Exercise-Induced Hypoalgesia of Low-Intensity Blood Flow Restriction Exercises

Subjects: Rehabilitation

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Low-intensity exercise with blood flow restriction (LIE-BFR) has been proposed as an effective intervention to induce hypoalgesia in both healthy individuals and patients with knee pain.

Keywords: KAATSU training ; exercise ; occlusion training ; pain threshold

1. Introduction

Physical exercise is considered a beneficial intervention to reduce pain sensitivity in healthy individuals and patients with chronic pain conditions [1]. Clinically important changes in pain reduction are reported during or after a single bout of exercise, a phenomenon widely known as exercise-induced hypoalgesia (EIH) [2][3]. Based on experimental studies, the magnitude of EIH varies according to different factors, such as exercise parameters (i.e., type, dose, duration, and intensity), the type of noxious stimulus used for assessment (pressure, thermal, or electrical), the site of measurement (local or remote, muscle, or bone), and the timing of assessment (during or after exercise) [3][4][5][6][7]. Evidence suggests that EIH increases when the intensity of exercise is higher and over the exercising limb compared to remote sites in individuals with or without chronic pain [2][6].

During the last two decades, a new training method using low-intensity exercise with blood flow restriction (LIE-BFR) has been suggested to produce significant improvements in muscle strength, hypertrophy, and endurance in healthy individuals [8][9][10][11]. LIE-BFR is used during voluntary resistance exercises (using 20–40% of one repetition maximum [RM]) or aerobic exercises (using 50% of heart rate or VO_2max) [12]. BFR training involves partial restriction of arterial blood flow, applying 40% to 80% of limb occlusive pressure using elastic or inflatable air cuffs of different diameters [12][13]. When air cuffs are used, external pressure is achieved with pneumatic tourniquet systems or a manual pump system [14][15]. Recently, the effectiveness of LIE-BFR has been investigated in various musculoskeletal pathologies, suggesting comparable improvements in muscle strength, hypertrophy, and function compared to traditional exercise programs [16][17][18][19]. Hence, the method has been proposed as a useful alternative in rehabilitation when high-intensity conventional exercises are contraindicated or should be avoided [20][21][22][23][24].

In addition to the positive effects on skeletal muscles, LIE-BFR has shown significant reductions in pain intensity in patients with knee problems or lateral elbow tendinopathy [16][18][23][25]. As a result, it has been suggested that the BFR component may trigger a hypoalgesic response similar to high-load resistance exercise [26][27]. Further investigations have demonstrated that LIE-BFR induces greater reductions in pressure pain thresholds compared to conventional training [28][29]. These hypoalgesic responses were partially explained by endogenous opioid and endocannabinoid system pain-modulation mechanisms [28][29]. However, other studies have supported that the addition of BFR to LIE did not provide an additional hypoalgesic response when the exercise was performed to failure [30][31]. Additionally, based on a recent randomized controlled trial (RCT), elbow flexion LIE-BFR produced a similar reduction in pain perception compared to HIE only in the exercising limb [32]. Despite growing research evidence in the current field, it remains unclear whether BFR exercises induce a significant hypoalgesic effect compared to other interventions or how different types of applications may influence the hypoalgesic response.

2. Participants

A total of 189 healthy participants were included with a mean age of 24.1 years. Of the participants, 44% were women and 56% were men, and the sample sizes ranged from 12 to 60 healthy individuals. All subjects were asked to maintain normal dietary habits during participation in the experimental protocols and refrain from caffeine, alcohol, and intense exercise the day before the experimental trials. All eligible studies described some common exclusion criteria, such as serious cardiovascular diseases, venous deficiency, lymphoedema, history of heart surgery, pulmonary embolism, cancer, or thrombosis [28][29][30][31][32]. **Table 1** shows the characteristics and main results of the included trials.

Table 1. Included studies, demographics and results.

Study (Year)	Design	Total Sample Size N (Mean Age ± SD, Sex)	Interventions	Equipment	Follow-Up	Outcome Measures	Results
Hill et al. (2019) [33]	Parallel design	25 healthy individuals (25 women) Ecc LIE-BFR (n = 12; 21.7 years ± 1.0) Con LIE-BFR (n = 13; 22.0 years ± 1.6)	Unilateral isokinetic elbow flexion (120° s) (1) Ecc LIE-BFR(40% AOP) at 30% of eccentric peak torque (30-15-15-15 reps) (2) Con LIE-BFR(40% AOP) at 30% of concentric peak torque (30-15-15-15 reps)	Inflatable cuffs with a manual pump (KAATSU Master, Sato Sports Plaza, Tokyo, Japan)	Between 7 testing days	PPTs at the biceps brachii muscle	There was no significant group × testing day interaction (p = 0.682)
Hughes et al. (2020) [29]	Cross-over design	12 healthy individuals (29 ± 6 years; 10 men and 2 women)	Unilateral leg press (1) LIE using at 30% 1RM (30-15-15-15 reps) (2) LIE-BFR(40% AOP) at 30% 1RM (30-15-15-15 reps) (3) LIE-BFR(80% AOP) at 30% 1RM (30-15-15-15 reps) (4) HIE at 70% 1RM (4 sets × 10 reps)	Personalized Tourniquet system (Delfi Medical Inc, Vancouver, BC, Canada)	5 min post-exercise 24 h post-exercise	PPTs at the dominant and nondominant quadriceps, dominant biceps brachii, nondominant upper trapezius muscles	LIE-BFR (80% AOP) showed significantly higher PPTs compared to all trials (p < 0.05) at all measurements sites 5 min post-exercise LIE-BFR (40% AOP) showed significantly higher PPT compared to LIE (p < 0.05) at all measurements sites 5 min post-exercise HIE showed higher PPTs compared to LIE (p < 0.05) at all measurements sites 5 min post-exercise
Hughes et al. (2021) [28]	Cross-over design	12 healthy individuals (27 ± 6 years; 12 men)	Static bicycle X 20 min (1) LIE (2) LIE-BFR(40% AOP) at 40% VO_2max (3) LIE-BFR(80% AOP) at 40% VO_2max (4) HIE at 70% VO_2max	Personalized tourniquet system (Delfi Medical Inc, Vancouver, BC, Canada)	5 min post-exercise 24 h post-exercise	PPTs at the dominant and nondominant quadriceps, dominant biceps brachii, nondominant upper trapezius muscles	PPTs were significantly increased following BFR (40% AOP) and BFR (80% AOP) compared with LIE (p < 0.05). BFR (80% AOP) presented higher increase in PPTs compared to BFR (40% AOP) (p < 0.05). BFR (80% AOP) and HI-AE presented increased PPTs in remote areas of the body.

Study (Year)	Design	Total Sample Size N (Mean Age ± SD, Sex)	Interventions	Equipment	Follow-Up	Outcome Measures	Results
Karanasios et al. (2022) [32]	Parallel design	40 healthy individuals (26.6 years ± 6.8; 17 women and 23 men)	Elbow flexion with dumbbells (1) LIE-BFR(40% AOP) at 30% RM (30-15-15-15 reps) (2) HIE at 70% RM (4 sets × 10 reps)	Personalized tourniquet system (Mad-Up Pro, France)	5 min post-exercise	PPTs at the dominant and nondominant quadriceps, biceps brachii and upper trapezius muscles	Non-significant between-group changes in PPTs at all measurement sites Statistically significant reductions between pre- and post-exercise in LIE–BFR and HIE at dominant biceps brachii
Song et al. (2022) [31]	Cross-over design	60 healthy individuals (21.8 years ± 3.2; 21 men, 39 women)	Isometric handgrip contraction (1) LIE-BFR (50% AOP) at 30% of max strength (4 sets × 2 min contraction) (2) LIE at 30% of max strength (4 sets × 2 min contraction) (3) control	Inflatable cuffs with a manual pump (E20, Hokanson Inc., Bellevue, WA, USA)	5 min post-exercise	PPTs at the dominant forearm and ipsilateral tibialis anterior	PPTs increased similarly in both exercise groups compared to control at a local and non-local site. Non-significant differences between exercise conditions.
Song et al. (2022) [30]	Cross-over design	40 healthy individuals (23.7 years ± 4.3; 18 men, 22 women)	Unilateral knee extension (1) LIE-BFR (80% AOP) at 30% RM (to failure) (2) LIE at 70% RM (to failure) (3) control	Inflatable cuffs with a manual pump (E20, Hokanson Inc., Bellevue, WA, USA)	5 min post-exercise	PPTs at the dominant forearm and ipsilateral tibialis anterior	Both exercise conditions presented greater changes in PPTs compared to control ($p > 0.05$) Non-significant differences between exercise conditions

3. Interventions

Five studies evaluated the effectiveness of LIE-BFR alone compared to other exercise interventions [28][29][30][31][32], while only two of them included a control group [30][31]. One study compared the effectiveness of LIE-BFR between concentric and eccentric isokinetic contractions [33]. Four of the eligible studies investigated the effect of dynamic resistance exercises with BFR and one investigated the effect of low-intensity aerobic exercise with BFR [28][29][30][31][32]. Three studies used lower-limb exercises with BFR, including a leg press [29], knee extension [30], and cycling [28]. Three studies included upper-limb exercises, of which two used a dynamic elbow flexion resistance exercise [32][33] and one used an isometric handgrip contraction [31].

Three of the eligible studies used a pneumatic tourniquet system to apply the BFR condition [28][29][32]. The rest of the studies used inflatable air cuffs and determined arterial occlusive pressure with the help of a hand-held Doppler ultrasound [30][31][33]. Three studies used LIE-BFR with low occlusive pressure (40–50% AOP) [31][32][33], two studies included exercise with both low and high occlusive pressures (40% and 80% AOP, respectively) [28][29], and one trial included only high occlusive pressure (80% AOP) [30].

4. Outcome Measures

Pain sensitivity was assessed using pressure pain thresholds across all studies. Hand-held pressure algometers with a stimulation area of 1 cm diameter were used across all trials. Five studies included measurements at the exercising limb and remote sites [28][29][30][31][32] and one trial investigated the effects of exercise with BFR only at a local site (biceps brachii muscle) [33]. Five studies [28][29][30][31][32] included a follow-up measurement 5 min after exercise trials, while two studies added a follow-up assessment 24 h post-intervention [28][29]. One study examined PPTs throughout a 2-week isokinetic training program [33].

5. Methodological Quality

Table 2 shows the results of the methodological assessment based on the PEDro criteria. Out of six studies, two were rated as ‘high’, one was rated as ‘moderate’ and one was rated as ‘low quality’. Blinding therapists was not feasible in all trials due to the nature of the interventions. Four out of six studies did not ensure the blinding of the participants. One study included the blinding of outcome assessors. There was a low to no drop-out rate among the trials.

Table 2. Methodological quality assessment using the PEDro scale.

	1	2	3	4	5	6	7	8	9	10	11	Total Score
Hill et al. (2019) [33]	+	+	−	−	−	−	−	−	−	+	+	**4/10**
Hughes et al. (2020) [29]	+	+	+	+	−	−	−	+	+	+	+	**7/10**
Hughes et al. (2021) [28]	+	+	+	+	−	−	−	+	+	+	+	**7/10**
Karanasios et al. (2022) [32]	+	+	+	+	+	−	+	+	+	+	+	**9/10**
Song et al. (2022) [31]	+	+	+	−	−	−	−	+	+	+	+	**6/10**
Song et al. (2022) [30]	+	+	+	+	+	−	−	+	+	+	+	**8/10**

6. Effects on Pain Perception

Five studies reported significant within-group increases in PPTs after a single bout of LIE-BFR at a short-term follow-up (5 min post-intervention) [28][29][30][31][32]. Pain sensitivity was significantly decreased after a LIE-BFR using knee extension, leg press, isometric handgrip, or 20 min of cycling at both the exercising limb and distal areas of the body [28][29][30][31][32]. Based on the results of a single RCT, an elbow flexion isotonic LIE-BFR resulted in a significant increase in PPTs only at the brachialis brachii muscle and without significant changes at remote areas [32]. One RCT using elbow flexion isokinetic LIE-BFR reported no changes in PPTs at a local site of measurement throughout a 2-week training program [33].

Significantly greater increases in PPTs at local and distal sites of the body were found in favor of lower-limb LIE-BFR with 80% arterial occlusive pressure (AOP) compared to LIE-BFR with 40% AOP, HIE, and LIE alone [28][29]. Based on the same studies, LIE-BFR with 40% AOP had better results in reducing pain sensitivity than LIE alone [28][29]. Notably, the differences did not remain statistically different at the 24 h follow-up.

In contrast to previous findings, two cross-over trials found comparable decreases in PPTs between LIE-BFR and LIE, using either a resistance leg extension or a handgrip isometric exercise [30][31]. A similar hypoalgesic effect between elbow flexion LIE-BFR and HIE was found only at the biceps brachii muscle immediately after intervention [32]. No differences were found in PPTs between concentric LIE-BFR and eccentric LIE-BFR at the biceps brachii muscle using elbow flexion isokinetic exercises during a two-week training program [33].

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