise (weeks 1-16)

4 weeks of SMT intervention (weeks 5-8)

Ethics approval: SESLHD HREC (approval no:13/004)  Trial registration: ANZCTR:12614000766617

Data collection October 2014 - February 2019
Statistical analysis

- Linear mixed effects model to examine change over time between groups
- $P < 0.004$ (0.05/12 to account for multiple comparisons – Bonferroni)
- Intention-to-treat (ITT) analysis undertaken via linear mixed-effects model
- Tukey all-pairwise comparisons used to compare time points
Volunteers (175)

Excluded (104)
Outside age range = 15
Outside lung function range = 32
Unable to attend trial = 37
Contra-indicated for SMT = 20

Enrolled (71)

Baseline measurements

Randomisation

Group 1
Exercise (35)
Withdrew < 16 weeks (7)
Work/family commitments = 5
Medical not related to trial = 2
Withdrew > 16 weeks (9)
Work/family commitments = 7
Medical not related to trial = 2
Completed 48 weeks (19)

Group 2
SMT + Exercise (36)
Withdrew < 16 weeks (4)
Work/family commitments = 3
Medical not related to trial = 1
Withdrew > 16 weeks (7)
Work/family commitments = 3
Medical not related to trial = 4
Completed 48 weeks (25)

Volunteers

Withdrew < 16 weeks (4)
Work/family commitments = 3
Medical not related to trial = 1

Work/family commitments = 5
Medical not related to trial = 2

Completed 48 weeks (19)

Completed 48 weeks (25)
## Baseline characteristics

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Group 1: Ex n = 35</th>
<th>Group 2: MT+Ex n = 36</th>
<th>All groups n = 71</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age (years)</strong></td>
<td>58.5 (4.0)</td>
<td>58.6 (3.8)</td>
<td>58.5 (3.9)</td>
</tr>
<tr>
<td><strong>Gender (F:M)</strong></td>
<td>29:6</td>
<td>24:12</td>
<td>53:18</td>
</tr>
<tr>
<td><strong>FEV\textsubscript{1} (litres)</strong></td>
<td>2.31 (0.43)</td>
<td>2.59 (0.66)</td>
<td>2.46 (0.56)</td>
</tr>
<tr>
<td><strong>FVC (litres)</strong></td>
<td>3.16 (0.57)</td>
<td>3.71 (1.00)</td>
<td>3.5 (0.87)</td>
</tr>
<tr>
<td><strong>SGRQ total</strong></td>
<td>25.2 (15.0)</td>
<td>19.0 (14.4)</td>
<td>21.8 (14.9)</td>
</tr>
<tr>
<td>symptoms</td>
<td>33.4 (23.2)</td>
<td>30.1 (20.4)</td>
<td>31.8 (21.5)</td>
</tr>
<tr>
<td>activity</td>
<td>37.9 (19.8)</td>
<td>23.4 (16.5)</td>
<td>29.9 (19.3)</td>
</tr>
<tr>
<td>impact</td>
<td>14.8 (13.3)</td>
<td>11.8 (14.3)</td>
<td>13.2 (13.9)</td>
</tr>
<tr>
<td><strong>HAD anx</strong></td>
<td>6.5 (4.1)</td>
<td>4.5 (2.3)</td>
<td>5.5 (3.4)</td>
</tr>
<tr>
<td><strong>HAD dep</strong></td>
<td>4.0 (3.4)</td>
<td>2.7 (2.4)</td>
<td>3.3 (2.9)</td>
</tr>
<tr>
<td><strong>6 MWT (metres)</strong></td>
<td>575 (59)</td>
<td>615 (59)</td>
<td>597 (66)</td>
</tr>
</tbody>
</table>

\( ^a \) All values except gender are given as means with standard deviation in parentheses. Ex, exercise; MT+Ex, manual therapy plus exercise; FEV\textsubscript{1}, forced expiratory volume in the 1\textsuperscript{st} second; FVC, forced vital capacity; SGRQ, St George’s respiratory questionnaire; HAD anx, hospital anxiety and depression scale – anxiety score; HAD dep, hospital anxiety and depression scale – depression score; 6MWT, 6-minute walking test.
Results

- No difference in effect between groups over time \( (p>0.08) \)
  - SMT did not produce any additional benefits
  - Breathing mechanics not as affected in mild v moderate COPD
  - Limited scope for increasing thoracic compliance

- Change over time (no interaction model)
  - Improvements in:
    - Lung function (\( \text{FEV}_1 \& \text{FVC}; p<0.001 \))
    - Exercise capacity (\( 6\text{MWT}; p<0.001 \))
    - Quality of Life (\( \text{SGRQ activity, impact & total}; p<0.001 \))
    - Anxiety and Depression (\( \text{HAD}; p<0.001 \))

- Clinically meaningful average change from baseline (weeks)
  - FVC: 32 & 48 (MCID: 200 mL)
  - 6MWT: 8,16,24,32 & 48 (MCID: 25m)
  - SGRQ activity, impact & total: 16,24,32 & 48 (MCID: 4 units)
  - HAD anxiety: 24 & 32 (MCID: 1.5 units)
Safety - Adverse events related to Thoracic SMT

Total of 512 x thoracic mobilisations/manipulations

- 32 participants received SMT + Ex intervention
- 2 x mobilisations/manipulations per session x 8 sessions

Adverse Events (AE)
- No severe
- No moderate
- 21 mild AEs from 14 participants
- Incidence rate = 4.1% (very low compared to previous studies in COPD)
In summary

- Exercise delivers medium to long-term benefits in lung function, exercise capacity and quality of life in mild COPD

- Potential to improve prognosis of mild COPD
  Exercise capacity is a prognostic indicator for long-term survival

- In mild COPD, Thoracic Manual Therapy does not deliver additional benefits in LF, EC and QoL compared to exercise alone
  Different to previous results for moderate/severe COPD

- Thoracic SMT appears to be relatively safe for 50-65 year olds with mild COPD
  Similar to results for moderate COPD
References


Thank you

END