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Warm-up exercise can reduce exercise-induced bronchoconstriction

▸ **Stickland MK**, Rowe BH, *et al. Medicine & Science in Sports & Exercise* 2012;**44**(3):383–91.

BACKGROUND

Exercise-induced bronchoconstriction (EIB) is a transient narrowing of the lower airways after vigorous exercise.[1] Exercise requires increased ventilation, which results in respiratory water loss leading to airway drying and cooling. Evaporative water loss leading to an increase in the osmolarity of the airway surface liquid and consequent release of mediators is thought to be the major stimulus and mechanism for EIB.[2] Mast cell mediators include histamine, leukotrienes and prostaglandins, which act on specific receptors on the bronchial smooth muscle causing bronchoconstriction.[3] Leukotrienes from eosinophils and neuropeptides from sensory nerves may also be involved in EIB. EIB can occur in people with or without chronic asthma, although it is highly prevalent in people with asthma.[1]

The intensity and duration of exercise are key determinants of the airway response.[2] Guidelines therefore recommend an exercise challenge of 6–8 min at 80–90% of the predicted maximum heart rate.[4] However, laboratory exercise may have poor sensitivity to identify EIB if the intensity does not induce enough ventilation to achieve an adequate rate of respiratory water loss. In athletes, field exercise, eucapnic hyperventilation or osmotic challenge may be more appropriate tests.[3]

A decrease in the forced expiratory volume in 1 s (FEV_1) of 10–15% after exercise is the threshold for the diagnosis of EIB.[4 5] EIB may be associated with cough, wheeze, chest pain or tightness, dyspnoea or excessive mucus production.[6] However, the amount of bronchoconstriction does not always correlate well with the baseline level of lung function or presence or severity of symptoms.[7 8] Nevertheless, these symptoms or the effect of bronchoconstriction on ventilation could limit athletic performance.

An initial airway response to exercise inducing a significant fall in FEV_1 may result in a refractory period of 3–4 h following spontaneous recovery from the bronchoconstriction. During this refractory period, the airways have reduced responsiveness to subsequent exercise. Around 50% of persons with EIB have about a 50% inhibition in the fall in FEV_1 during a subsequent exercise challenge.[9] Initially, this inhibition was explained by the depletion of bronchoconstricting mediators from mast cells; however, it was later attributed to the release of the bronchoprotective prostaglandin E2 because the refractory period is prevented by a cyclooxygenase inhibitor indomethacin.[10] However, the bronchial provocation test inhaled mannitol, which is used as a model of EIB, suggests that the refractory period is a transient tachyphylaxis at the level of the airway smooth muscle to the mediators of bronchoconstriction, rather than mediator depletion.[11] These studies suggest that warm-up exercise may offer a free, non-pharmacological means of reducing EIB in some subjects, but results from individual trials are not consistent.

AIM

This systematic review was performed to determine whether warm-up exercise attenuates EIB in a subsequent exercise period.

SEARCHES AND INCLUSION CRITERIA

Cochrane CENTRAL, MEDLINE, Embase, CINAHL, AMED and PsycINFO were searched with search terms related to exercise, asthma, bronchoconstriction, hyperreactivity and training. Twenty respiratory journals, 12 conference proceedings and reference lists of included articles were also searched. Two reviewers applied the selection criteria and extracted the relevant data, including information about method of randomisation, blinding and allocation concealment. Studies were not excluded on the basis of their language or date of publication.

To be eligible for inclusion in the review, studies were required to have used a randomised design to examine the effect of warm-up exercise in adults and/or children of any fitness level with confirmed EIB.

INTERVENTIONS

Any form of warm-up exercise routine was eligible as the study intervention if the comparator was no intervention or a placebo. These randomised interventions were each required to be followed by a 5 to 10-minute exercise challenge test.

MAIN OUTCOME MEASURES

The review considered two outcome measures for EIB: fall in FEV_1 from pre-exercise baseline as a continuous outcome, and the absence of EIB as a dichotomous outcome. The other outcomes considered by the review were symptoms, clinical protection and adverse effects.

STATISTICAL METHODS

Meta-analyses of continuous outcomes were reported as mean differences with 95% CIs. Random-effects models were used throughout the review and the I^2 statistic was used to assess heterogeneity. No sensitivity or subgroup analyses were conducted.

RESULTS

The search strategy identified seven eligible studies involving 128 participants. Three studies involved adults, one involved children and three involved both adults and children. Six of the trials involved participants with mild stable asthma; the seventh study did not specify asthma severity.

Five of the studies assessed multiple warm-up regimens, with 11 warm-up regimens being tested altogether. None of the included trials described their randomisation method or reported that blinding or allocation concealment were used.

Four 'interval' warm-up regimens (ie, several short intense sprints of about 30 s) were compared to control, with meta-analysis indicating that the sprints significantly attenuated the fall in FEV_1 by a mean of 11% (95% CI 7% to 15%). Three 'continuous low-intensity' warm-up regimens (ie, treadmill running at around 60% of peak workload) were compared to control. Again the meta-analysis identified a significant attenuation of the fall in FEV_1, by 13% (95% CI 2% to 27%). Two 'continuous high-intensity' warm-up regimens (ie, exercise

at 80–90% of peak workload) were compared to control, but the pooled effect was not statistically significant, attenuating the fall in FEV_1 by 10% (95% CI −6% to 26%). The final category was the 'variable intensity' warm-up (ie, continuous and interval exercise periods of varying intensity), which was assessed in two studies. Here, the result was statistically significant, attenuating the fall in FEV_1 by 11% (95% CI 8% to 14%).

While some studies reported the EIB dichotomously (ie, the number of participants who had a fall in FEV_1 greater than a specified threshold), these data were only reported for the treatment group. Therefore, between-group comparisons were not possible. No data were obtained from any of the studies for the remaining outcomes.

LIMITATIONS/CONSIDERATIONS

There was substantial heterogeneity among the trials included in this review. Apart from the variety in the warm-up regimens, the time between the warm-up and the standardised exercise test ranged between 1 and 49 min. Also, the time between the standardised exercise test and the follow-up measure of FEV_1 ranged from 10 to 90 min. Ten minutes is too short to see adequate recovery of FEV_1 to baseline following EIB while 90 min would be adequate for most subjects, still being within the time of the refractory period. Despite the noise created by this heterogeneity, the meta-analyses still identified statistically significant effects, suggesting that warm-up exercise has a bronchoprotective effect. The CIs around all the pooled results were wide, even for the warm-up regimens that had a significant effect, suggesting variability in the refractory responses within the population studied. The review does not analyse the protective effect based on the severity of EIB and while some subjects may have quantifiable protection on a second exercise test, they may still have significant EIB. It would have been useful for the data to be presented also as the percentage inhibition of the fall in FEV_1 due to warm-up exercise, similar to what is reported for drug interventions. Further it is unclear as to what proportion of subjects did and did not have protection due to warm-up exercise. For significant inhibition to be identified, the fall in FEV_1 of the second exercise challenge must be outside the range of reproducibility of the initial fall in FEV_1. Also, data about adverse effects would be helpful.

CLINICAL IMPLICATIONS

Although warm-up exercise appears to attenuate EIB, the refractory period does not occur in all subjects with EIB. Further, patients should be advised that the initial fall in FEV_1 could be severe, which has safety implications, particularly if exercise of a higher intensity is required. In these subjects appropriate pharmacological inhibition would be first-line prevention. Anti-inflammatory medication such as regular inhaled corticosteroids should be instituted in patients with chronic asthma symptoms that also occur apart from exercise, and may be useful in subjects with significant EIB alone. The β-2 agonists are also effective, however, they lose their efficacy as protection against EIB and as rescue bronchodilators with regular use, though this may not occur with intermittent use.[12] Leukotriene inhibitors are less effective at attenuating the response to exercise but shorten the duration of EIB. Mast cell stabilisers (eg, sodium cromoglycate) when taken immediately before exercise have been shown to be highly effective at inhibiting EIB in most subjects.[13] Other non-drug interventions such as breathing through the nose and covering the mouth in cold dry weather to minimise respiratory heat and water loss also appear effective.[5] These drug and non-drug therapies could also be used concurrently. For example, albuterol plus a warm-up gives better protection than the warm-up or albuterol alone.[14]

In summary, warm-up exercise can be considered as a possible free, non-pharmacological therapy to attenuate bronchoconstriction in subjects with mild EIB. EIB identifies the presence and activity of the key features of asthma—airway hyperresponsiveness and airway inflammation—which can be attenuated with regular inhaled corticosteroids.[15] Safety considerations may make warm-up exercise an inappropriate strategy to prevent EIB in persons with documented moderate-to-severe EIB and in others who have chronic asthma who are poorly controlled on anti-inflammatory therapy. Nevertheless, in many people with mild EIB, interval exercise, continuous high-intensity exercise and variable intensity exercise all appear to be effective regimens.

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