Advances in Pulmonary Rehabilitation: Peripheral and Respiratory Muscle Adaptations

Monday 4th June from 12:30-14:00
Dina Brooks, Darlene Reid, Richard Debiguare, Rik Gosselink

Objectives
• to appreciate the clinical consequences of peripheral and respiratory muscle dysfunction in COPD
• to realize the beneficial effects of inspiratory muscle training and pulmonary rehabilitation this population.

Definition of COPD
• A respiratory disorder largely caused by smoking, which is characterized by progressive, partially reversible airway obstruction, systematic manifestations and increasing frequency and severity of exacerbations.
• 2 main types: emphysema and chronic bronchitis

Common Signs and Symptoms of COPD

Physical
• Shortness of breath
• Physical deconditioning
• Fatigue
• Chronic cough
• Repeated respiratory infections

Psychosocial
• Depression
• Anxiety
• Social isolation
• Decreased perception of control
• Loneliness
**Prevalence**

- 1/5 smokers develop COPD
- 6% of men; 1-3% of women
- Prevalence underestimated by 50%
- >55 years of age: 10-15% have COPD
- Fourth leading cause of death

**Pulmonary Rehabilitation**

- “... is an evidence based multidisciplinary and comprehensive intervention for patients with chronic respiratory disease who are symptomatic and often have decreased daily life activities.”
  
  (ATS/ERS statement on PR, 2006)

**Pulmonary Rehabilitation Programs**

- Integrated into the individualized treatment of the patient, PR is designed to reduce symptoms, optimize functional status, increase participation, and reduce health care cost through stabilizing or reversing manifestations of the disease”. (ATS/ERS statement on PR, 2006)

- Spectrum of strategies integrated into lifelong management to address primary and secondary impairments
  - Patient Assessment
  - Exercise training
  - Education
  - Psychological support
Training, Fatigue, and Injury of the Inspiratory Muscles in COPD

Darlene Reid
Associate Professor
Department of Physical Therapy
University of British Columbia
Darlene.reid@ubc.ca
www.muscle.rehab.ubc.ca

Acknowledgements

IMT Systematic Review
Lynne Geddes
Kelly O’Brien
Jean Crowe
Dr. Dina Brooks

Diaphragm Morphology Studies
Thoracotomy and post-mortem
Dr. Nori MacGowan
Alex Scott
Anju Sharma
Dr. Ken Evans
Dr. Jenny Davis
Dr. Jeremy Road
Dr. Mark Elliot

Vancouver Foundation
University of British Columbia
The Lung Association
Ontario Respiratory Care Society
Ontario Lung Association

Outline of Presentation

• Systematic Review on IMT
• Diaphragm injury in People
• How to prescribe inspiratory muscle training

Clinical Relevance of Inspiratory muscle training (IMT)

COPD:
• Is common and results in
  – significant morbidity and mortality
  – decreased functional capacity and quality of life
  – Weak, injured, or fatigued inspiratory muscles
• Training will potentially reverse some muscle weakness of peripheral and inspiratory muscles
• Inspiratory muscle training may decrease dyspnea and increase exercise tolerance
Evidence supporting IMT

Systematic Review:
- 274 retrieved
- 16 met inclusion criteria that compared IMT with ‘sham’
  - 10 used targeted/threshold IMT
  - 6 used ‘other’ IMT without target


Categorized Types of Inspiratory Muscle Training (IMT)

1. Threshold ® device (Respironics HealthScan) or IMT device with a target e.g. Incentive spirometer with P-Flex inline

2. DHD Trainer or P-Flex without target

1. Threshold ® IMT

- Spring-loaded valve
- Black Disc
- Mouthpiece

2. IMT with no Target

- While breathing against the resistive trainer, patients can slow their breathing and thus, do not have to breathe as hard to train using this device.
Estimate of Inspiratory Muscle Force

Maximal Inspiratory Pressure abbreviated as \( P_{\text{Imax}} \) or MIP
- Measured at standard lung volume
- Usually at RV unless FRC can be reliably determined.

Inspiratory Threshold Loading
- Every 2-3 minutes, a weight is added imposing a higher inspiratory threshold load.
- The person breathes against progressively greater loads until they can no longer continue.

Results of Systematic Review—Targeted/threshold IMT vs Sham

Meta-analyses results (weighted mean difference):

1. **Inspiratory muscle strength**
   - \( P_{\text{Imax}} \) improved by 12.3 cm H\(_2\)O
   - \( P_{\text{Imax}} \% \) predicted improved by 27.23%

2. **Inspiratory muscle endurance**
   - Inspiratory threshold loading improved by 10 cmH\(_2\)O (1.0 kPa).

Targeted/threshold IMT vs Sham

Meta-analyses Results (weighted mean difference):

3. **Exercise capacity**
   - Borg score for effort decreased by 2.3
   - Max work rate increased by 13.75 W

4. **Dyspnea**
   - TDI increased by 3.4

5. **Quality of Life** - 2/10 studies
   - Improvement in CRQ (Sanchez Riera et al 2001)
   - No change in Profile of Mood States, Sickness Impact Pro or Health Perceptions Questionnaire (Larson et al 1988)
Results - IMT with no Target

- Most studies (4/6) showed no improvements
- Only one study showed improved dyspnea and increased endurance time on cycle ergometer

Summary of Systematic Reviews

- **IMT is effective** in management of people with COPD
- **IMT must use targeted or threshold** device
- **IMT is under-utilized** in practice

Can the inspiratory muscles undergo injury?

Exertion-induced Muscle Injury

- usually defined as structural disruption
  - Light microscope
  - Electron microscope
- Can manifest as muscle weakness
**Abnormal Diaphragm Morphology – after thoracotomy and post-mortem**

**Light Microscope**
- disruption of cytoplasm
- nuclearity (inflammation & regenerative cells),
- ↑ connective tissue

**Post-mortem changes in COPD**

Greater cross-section area of collagen & more abnormal fibres in costal diaphragm.

Scott, Wang, Road, Reid. *Eur Respir J* 2006

---

**Human Studies**

**In patients going for thoracotomy**
- Some injury and inflammation
- COPD and more so after inspiratory loading had more sarcomeric disruption.

**Post-mortem**
- More injury and some people have increased connective tissue

---

**Inspiratory Muscle Exercise Prescription**

**Fatigue**

**Chronic Injury**

**Adaptive Response**

**Muscle Promoters**
- titrated exercise intensity
- progressive eccentric exercise
- progressive sustained exercise
- anabolic agents
- selective anti-inflammatories

**Progressive Disability**
- Falls
- Weakness
- Irreversible Muscle Atrophy
- Connective Tissue Replacement

**Enhanced Strength & Endurance**
- Hypertrophy
- Enhanced connective tissue harness and cytoskeleton
- Improved oxidative capacity
How to Prescribe IMT

• **Patient selection** – stable COPD
  – Studies included mostly moderate to severe COPD (some included mild)
  – Not during acute exacerbation
  – Not immediately following exacerbation
  – Extreme caution should be used for those with stable hypercapnic ventilatory failure
  – Lotters – those with MIP less than 60 cmH₂O

Training Device

• **Targeted** – Threshold ® or P-Flex with an incentive spirometer

• Do not use DHD or P-Flex alone (without the IS to provide a target) – user alters breathing pattern and does not get training effect

Frequency

• 30 mins per day (may be in 2-3 sessions)

• 4-6 days per week

• For continued benefit – continue indefinitely!

Intensity of training

• From research studies
  – Generally accepted 40 – 70% P₁₅₀
  – Some studies as low as 22% - but subjects were closely supervised

  **Clinical recommendation**
  – begin at 7 cm H₂O and increase no more than 2 cm H₂O per week

• Progress slowly
Outcomes

• Inspiratory muscle
  – Strength - PImax
  – Endurance – incremental test using on threshold trainer
• Dyspnea scale – TDI, Borg
• Exercise capacity – walk test
• Quality of life - CRQ

Precautions/Monitoring

<table>
<thead>
<tr>
<th>Precautions/Monitoring</th>
<th>To ensure adequate training protocol</th>
<th>Intensity of Load</th>
<th>Begin at a low % of ${P}^{\text{Imax}}$ (&lt; 50%), progress as tolerated. Less than 5% per week to a max 70% ${P}^{\text{Imax}}$ according to patient tolerance.</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mode of Load</td>
<td>Targeted inspiratory resistive or threshold trainer.</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Duration</td>
<td>Begin at low duration as tolerated (≤ 15 min) and progress to 30 minutes per day</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Frequency</td>
<td>4-6 times per wk for endurance effect. 1-2 days rest per week to avoid staleness, fatigue, and muscle injury</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Length of Training</td>
<td>Indefinitely</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Signs of exercise intolerance</td>
<td>BP, HR, RR, other signs and symptoms of respiratory distress or inability to tolerate exercise load.</td>
<td>For details of signs of cardiovascular and respiratory distress, see ACSM guidelines.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>To avoid fatigue</th>
<th>Dis-coordinated chest wall movement</th>
<th>Observation</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Excessive dyspnea during training</td>
<td>Observation; monitoring respiratory rate</td>
</tr>
<tr>
<td></td>
<td>Long-lasting fatigue after training</td>
<td>Interview</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>To avoid muscle injury</th>
<th>Signs of delayed onset muscle soreness</th>
<th>Interview</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Reduced strength</td>
<td>Reassessment of ${P}^{\text{Imax}}$</td>
</tr>
<tr>
<td></td>
<td>Reduced endurance</td>
<td>Inability to tolerate usual training load intensity and duration</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>To avoid hypercapnea</th>
<th>End-tidal CO$_2$, SpO$_2$</th>
<th>End-tidal CO$_2$ monitor, Pulse oximeter</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Signs of headache, confusion</td>
<td>Interview</td>
</tr>
</tbody>
</table>

If possible, should be combined with aerobic & resistance training of the extremities
Summary

- Like other skeletal muscle, inspiratory muscles can be trained.
- People with stable COPD can benefit from IMT.
- IMT is under-utilized by PTs.
- Appropriate parameters (FITT) are needed, including a targeted or threshold device.
- Ideally IMT should be in conjunction with pulmonary rehabilitation.

References


PERIPHERAL MUSCLE ATROPHY DEVELOPMENT IN COPD

Richard Debigaré, PT, PhD
Adjunct professor
Université Laval, Hôpital Laval
Québec, Canada
Prevalence of muscle atrophy

- Normal BM and FFM
- Normal BM, low FFM
- Low BM and FFM
- Low BM, normal FFM

Impacts on clinical outcomes

- Muscle weakness
- Decreased quality of life
- Lower functional capacity
- Increased mortality risk
- Accentuated inflammation and ROS production after exercise

Muscle weakness

- CPBD
- Control

Decreased quality of life

- BMI ≤ 21 and FFM ≤ 15 (♀)/16 (♂)
- BMI ≥ 21
- BMI > 21 and FFM > 15 (♀)/16 (♂)
Lower functional capacity

BMI ≤ 21 and FFMI ≤ 15 (♀)/16 (♂)
BMI ≤ 21 and FFMI > 15 (♀)/16 (♂)
BMI > 21 and FFMI ≤ 15 (♀)/16 (♂)

Increased mortality risk

Probability of surviving

AJRCCM, 166:809-13; 2002

Accentuated inflammation and ROS production after exercise

How muscle atrophy initiates and progresses in patient with COPD?
**Muscle atrophy initiation**

- Inactivity
- Low level of anabolic hormones
- Inflammation
- Oxidative stress
- Hypoxia

**Inactivity**

Left leg immobilization in a cast for two weeks.

**Low level of anabolic hormones**

Testosterone

---

*Faseb J, 18:1025-27, 2004*

*AJRCCM, 172:1105-11, 2005*
Low level of anabolic hormones
Growth hormone/IGF-1

<table>
<thead>
<tr>
<th></th>
<th>Controls</th>
<th>ncCOPD</th>
<th>cCOPD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, years</td>
<td>54.5 ± 1.4</td>
<td>60.7 ± 1.6</td>
<td>58.0 ± 2.1</td>
</tr>
<tr>
<td>BMI, kg/m²</td>
<td>25.2 ± 1.1</td>
<td>25.6 ± 0.7</td>
<td>19.0 ± 0.5*</td>
</tr>
<tr>
<td>FEV₁, % pred</td>
<td>106.0 ± 3.2</td>
<td>42 ± 2.2**</td>
<td>30.7 ± 2.3*</td>
</tr>
<tr>
<td>GH, µg/ml</td>
<td>383 ± 213</td>
<td>912 ± 158**</td>
<td>1658 ± 412**</td>
</tr>
<tr>
<td>IGF-1, ng/ml</td>
<td>132 ± 11</td>
<td>133 ± 9</td>
<td>118 ± 11</td>
</tr>
</tbody>
</table>

*p < 0.05 vs controls and ncCOPD
** p < 0.005 vs controls

Int J Cardiol in press; 2007

Systemic inflammation

Findings are inconsistent among studies.
Overall,
• ↑ TNFα
• ↑ IL-8
• ↑ CRP

Peripheral muscle inflammation

TNFα

Macrophage infiltration

Systemic oxidative stress

Lipid damage

Protein damage

* Activation of NF-κB has also been reported.

Thorax, 59:483-7; 2004

AJRCCM, 167:1644-9; 2003
Peripheral muscle oxidative stress

Eur Respir J, 26:390-7; 2005

Is it reversible?

Muscle training

Muscle mass and strength

Faseb J, 18:1025-27; 2004

Pulmonary rehabilitation

AJRCM, 159:896–901; 1999
Acknowledgments

• Canadian Lung Association
• François Maltais
• Sabah N.A. Hussain
• Aaron P. Russell
• Mariève Doucet
• Marc-André Gagnon
• Marie-Ève Paré
• Annie Michaud

SUCCESSFUL REHABILITATION OF COPD PATIENTS: THE CHALLENGE OF ADJUSTING THE SAILS

Rik Gosselink, PT, PhD
Faculty of Kinesiology and Rehabilitation Sciences
Katholieke Universiteit Leuven

Questions

• Physical activity in COPD patients
• Pulmonary rehabilitation: which patient or which program?

Characteristics of physical activity in COPD patients

Pitta et al AJRCCM 2005
**Active / Passive Time**

Langer et al ERS 2006

Pitta et al AJRCCM 2005

---

**Inactivity and mortality in COPD**

Garcia Aymerich Thorax 2006

- Very low: mainly sitting work no activity during leisure time
- Low: Less than 2h/week light physical activity

---

**Inactivity and morbidity in COPD**

Garcia Aymerich Thorax 2006
Exacerbations and inactivity

Clinical benefits

- Maximal Exercise Capacity
- Walking distance - Endurance capacity
- Relief of symptoms (dyspnea and fatigue)
- Quality of life
- Utilization of health care resources
- Mortality?

ATS/ERS Statement on Pulmonary Rehabilitation 2006

How successful is pulmonary rehabilitation in individual patients?

Keys for successful pulmonary rehabilitation?

- Patient selection
- Program components
**Selection of Candidates**

- AGE?
- PULMONARY FUNCTION?
- SMOKING?
- CO-MORBIDITY?
- PSYCHOSOCIAL CONDITION?
- OTHER: MUSCLE FORCE, EXERCISE IMPAIRMENT, ...

NO, but ADAPT the PROGRAM!

**Guidelines for Training**

- INTENSITY: 55 - 90% HRmax or 40 - 85% VO2max
- DURATION: 20 - 60 MIN
- FREQUENCY: 3 - 5 TIMES/WEEK

Limitations for high intensity exercise training

- REDUCED VENTILATORY CAPACITY
  - Airflow obstruction
  - Dynamic hyperinflation
  - Respiratory muscle weakness
- INCREASED VENTILATORY REQUIREMENT
  - Early onset lactate accumulation
  - Increased dead space ventilation

Solutions

- INCREASE VENTILATORY CAPACITY
- REDUCE THE VENTILATORY REQUIREMENT

Interval training, a valid option

<table>
<thead>
<tr>
<th></th>
<th>Interval (n = 10)</th>
<th>Continuous (n = 9)</th>
</tr>
</thead>
<tbody>
<tr>
<td>FEV₁ % pred</td>
<td>44 ± 6</td>
<td>39 ± 6</td>
</tr>
<tr>
<td>T_LCO % pred</td>
<td>51 ± 9</td>
<td>47 ± 8</td>
</tr>
<tr>
<td>Wpeak W</td>
<td>53 ± 9</td>
<td>61 ± 8</td>
</tr>
<tr>
<td>Peak VE/MVV %</td>
<td>88 ± 7</td>
<td>86 ± 6</td>
</tr>
<tr>
<td>Change in IC L</td>
<td>-0.49 ± 0.09</td>
<td>-0.63 ± 0.07</td>
</tr>
</tbody>
</table>


Vogiatzis Chest 2006
Peripheral muscle electrical stimulation

SUPPLEMENTAL OXYGEN

\[ \Delta \text{Work (O}_2\text{-Air)} = \text{Training effect (R=0.50, p<0.01)} \]

Emtner et al. AJRCCM: 2003; 168:1034-1042

DYNAMIC HYPERINFLATION

- PURSED LIPS BREATHING
- ACTIVE EXPIRATION

Casaburi et al. Chest 127: 809, 2005
<table>
<thead>
<tr>
<th></th>
<th>PLB</th>
<th>Non-PLB</th>
</tr>
</thead>
<tbody>
<tr>
<td>End RR (bpm)</td>
<td>20.9</td>
<td>27.2***</td>
</tr>
<tr>
<td>Change in RR from pre-exercise to post exercise</td>
<td>1.7</td>
<td>6.6**</td>
</tr>
<tr>
<td>Time to recovery (seconds)</td>
<td>189.5</td>
<td>214.5*</td>
</tr>
<tr>
<td>ISWT (m)</td>
<td>298.5</td>
<td>292.5</td>
</tr>
<tr>
<td>SpO2 postwalk (%)</td>
<td>90.5</td>
<td>90.4</td>
</tr>
<tr>
<td>Borg breathlessness score</td>
<td>3.8</td>
<td>4.0</td>
</tr>
<tr>
<td>Change in heart rate</td>
<td>18.9</td>
<td>21.3</td>
</tr>
</tbody>
</table>

from pre-exercise to post exercise


NON-INVASIVE VENTILATORY SUPPORT

