Effect of Warm-Up Exercise on Exercise-Induced Bronchoconstriction

MICHAEL K. STICKLAND1, BRIAN H. ROWE2, CAROL H. SPOONER3, BEN VANDERMEER3, and DONNA M. DRYDEN3

1Department of Medicine, University of Alberta and Centre for Lung Health (Covenant Health), Edmonton, Alberta, CANADA; 2Department of Emergency Medicine and School of Public Health, University of Alberta, Edmonton, Alberta, CANADA; and 3Department of Pediatrics and University of Alberta Evidence-Based Practice Center, University of Alberta, Edmonton, Alberta, CANADA

ABSTRACT

STICKLAND, M. K., B. H. ROWE, C. H. SPOONER, B. VANDERMEER, and D. M. DRYDEN. Effect of Warm-Up Exercise on Exercise-Induced Bronchoconstriction. Med. Sci. Sports Exerc., Vol. 44, No. 3, pp. 383–391, 2012. Purpose: Exercise-induced bronchoconstriction (EIB) occurs when vigorous exercise induces bronchoconstriction. Preexercise warm-up routines are frequently used to elicit a refractory period and thus reduce or prevent EIB. This study aimed to conduct a systematic review to evaluate the effectiveness of preexercise routines to attenuate EIB. Methods: A comprehensive literature search was performed, with steps taken to avoid publication and selection bias. Preexercise warm-up routines were classified into four groups: interval high intensity, continuous low intensity, continuous high intensity, and variable intensity (i.e., a combination of low intensity up to very high intensity). The EIB response was measured by the percent fall in the forced expiratory volume in 1 s (FEV1) after exercise, and the mean differences (MDs) and 95% confidence intervals (CI) are reported. Results: Seven randomized studies met the inclusion criteria. The pooled results showed that high-intensity (MD = 10.6%, 95% CI = −14.7% to −6.5%) and variable intensity (MD = −10.9%, 95% CI = −14.37% to −7.5%) exercise warm-up attenuated the fall in FEV1. However, continuous low-intensity warm-up (MD = −12.6%, 95% CI = −26.7% to 1.5%) and continuous high-intensity warm-up (MD = −9.8%, 95% CI = −26.0% to 6.4%) failed to result in a statistically significant reduction in bronchoconstriction. Conclusions: The most consistent and effective attenuation of EIB was observed with high-intensity interval and variable intensity preexercise warm-ups. These findings indicate that an appropriate warm-up strategy that includes at least some high-intensity exercise may be a short-term nonpharmacological strategy to reducing EIB. Key Words: EXERCISE-INDUCED ASTHMA, SPIROMETRY, EXERCISE, ASTHMA, WARM-UP

Exercise-induced bronchoconstriction (EIB) is defined as a transient narrowing of the lower airway after exercise in the presence or absence of clinically recognized asthma (25). In subjects who develop EIB, acute airflow obstruction, as measured by the forced expiratory volume in 1 s (FEV1), is typically most severe 3–15 min after exercise termination and then remits spontaneously within 20–60 min (11). In addition to pharmacological interventions, many athletes, trainers, and researchers advocate specific warm-up routines as a method to trigger a refractory period, that is, a period after warm-up exercise during which further vigorous exercise results in significantly less severe or no EIB. Approximately 40%–50% of individuals who have an initial episode of EIB experience a refractory period of diminished responsiveness that can last 1–4 h after the initial warm-up exercise (19). The cause of this refractory period is not fully understood but may be due to the depletion of catecholamines, increased circulation of prostaglandin, or degranulation of mast cell mediators (4).

The use of a warm-up to induce a refractory period to limit the magnitude of EIB in subsequent vigorous exercise is appealing, as it could result in fewer symptoms, decreased medication use, and improved exercise performance. A variety of warm-up protocols have been used to elicit the refractory period, and the purpose of this systematic review was to summarize the evidence on the effectiveness of each protocol to cause a refractory period.

METHODS

This review was part of a larger report (7) conducted for the Agency for Healthcare Research and Quality (Bethesda, MD) that 1) assessed the diagnostic characteristics of six alternative tests for EIB, 2) examined the efficacy of a single
prophylactic dose of four pharmacologic interventions and one nonpharmacologic intervention to attenuate EIB, and 3) determined whether regular daily treatment with short-acting or long-acting β-agonists causes patients with EIB to develop tachyphylaxis.

Search Strategy

A comprehensive search was performed in the Cochrane Airways Register, which contains references to controlled clinical trials from systematic searches of the Cochrane Central Register of Controlled Trials, MEDLINE®, Embase, CINAHL®, AMED, and PsycINFO as well as results from hand searches of the top 20 respiratory journals and meeting abstracts. The original search was conducted on November 5, 2008, and was updated on August 4, 2009. To identify ongoing trials, we searched ClinicalTrials.gov and ClinicalStudyResults.org. In addition, we hand searched the following conference proceedings: American Academy of Asthma Allergy and Immunology (2007–2008), American Thoracic Society International Conference (2008), British Thoracic Society Winter Meeting (2008), Chest Meeting (2008), European Respiratory Society Annual Congress (2008), American College of Sports Medicine (2006–2008), and the Canadian Society for Exercise Physiology (2006–2008). We also hand searched the reference lists of included studies.

Search terms included a combination of subject headings and text words: (exerc* OR train* OR fitness OR physical OR athlete* OR sport*) AND (bronchoconstrict* OR asthma* OR antiasthma* OR wheeze* OR “Respiratory Sounds” OR “Bronchial Spasm” OR bronchospas* OR “Bronchial Hyperreactivity” OR “Respiratory Hypersensitivity” OR (bronch* AND spasm*) OR (bronch* AND constrict*) OR (bronchial* OR respiratory OR airway* OR lung*) AND (hypersensitiv* OR hyperreactiv* OR allerg* OR insufficiency)) OR EIB OR exercise-induced asthma. We did not apply language or date restrictions.

Study Selection

We selected randomized controlled trials (RCTs; parallel or crossover) that included adults and children (≥6 yr) with confirmed EIB. Both recreational and elite athletes were eligible for inclusion. The intervention was a preexercise warm-up period compared with no treatment or placebo. Outcomes of interest were the maximum percent fall in FEV1 from preexercise baseline, symptoms, presence or absence of EIB (complete protection), clinical protection, and adverse effects. Two reviewers independently screened the search results (titles and abstracts) to determine whether a study met broad inclusion criteria. Two reviewers independently assessed the full-text of potentially relevant studies using a standard inclusion/exclusion form. Disagreements were resolved through discussion or third-party adjudication, as needed.

Data Extraction and Analysis

Data extraction, methodological quality assessment (using the scale of Jadad et al. (14)), and evaluation of the adequacy of allocation concealment (1,24) were completed independently in duplicate. Reviewers resolved discrepancies by consensus or in consultation with a third party.

In all studies, the mean maximum percent fall in FEV1 measured after a control exercise challenge test (ECT) of 5–10 min with no warm-up was compared with the percent fall in an identical challenge after a designated warm-up routine. In one study, only peak flow was reported, and the change in peak flow was assumed to be equivalent to the change in FEV1 (6). The pooled results are presented as a mean difference (MD) in the maximum percent fall in FEV1 between the two challenges. All results are reported with 95% confidence intervals (CIs).

Most RCTs used a crossover design; therefore, SEM differences were either computed exactly using individual patient data or imputed using an estimated within-patient correlation of 0.5. Random-effects models were used for analyses in Review Manager 5.0 (The Cochrane Collaboration, Copenhagen, Denmark). The I² statistic was used to assess heterogeneity (13).

Where data were available, we also calculated the proportion of people who received complete protection from EIB with treatment compared with placebo. Results are reported as mean ± 95% CI.

RESULTS

Literature Search

The search identified 1653 citations from electronic databases and 8 citations through hand searching (Fig. 1). Seven trials involving 128 participants met the inclusion criteria (Table 1) (6,8,16–18,20,22).

Study and Population Characteristics

Six of the seven trials used a crossover design (6,16–18,20,22); for one abstract, the specific design could not be determined (8). The studies were published between 1979 and 2007. EIB was defined in the trials as a fall in FEV1 of at least 10% (8,17,18) or 15% (6,16,20). In three trials (6,8,20), it was not clear if the ECT that followed the warm-up met the American Thoracic Society criterion of a work rate equal to 80%–90% of an individually calculated HRmax (5). The time between warm-up and standardized ECT ranged from 1 to 49 min.

One study (6) included children only, three included adults only (16,17,20), and three included both children and adults (8,18,22). All participants were described as having mild stable asthma, except for one study (an abstract) where the asthma incidence and severity could not be determined (Table 2) (8).
Five studies investigated two or more warm-up protocols. The protocols were categorized into four subgroups based on the intensity of the routine. Four routines involved several short sprints and were designated “interval” warm-ups (6,16,17,22). Two studies involved two standardized challenges 45 min apart at 80%–90% of peak workload and were designated “continuous high-intensity” warm-ups (20,22). Three involved treadmill runs at work rates of 60% and were designated as “continuous low-intensity” warm-ups (16,18,20). The study by Eck et al. (8) and one arm of the study by Schnall and Landau (22) used a continuous routine followed by an interval routine and are reported separately as “variable-intensity” warm-ups. Study arms that involved drug therapy with or without a warm-up were not included in this analysis (17). See Table 1 for further description of warm-up protocols.

Overall, the methodological quality of the included studies was considered to be low with Jadad scores ranging from 1 to 2. No study described the randomization method. None stated that the assessors were blind. Concealment of allocation was unclear in all the trials.

Quantitative Results

Interval protocol. Four trials involving 52 patients compared the fall in FEV₁ in an ECT after an interval warm-up with the fall in an identical ECT with no previous warm-up (control challenge) (6,16,17,22). Spirometry was conducted up to 10 (6), 15 (17), 25 (16), and 80 min (22) after ECT. The interval warm-up protocols involved repetitive sprints of 26–30 s at 100% maximal oxygen consumption (V̇O₂max) or higher. The mean difference in the maximum percent fall in FEV₁ in the subsequent ECT ranged from an improvement of 4.8%–16.1% over the control challenge. The pooled results (Fig. 2) showed that a series of short, intense sprints attenuated the EIB response by a mean of −10.6% (95% CI = −14.7% to −6.5%, I² = 15%). One study (16) reported that 1 of the 12 participants had falls in FEV₁ <15% and would be classified as having obtained complete protection from EIB after the interval warm-up.

Continuous low-intensity protocol. Three trials involving 13 patients compared the fall in FEV₁ in an ECT after a continuous low-intensity warm-up that ranged from 3 (18) to 30 min (20) with an identical control challenge with no prior warm-up. The exercise intensity for the warm-up was 60% of HRmax (18), 60% of V̇O₂max (16), and reported as “low intensity” in the third study (20). Spirometry was conducted up to 25 (16), 30 (18), and 90 (20) min after ECT. The mean difference in the maximum percent fall in FEV₁ in the subsequent ECT ranged from no improvement to 20.6% over the control challenge. The pooled results (Fig. 2) showed that this type of warm-up failed to attenuate the EIB response (MD = −12.6%, 95% CI = −26.7% to 1.5%, I² = 90%). One study also reported that 6 of the 12 participants had falls in FEV₁ <15% and classified them as having obtained complete protection from EIB (16).

Continuous high-intensity protocol. Two trials involving 37 patients compared the fall in FEV₁ in an ECT after a continuous high-intensity warm-up with a control challenge with no warm-up (20,22). Exercise intensity for the warm-up was at HR = 180 bpm (22) and 98% ± 2% of predicted maximum (20). Spirometry was conducted up to 80 (22) and 90 min (20) after ECT. The mean difference in the maximum percent fall in FEV₁ in the subsequent ECT ranged from very little improvement (0.99%) to 17.6% over the control challenge. The pooled results (Fig. 2) showed that this type of warm-up failed to attenuate the EIB response (MD = −9.8%, 95% CI = −26.0% to 6.4%, I² = 89%).
<table>
<thead>
<tr>
<th>Author (yr)</th>
<th>Publication Status</th>
<th>Randomized [R]</th>
<th>Source</th>
<th>Country</th>
<th>Funding</th>
<th>Analyzed [A]</th>
<th>Trial Design</th>
<th>Withdrawals [W]</th>
<th>ECT Type/Duration (min) after No Warm-up or Warm-up</th>
<th>ECT: Temp; RH</th>
<th>No. of Protocols; Protocols per Day/WR</th>
<th>Withheld Asthma Med; Class; Time</th>
<th>Definition EIB (% Fall FEV₁)</th>
<th>Outcomes:</th>
<th>Secondary Adverse Events</th>
</tr>
</thead>
<tbody>
<tr>
<td>de Bisschop et al. (1999) (6)</td>
<td>Journal article NR</td>
<td>30</td>
<td>No warm-up or Protocol 1: interval: two sets of 5 × 26-s sprints, 1.5 min between, 5 min between sets (7.5% of the distance and 120% of the speed of FRAST)</td>
<td>Treatment center</td>
<td>Crossover 0</td>
<td>10-min rest</td>
<td>FRAST: running as fast as possible × 7 min (mean distance = 1171 ± 142 m)</td>
<td>4°C ± 5°C; 1.5 ± 0.5 mm Hg</td>
<td>2; 1;</td>
<td>≥15%</td>
<td>Primary: mean percent fall PEF</td>
<td>Secondary: complete protection</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Eck et al. (2002) (8)</td>
<td>Abstract NR</td>
<td>46</td>
<td>No warm-up or Protocol 1: continuous: 10-min steady training Protocol 2: interval: 10-min interval running Protocol 3: progressive: 10-min exercises with increasing intensity</td>
<td>Germany, Switzerland</td>
<td>Not clear NR</td>
<td>5-min stretching, no rest, plus Caffeine and exercise</td>
<td>Treadmill × 10-min steady running</td>
<td>SABA × 12 h</td>
<td>NR</td>
<td>≥10%</td>
<td>Primary: mean percent fall FEV₁</td>
<td>Secondary: complete protection</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>McKenzie et al. (1994) (16)</td>
<td>Journal article NR</td>
<td>12</td>
<td>No warm-up or Protocol 1: continuous: low-intensity; treadmill × 15 min at 60% VO₂max; 2-min rest; Protocol 2: interval: 8 × 30-s sprints at 100% VO₂max separated by 1.5-min rest; 2-min rest</td>
<td>Canada</td>
<td>NR</td>
<td>Volunteers</td>
<td>University and local community</td>
<td>Crossover 0</td>
<td>15-min rest (interval/intensity equal to VO₂max)</td>
<td>23°C ± 1.2°C; ambient room humidity 3; not clear (three sessions);</td>
<td>≥15%</td>
<td>Primary: max percent decrease FEV₁</td>
<td>Secondary: complete protection</td>
<td></td>
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</table>

Table 1. Description of RCTs included in the review.

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<table>
<thead>
<tr>
<th>Study</th>
<th>Protocol Type</th>
<th>Intensity</th>
<th>Duration</th>
<th>Rest</th>
<th>Temperature</th>
<th>Additional Information</th>
</tr>
</thead>
<tbody>
<tr>
<td>Morton et al. (1979) (18)</td>
<td>Continuous</td>
<td>Low</td>
<td>5 min</td>
<td>1 min</td>
<td>Room temp; NR</td>
<td>≥15%; Primary max percent decrease FEV₁, Secondary: FVC percent change FEV₁ times measured at 5, 10, 15, 20, and 30 min (1 AE)</td>
</tr>
<tr>
<td>Reiff et al. (1989) (20)</td>
<td>Continuous</td>
<td>High</td>
<td>6 min</td>
<td>45 min</td>
<td>HR = 97% ± 3% predicted max</td>
<td>≥15%</td>
</tr>
<tr>
<td>United Kingdom (NR)</td>
<td>Continuous</td>
<td>Low</td>
<td>30 min</td>
<td>21 min</td>
<td>19.9°C ± 0.7°C; 39%–50% ± 4.0%</td>
<td></td>
</tr>
<tr>
<td>Clinic volunteers (Crossover 0)</td>
<td>Progressive</td>
<td>Low</td>
<td>30 min</td>
<td>HR = 88% ± 32% predicted max</td>
<td>Two sessions within 1 wk at same time of day</td>
<td></td>
</tr>
<tr>
<td>Schnall and Landau (1980) (22)</td>
<td>Continuous</td>
<td>High</td>
<td>6 min</td>
<td>49 min</td>
<td>21°C–23.5°C ± 1.2°C; 0.55</td>
<td></td>
</tr>
<tr>
<td>Australia Government</td>
<td>Progressive</td>
<td>High</td>
<td>10 min</td>
<td>HR = 180 bpm; 10 min rest; 7 × 30-s sprints with 2.5 min between (speed 120%–130% of first run); 20 min rest</td>
<td>3; 1; Primary: max percent decrease FEV₁ and PEF</td>
<td></td>
</tr>
<tr>
<td>NR Crossover</td>
<td>Interval</td>
<td>Low</td>
<td>7 × 30-s</td>
<td>SABA and SCG × 8 h</td>
<td>Three sessions in 4 wk; FEV₁ (L); PEF (L·min⁻¹) measured at 0, 2, 5, 10, 15, 25 up to 80 min; Yes</td>
<td></td>
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</table>

AE, adverse events; AUC, area under the curve; FRAST, free-running asthma screening test; ICS, inhaled corticosteroid; NR, not reported; PEF, peak expiratory flow; RH, relative humidity; SABA, short-acting β-agonist; Sal, salbutamol; SCG, sodium chromoglycate; Temp, temperature; VO₂, oxygen consumption.
Variable-intensity protocols. Eck et al. (8) failed to identify significant difference among the three protocols they investigated in 52 patients—10 min of continuous low-intensity running, 10 min of running in intervals, and 10 min of exercising with increasing intensity (8). No data on the intensity of each warm-up were reported. Schnall and Landau (22) performed spirometry up to 80 min after ECT; Eck et al. (8) did not report timing of post-ECT spirometry. When combined, the three protocols protected 79% (36/46) of participants from EIB (cut point not reported). The combined mean maximum percent fall in FEV\textsubscript{1} on the challenges after all warm-up protocols was compared with an ECT with no warm-up and indicated a mean improvement of \(-11.0\% \) (95% CI = \(-14.6\% \) to \(-7.37\% \), \(I^2 = 0\% \)).

One of three protocols in the Schnall and Landau (22) trial involved a combination of continuous and interval segments: a 6-min treadmill run (HR = 180 bpm), a 10-min rest followed by 7 \times 30-s sprints (treadmill speed increased 120%–130% during the first run), and then a 20-min rest before the final challenge of the same intensity as the original 6-min run. The mean difference in the maximum percent fall in FEV\textsubscript{1} compared with results of a no-warm-up ECT was an improvement of \(-10.4\% \) (95% CI = \(-21.1\% \) to \(0.24\% \)). The pooled results (Fig. 2) showed that variable-intensity warm-up protocols attenuated the EIB response by a mean of \(-10.9\% \) (95% CI = \(-14.4\% \) to \(-7.5\% \), \(I^2 = 0\% \)).

No data/results were presented for any preexercise routine for symptom relief, clinical protection, or adverse effects.

**DISCUSSION**

Using a comprehensive search strategy and concerted efforts to avoid publication and selection bias, this systematic review identified all the available evidence that compared various forms of warm-up activities with no warm-up in the preexercise treatment of EIB. A total of seven RCTs were identified, involving 128 patients with documented EIB after vigorous exercise. The evidence suggests that, compared with no warm-up, high-intensity interval or variable-intensity warm-up exercise before vigorous exercise offers a statistically significant attenuation in the percent fall in FEV\textsubscript{1} for up to 80 min, with the response fairly consistent across studies.

Interval exercise resulted in a mean attenuation in FEV\textsubscript{1} of 10.61%, ranging from \(-4.80\% \) (16) to 16.10% (22). The warm-up exercise could be considered a physiological stress, and therefore, variations in warm-up protocol or environmental conditions may affect the stress on the airways and, correspondingly, the protective effect of the preexercise warm-up. The study by McKenzie et al. (16) showed the least protection for EIB, although the warm-up protocol and the environmental conditions were similar to those described in the other included studies. Further, there were no apparent differences in subject characteristics among studies. It is unclear why the interval protocol used by McKenzie et al. (16) resulted in less attenuation of FEV\textsubscript{1} after the exercise challenge.

<table>
<thead>
<tr>
<th>Author (yr)</th>
<th>Age (Mean SD)</th>
<th>Pulmonary Function: Baseline FEV\textsubscript{1}</th>
<th>Max Percent Fall FEV\textsubscript{1}</th>
<th>Asthma Status</th>
<th>Atopic Status</th>
<th>ICS History</th>
<th>Smoking Status</th>
<th>Male, n (%)</th>
<th>Max Percent Fall PEF, n (%)</th>
<th>Max Percent Fall PEF, %</th>
</tr>
</thead>
<tbody>
<tr>
<td>de Bisschop et al. (1999) (6)</td>
<td>12; range 8–15</td>
<td>PEF: 99 ± 15%</td>
<td>4.2 ± 1.8</td>
<td>Stable, mixed severity</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>8/30 (26.7)</td>
<td>PEF: 37 ± 14.5</td>
<td></td>
</tr>
<tr>
<td>Eck et al. (2002) (8)</td>
<td>Range 6–19</td>
<td>NR</td>
<td>8 ± 1.1</td>
<td>Stable</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td></td>
</tr>
<tr>
<td>McKenzie et al. (1994) (16)</td>
<td>Stable</td>
<td>Stable</td>
<td>3.4 ± 0.5</td>
<td>Stable, mild to persistent</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>3/12 (33.3)</td>
<td>FEV\textsubscript{1}: 48 ± 6.8; PEF: 51 ± 10.6</td>
<td></td>
</tr>
<tr>
<td>Morton et al. (1979) (18)</td>
<td>Stable</td>
<td>Stable</td>
<td>9 ± 1.0</td>
<td>Stable, mild to persistent</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>10/18 (55.6%)</td>
<td>FEV\textsubscript{1}: 22.8 ± 8.0; PEF: 12.3 ± 7.1</td>
<td></td>
</tr>
<tr>
<td>Reiff et al. (1989) (20)</td>
<td></td>
<td></td>
<td>8 ± 1.0</td>
<td>Stable</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>7/7 (100)</td>
<td>FEV\textsubscript{1}: 84 ± 7.7; PEF: 22 ± 11</td>
<td></td>
</tr>
<tr>
<td>Schnall and Landau (1980) (22)</td>
<td></td>
<td></td>
<td>8 ± 1.0</td>
<td>Stable</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>4/6 (66.7)</td>
<td>FEV\textsubscript{1}: 8 ± 1.0; PEF: 22 ± 11</td>
<td></td>
</tr>
</tbody>
</table>

NR, not reported.
In the two studies that examined continuous high-intensity warm-up, the mean attenuation in FEV₁ was -9.79%, with one study (20) showing significant protection (-17.57%), while the other study showing minimal protection (-0.99%) (22). In the study by Reiff et al. (20), the preexercise warm-up was 6 min at 98% of HRmax. In contrast, Schnall and Landau (22) had subjects exercise for 6 min at an absolute HR of 180 bpm. Schnall and Landau (22) report only an age range for their subjects (12–31 yr). Taking the median of the age range (22 yr), the predicted maximal HR would be ~198 bpm (220 - mean age), and therefore, 180 bpm represents ~91% of maximum. In addition, the relative humidity during all of the exercise conducted by Schnall and Landau (22) report only an age range for their subjects (12–31 yr). Taking the median of the age range (22 yr), the predicted maximal HR would be ~198 bpm (220 - mean age), and therefore, 180 bpm represents ~91% of maximum. In addition, the relative humidity during all of the exercise conducted by Schnall and Landau (22) may be explained by the reduced preconditioning airway stress during the warm-up, that is, lower exercise intensity and higher relative humidity.

The results of the three studies that examined continuous low-intensity warm-up showed a mean attenuation in FEV₁ of -12.60%, with two studies showing similar responses (-18.25% and -20.57%) (16,20), whereas one study showed no effect on FEV₁ (18). In the study by McKenzie et al. (16), subjects exercised for 15 min at 60% of VO₂max whereas in the study by Reiff et al. (20), subjects exercised for 30 min at an average HR of 88% of maximum. In contrast, the study by Morton et al. (18), which showed no attenuation in the fall in FEV₁, had subjects exercise at 60% of maximum predicted HR for only 3 min. These results suggest that, in order for a continuous exercise warm-up to be effective in attenuating EIB, subjects may need to exercise longer (e.g., for at least 15 min).

Results of the variable intensity warm-up show a mean attenuation in FEV₁ of -10.94%. Of note, these studies need to be interpreted with caution. The study by Eck et al. (8) was a larger study (n = 46); however, it was a published abstract, and therefore, pertinent information such as EIB status and environmental conditions is absent. The “combination warm-up” arm of the study of Schnall and Landau (22) includes only six subjects and seems to have a high degree of variability in the change in FEV₁ (95% CI = -21.08% to 0.24%). In addition, because of the varying nature of the warm-up intensity, these protocols would be difficult to replicate as a standardized warm-up for subjects.

**PHYSIOLOGICAL MECHANISM FOR REFRACTORY PERIOD**

Potential physiological mechanisms have been proposed as to why exercise would cause a refractory period of EIB. Exercise is believed to result in dehydration of the airway...
surface, which increases airway osmolarity, releasing inflammatory mediators (prostaglandins, leukotrienes, and histamine) from the mast cell, and it is the release of these mediators that causes bronchoconstriction (4). Of note, the pathophysiology of EIB in a patient with asthma may be different from bronchoconstriction in an athlete after exercise (4). The cause of this refractory period is not fully understood but may be due to depletion of catecholamines, increased circulation of prostaglandin, or degradation of mast cell mediators. Depletion of mast cell mediator stores is a popular theory to explain refractory period after exercise (9,15,23). It has been hypothesized that warm-up causes a gradual discharge of mast cell mediators, and a time would be required for replenishment (10). If exercise is resumed within this period, then mediator stores would not be replenished, and therefore, EIB would not occur. McKenzie et al. (16) have suggested that if depletion of mast cell mediators explains the refractory period, then the duration of the warm-up would seem to be most critical. As the most consistent response was observed after high-intensity interval exercise, it would seem that duration of warm-up exercise is not most critical at attenuating EIB.

LIMITATIONS

The results from this review should be interpreted cautiously due to the relatively small sample sizes, low methodological quality of the RCTs, and the variability in the warm-up protocols studied. Importantly, because of the small number of studies reviewed, and the small sample sizes contained within the studies, the power to detect differences between the various types of warm-up protocol was limited. As a result, we were not able to conduct comparisons among protocols. As shown in Figure 2, both interval and variable-intensity protocols resulted in attenuation in FEV$_1$ of approximately 10%. Based on previous work, this magnitude of protection is likely clinically significant (2,3,12,21). Unfortunately, most studies did not report individual results, and therefore, individual clinical EIB protection could not be determined. Of note, studies performed spirometry up to 80 min after ECT, and therefore, preexercise warm-up should be considered a short-term strategy to prevent EIB.

In addition, limitations associated with systematic reviews should be discussed. First, there is a possibility of publication bias (i.e., that only positive studies were published). Importantly, we conducted comprehensive and systematic searches of the published literature for potentially relevant studies; these were supplemented by hand searching for gray literature (i.e., unpublished or difficult to find studies). Despite these efforts, we recognize that we may have missed some studies. In addition, EIB literature is not indexed well, and authors do not use consistent terms. To control for this, the search strategy was designed to be highly sensitive to avoid missing potentially relevant articles and 18 electronic databases were searched to retrieve as many studies as possible. More high-quality studies examining the efficacy of warm-up strategies to reduce EIB are needed.

CONCLUSIONS

From the available evidence, the attenuation in the fall in FEV$_1$ was similar whether high-intensity interval or variable intensity warm-up exercise was used. The attenuation in FEV$_1$ seems consistent with either warm-up strategy; however, interval exercise may be superior as it is a more easily standardized for the athlete/coach, and there is more evidence for this strategy. These findings indicate that an appropriate warm-up strategy, which includes at least some exercise close to peak oxygen consumption or maximal HR, may be a short-term nonpharmacological alternative to reducing EIB.

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REFERENCES