

EFFECT OF A LOW-INTENSITY RESISTANCE EXERCISE PROGRAMME WITH BLOOD FLOW RESTRICTION ON GROWTH HORMONE AND INSULIN-LIKE GROWTH FACTOR-1 LEVELS IN MIDDLE-AGED WOMEN

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ABSTRACT

The effect of a 12-week low-intensity resistance exercise programme with blood flow restriction (LI-BFR) on growth hormone (GH) and insulin-like growth factor-1 (IGF-1) levels in middle-aged women (52.7±7.8 years) was examined. Subjects (N=44) were randomly assigned to the following five groups: control group (CG; n=8), low-intensity (40% of 1RM) resistance exercise group (LI; n=9), high-intensity (70% of 1RM) resistance exercise group (HI; n=9), low-intensity (20% of 1RM) resistance exercise group with a 5% reduction in cuff circumference for blood flow restriction (LI-5% BFR; n=7), and a low-intensity (20% of 1RM) resistance exercise group with a 3% reduction in cuff circumference (LI-3% BFR; n=11). Subjects completed pre- and post-assessments of body weight, percentage body fat, waist-to-hip ratio, muscle strength, GH hormone and IGF-1 levels. A significant effect ($p<0.05$) was observed for waist-to-hip ratio, GH, IGF-1, biceps curls, triceps extensions, leg curls and leg extensions. A significant elevated GH level was observed in HI and LI-5% BFR groups when compared with the control group ($p<0.05$). A significant increase in IGF-1 levels was observed in the HI, LI-5% and LI-3% BFR groups when compared with the LI group ($p<0.05$). Portable cuffs reducing arm and thigh circumferences by 5% were effective in improving GH and IGF-1 levels in middle-aged women.

Key words: Blood flow restriction; Growth hormone; Insulin-like growth factor-1; Resistance exercise; Middle-aged women.

INTRODUCTION

Low-intensity resistance exercise with blood flow restriction can facilitate greater muscular gains than equivalent training without blood flow restriction (Scott *et al.*, 2014). Previous studies have suggested that even low-intensity resistance exercise may have a positive effect on skeletal muscles, such as improving muscle mass and strength (Takarada *et al.*, 2000b; Madarame *et al.*, 2008; Abe *et al.*, 2010; Yasuda *et al.*, 2010; Loenneke *et al.*, 2011). These findings led to the development of blood flow restriction exercise to achieve muscle hypertrophy with 20 to 30% of 1RM intensity (Yasuda *et al.*, 2012). It has also been

suggested that performance of low-intensity resistance exercise with blood flow restriction (LI-BFR) presents no greater risk than traditional high-intensity resistance exercise (Loenneke *et al.*, 2011). As a result, LI-BFR exercise may be an appropriate way to achieve improvement in muscle mass and strength. For example, elderly people need to maintain their strength and muscle mass to decrease the prevalence of osteoporosis (Czarkowska-Paczek *et al.*, 2011) and sarcopenia (Forbes *et al.*, 2012). However, due to the risk of injury, older people should not maintain a high intensity during resistance exercise. Moreover, for people wishing to gain muscle without having to perform high-intensity resistance exercise (like people needing skeletal muscle rehabilitation), LI-BFR exercise should be of a suitable intensity to achieve their goals.

Even though LI-BFR exercise is beneficial for muscle hypertrophy and gaining strength, the BFR method is not simple. Controlling pressure levels during exercise must always be considered (Loenneke *et al.*, 2013a). Therefore, more simple criteria are needed for measuring the pressure during BFR exercise. Previous studies have suggested many different BFR exercise devices, such as elastic wraps, elastic belts with a pneumatic bag inside, nylon pneumatic cuffs, or traditional nylon blood pressure cuffs (Crenshaw *et al.*, 1988; Graham *et al.*, 1993; Laurentino *et al.*, 2008; Karabulut *et al.*, 2011; Loenneke *et al.*, 2013b;). However, the criteria for pressure levels during BFR are not yet clear. In general, the range of pressure used is higher than that of systolic brachial blood pressure (>120mmHg) (Loenneke *et al.*, 2012a; Loenneke *et al.*, 2013a).

Most devices are not customised, but instead are set to a universal pressure for all study participants. When using BFR, pressure should differ depending on the individual. During concentric and eccentric contraction, pressures differ among individuals because of differences in arm and leg circumferences (Loenneke *et al.*, 2012a; Loenneke *et al.*, 2013a). Therefore, the application of the circumference ratio by limiting the blood flow on an individual basis is suggested. This can be accomplished by making the belt shorter than the limb circumference of the subject and marking the length on the belt. It is more convenient to wear a belt fitting the limb circumference of a subject than using an existing pressure regulator.

PURPOSE OF THE STUDY

The purpose of this study was to examine the effects on growth hormone (GH), insulin-like growth factor-1 (IGF-1) and muscle strength in middle-aged women during 12 weeks of LI-BFR by tightening the belt shorter than the limb circumference (3 to 5%) of the subject.

METHODOLOGY

Participants

Forty-four healthy middle-aged women (52.7±7.8 years) were recruited from a gymnasium in Seoul, Republic of Korea and screened with a Physical Activity Readiness Questionnaire (PAR-Q), before participation in this study. Informed and written consent was obtained from all participants prior to starting the study and the Institutional Review Board of the Institute of Sports Science of Dongguk University approved this study. The body mass index of the

subjects was $22.7 \pm 2.8 \text{ kg/m}^2$. Exclusion criteria included any known orthopaedic problem or cardiovascular, pulmonary, or metabolic disease. None of the subjects were on any medication.

Research design

The subjects (N=44) were randomly assigned to 1 of the following 5 groups: the Control Group (CG; n=8), a Low-Intensity resistance exercise group (LI; n=9), a High-Intensity resistance exercise group (HI; n=9), a Low-Intensity resistance exercise group with 5% reduction in circumference of cuff length for Blood Flow Restriction (LI-5% BFR; n=7), and a Low-Intensity resistance exercise group with 3% reduction in circumference of cuff length for Blood Flow Restriction (LI-3% BFR; n=11). The blood flow was limited by tightening the belt shorter than the limb circumference (3 to 5%) of the subject and marking the length on the belt. All training groups completed pre- and post-training assessments of all variables, including GH, IGF-1 and muscle strength (Figure 1).

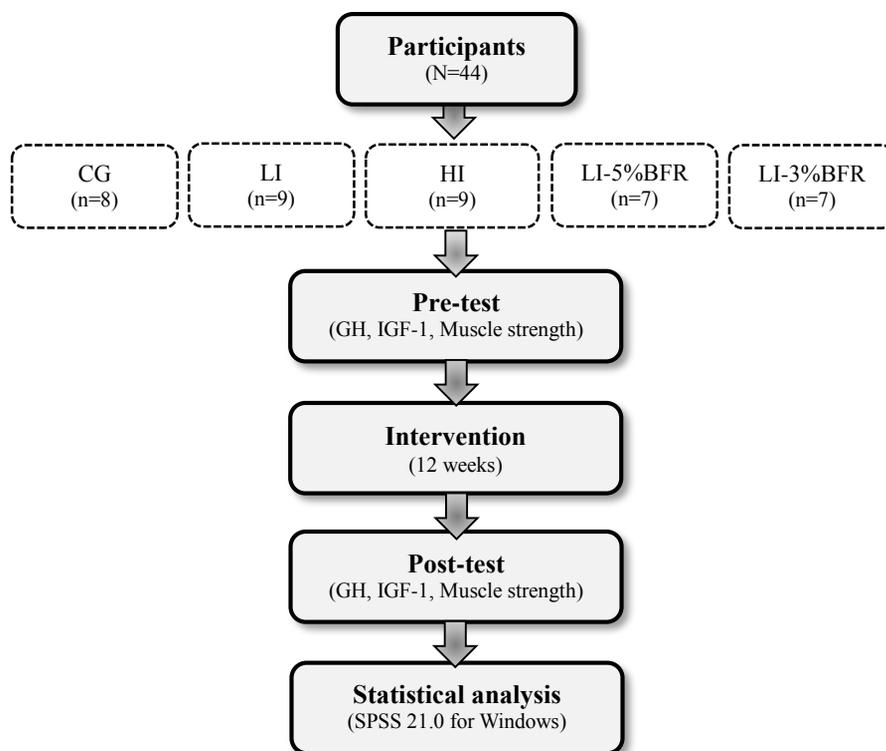


Figure 1. EXPERIMENTAL DESIGN

Measurement variables

Anthropometric measures

Height and weight were measured to the nearest 0.1cm and 0.1kg respectively, by using

InBody 720 (Biospace, Seoul, Korea), and the body mass index (BMI) was calculated in kg/m². Waist-to-Hip Ratio (WHR) was calculated by dividing the waist circumference by the hip circumference as measured to the nearest 0.1cm by using a standard measuring tape (Hoechstmass, Germany). Body fat was measured by means of bioelectrical impedance analysis (InBody 720, Biospace, Seoul, Korea).

Muscle strength

All subjects warmed up before testing by cycling for 5 minutes on a stationary bicycle. 1RM testing was performed using leg extensions, lying leg curls, biceps curls, and triceps extensions (Cybex, USA), using standard 1RM procedures (Seo *et al.*, 2012). After a 1-minute rest period, subjects were familiarised with each of the resistance machines by performing 8 to 10 repetitions with a light load (approximately 50% of predicted 1RM). After a 1-minute rest, subjects performed the full range of exercises with a load approximately 80% of their estimated 1RM. After each successful performance, the weight was increased by 2 to 5kg for each following attempt. The exercises were performed until a failed attempt occurred. Rest periods of 1 minute were taken between each attempt, and 1RM was attained within 5 attempts and a 5-minute rest period separated each test from the next. To facilitate recovery and reduce the effect of fatigue, upper and lower body tests were alternated. All 1RM measurements were recorded in kilograms for subsequent data analysis.

Blood assay

Blood samples were obtained in the morning after a 12-hour fast and collected in Vacutainer® tubes with ethylenediaminetetraacetic acid pre- and post-training. The samples from the subjects were packed in ice and sent to the NEODIN Medical Institute in Seoul, Korea. An immunometric assay (Immulate Analyzer, Diagnostic Products Corp., DPC, Los Angeles, CA, USA), was used for the measurement of serum GH concentrations. The sensitivity of this method was 0.01ng/mL, having intra- and inter-assay coefficient variance percentage of 5.2 and 5.9, respectively. The enzyme-linked immunosorbent assay (ELISA, Diagnostic Systems Laboratories, Dallas, TX, USA), was used to determine serum IGF-I levels. This method had a sensitivity of 0.01 ng/mL, and it had an intra- and inter-assay coefficient variance percentage of 4.9 and 7.7, respectively (Daughaday & Rotwein, 1989).

Exercise training programme with the BFR belt

Subjects in the CG underwent a supervised major muscle stretching exercise programme. Subjects in all training groups performed dumbbell biceps curls, triceps extensions, leg curls and leg extensions 3 times per week for 12 weeks. In the LI group, exercises were performed with an intensity of 40% of 1RM; in the HI group, exercises were performed with an intensity of 70% of 1RM. In the LI-5% BFR and the LI-3% BFR groups, subjects performed exercises with an intensity of 20% of 1RM. They performed 15 repetitions per set and 3 sets per day.

All subjects in the training groups stretched major muscles before and after each training session for 5 minutes. For the BFR exercise group, subjects wore a specially designed BFR belt (SONU KAAP BELT, Seoul, Korea), on the most proximal portion of both legs and arms during exercise training only. The belt was not the usual rubber material with a high flexibility, but instead was a rigid nylon belt with almost no elasticity. The blood flow was reduced by tightening the belt shorter than the limb circumference (3 to 5%) of the subject and marking the length on the belt. The BFR belt width was 3cm for the arms and 5cm for the

thighs (Figure 2).



Figure 2. BLOOD FLOW RESTRICTION BELTS FOR ARMS AND LEGS

Statistical analysis

On the basis of the 5×2 (group \times time), repeated measures design and an anticipated statistical power of 0.80 with an effect size of 0.3, a total sample number of 40 subjects was estimated to be needed for this study (G power program 3.12, Germany). Descriptive variables are presented as mean and SD. One-way analysis of variance (ANOVA) was used to examine baseline differences in participant characteristics between groups. Data analysis was performed by using 5×2 repeated-measures ANOVA. When main effects and interactions were significant, 1-way ANOVA was used for identifying significant differences between the groups. Statistical significance was set at $p < 0.05$. SPSS 21.0 (SPSS Inc., Chicago, IL, USA) was used to perform all analyses.

RESULTS

Table 1. PHYSICAL CHARACTERISTICS OF ALL GROUPS

| Variables | CG (n=8) | LI (n=9) | HI (n=9) | LI-5%BFR (n=7) | LI-3%BFR (n=11) | p# |
|--------------------------|-----------------|-----------------|-----------------|-------------------|--------------------|------------|
| Age (years) | 47.8 \pm 6.8 | 55.3 \pm 6.2 | 52.0 \pm 2.8 | 51.7 \pm 7.6 | 53.6 \pm 11.3 | NS (0.351) |
| Height (cm) | 160.5 \pm 3.8 | 155.7 \pm 4.1 | 158.2 \pm 2.7 | 160.9 \pm 6.2 | 158.5 \pm 5.7 | NS (0.185) |
| Weight (kg) | 61.5 \pm 10.1 | 54.7 \pm 8.6 | 56.0 \pm 4.7 | 59.1 \pm 5.5 | 55.6 \pm 4.6 | NS (0.255) |
| BMI (kg/m ²) | 23.8 \pm 3.5 | 22.6 \pm 3.6 | 22.4 \pm 2.1 | 22.9 \pm 2.1 | 22.2 \pm 2.8 | NS (0.806) |
| Body fat (%) | 32.3 \pm 5.4 | 30.5 \pm 5.4 | 31.4 \pm 5.2 | 28.6 \pm 4.0 | 27.3 \pm 5.0 | NS (0.218) |

BMI=Body Mass Index, CG=Control Group, LI=Low Intensity resistance group, HI=High Intensity resistance group, LI-5% BFR=Low Intensity resistance with 5% reducing circumference for blood flow restriction, LI-3% BFR=Low Intensity resistance with 3% reducing circumference for blood flow restriction, NS=Not Significant # Tested using one-way analysis of variance

Table 2. CHANGES IN VARIABLES AFTER 12-WEEK INTERVENTION

| Variables | Test | CG | LI | HI | LI-5% BFR | LI-3% BFR | p |
|------------------------|------|------------|-------------|--------------|--------------|--------------|---------|
| Weight (kg) | Pre | 61.5±10.1 | 54.7±8.6 | 56.0±4.7 | 59.1±5.5 | 55.6±4.6 | NS |
| | Post | 62.1±10.0 | 54.8±8.8 | 56.1±4.8 | 59.1±5.1 | 55.4±4.1 | |
| Body fat (%) | Pre | 32.3±5.4 | 30.5±5.4 | 31.4±5.2 | 28.6±4.0 | 27.3±5.0 | a |
| | Post | 32.6±5.2 | 30.5±5.9 | 30.1±3.7 | 27.9±4.1 | 26.6±5.5 | |
| WHR | Pre | 0.99±0.18 | 0.95±0.05 | 0.96±0.03 | 0.95±0.03 | 0.86±0.07 | b, c |
| | Post | 1.00±0.18 | 0.95±0.05 | 0.92±0.04# | 0.93±0.04 | 0.87±0.06 | |
| GH (ng/ml) | Pre | 1.29±0.76 | 1.09±0.62 | 1.16±0.96 | 1.37±0.96 | 1.03±1.34 | a, c |
| | Post | 1.30±0.80 | 1.14±0.78 | 2.12±1.92*# | 1.97±1.30* | 0.98±1.32 | |
| IGF-1 (ng/ml) | Pre | 177.0±63.0 | 129.0±35.0 | 138.0±35.0 | 167.0±53.0 | 154.0±53.0 | a, c |
| | Post | 175.0±61.0 | 134.0±36.0* | 203.5±56.0*# | 226.3±54.0*# | 196.0±32.0*# | |
| Biceps curl (kg) | Pre | 20.8±6.0 | 18.9±3.1 | 23.2±2.9 | 22.1±4.5 | 23.1±3.4 | b, c |
| | Post | 17.9±8.3 | 18.8±3.7 | 26.2±3.1*# | 24.9±4.5*# | 23.2±2.9 | |
| Triceps extension (kg) | Pre | 16.9±3.9 | 16.4±3.9 | 20.1±3.5 | 22.7±4.5 | 21.2±5.6 | a, b, c |
| | Post | 16.1±3.9 | 15.6±2.9 | 22.8±2.9*# | 25.1±4.8*# | 21.4±5.1 | |
| Leg curl (kg) | Pre | 40.7±4.6 | 36.3±6.0 | 39.2±5.5 | 30.8±3.3 | 34.7±3.8 | a, b, c |
| | Post | 40.2±4.5 | 35.7±5.8 | 43.5±7.2*# | 34.9±3.2*# | 34.5±3.2 | |
| Leg extension (kg) | Pre | 48.5±7.2 | 47.2±5.5 | 51.4±7.5 | 47.3±4.8 | 48.3±6.2 | a, c |
| | Post | 47.8±6.6 | 47.0±5.8 | 54.6±7.0*# | 50.9±3.0*# | 48.2±5.2 | |

a=time b=group c=time x group CG=Control Group LI=Low Intensity resistance group HI=High Intensity resistance group

LI-5% BFR=Low Intensity resistance with 5% reducing circumference for Blood Flow Restriction

LI-3% BFR=Low Intensity resistance with 3% reducing circumference for Blood Flow Restriction; WHR; waist-hip ratio.

NS=Not Significant * p<0.05 versus CG # p<0.05 versus LI Tested 5×2 (group × time) repeated measures analysis of variance

Physical characteristics of the study subjects are shown in Table 1. Average age and height for participants (N=44) were 52.3 ± 7.8 years and 158.6 ± 4.8 cm respectively. Differences between groups were not statistically significant at baseline.

A significant ($p < 0.05$) interaction effect was observed for WHR, GH, IGF-1, biceps curl, triceps extension, leg curl and leg extension ($p < 0.05$). A repeated measure ANOVA revealed a significant ($p < 0.05$) main effect over time for percentage body fat, GH, IGF-1, triceps extensions, leg curls and leg extensions. A main effect for the group was also observed for WHR, GH, IGF-1, biceps curls, triceps extensions, leg curls and leg extensions ($p < 0.05$). A significant interaction effect ($p < 0.05$) was observed for a reduction in WHR in the HI group compared with the LI group. GH showed a significant interaction effect ($p < 0.05$) in the HI group compared with the LI and CG group. Elevated GH was observed in the HI group and LI-5% BFR group compared to the CG group ($p < 0.05$). In addition, elevated GH was found in the HI group compared to the LI group ($p < 0.05$). Elevated IGF-1 was observed in the LI, HI, LI-5% BFR and LI-3% BFR groups compared with the CG group ($p < 0.05$). Moreover, increased IGF-1 was observed in the HI, LI-5% BFR and LI-3% BFR groups compared with the LI group ($p < 0.05$). For muscle strength, a significant interaction effect ($p < 0.05$) was observed for biceps curls, triceps extensions, leg curls and leg extensions. Muscle strength showed improvement in the HI and LI-5% BFR groups compared with the CG group ($p < 0.05$). Furthermore, biceps curls, triceps extensions, leg curls and leg extensions increased in the HI and LI-5% BFR groups when compared with the LI group ($p < 0.05$) (Table 2).

DISCUSSION

The main finding of this study was that using both traditional HI as well as LI-BFR resistance exercise with a 5% reduction in circumference result in increased GH, IGF-1, and muscle strength in middle-aged women. Further, a 5% reduction in the length of the portable cuff was more effective than a 3% reduction of circumference for performance of individual BFR resistance exercises.

Findings reported in previous studies have suggested that LI-BFR provides a unique beneficial training mode that promotes muscle hypertrophy and strength (Madarama *et al.*, 2008; Loenneke *et al.*, 2010; Yasuda *et al.*, 2010). Training at intensities as low as 20% of 1RM with moderate vascular occlusion has been reported to result in increased muscle strength within one month because of neuromuscular adaptation (Loenneke *et al.*, 2012b). In the current study, using a 5% reduction in belt length lead to improvement in muscle strength ($p < 0.05$), GH and IGF-1 levels ($p < 0.05$). This suggests that BFR pressure should be applied on an individual basis when using a portable BFR belt. Previous studies reported numerous cuff pressures, such as beginning training pressures of 140 to 160 mmHg and final training pressures of 160 to 240 mmHg (Takarada *et al.*, 2000b; Madarama *et al.*, 2008; Abe *et al.*, 2010; Yasuda *et al.*, 2010; Loenneke *et al.*, 2011). However, the pressure of the portable cuffs was unknown, which is why the results of the current study are suitable for individual application.

The potential mechanisms by which BFR exercise stimulates growth include metabolic accumulation, which stimulates a subsequent increase in anabolic growth factors (Pierce *et al.*, 2006), fast-twitch fibre recruitment (Takarada *et al.*, 2000b), and increased protein synthesis

through the mammalian target of rapamycin (mTOR) pathway (Fujita *et al.*, 2007). Increased levels of heat shock protein 72 and nitric oxide synthase-1 and decreased expression of myostatin have also been reported (Kawada & Ishii, 2005).

In general, it is understood that only muscle fibres that are activated during exercise grow because of strength training (Kraemer *et al.*, 1996). According to the size principle of motor unit recruitment, small units composed of slow but fatigue-resistant fibres are recruited first; with increasing demands for force or power, increasingly larger units are recruited (Henneman *et al.*, 1965). Therefore, the heavy loads typically used in resistance exercise are required to ensure recruitment of the most motor units that are thus exposed to strength training stimulus. However, numerous studies have suggested that recruitment thresholds for motor units decrease during fatiguing exercise at submaximal loads, in order that type II fibres are increasingly recruited as the point of torque failure draws closer (Vøllestad *et al.*, 1984; Sahlin *et al.*, 1997; Houtman *et al.*, 2002).

Restriction of muscle blood flow has been shown to result in decreased endurance and increased electrical activity of working muscle during performance of low-intensity exercise (Takarada *et al.*, 2000b). Thus, it can be postulated that type II muscle fibres are also recruited during very LI-BFR exercise training. These novel theories may explain why an increase in muscle strength was observed in the current study.

Previous studies have demonstrated that circulating GH stimulates synthesis and secretion of IGF-1 within the muscle acting on itself to promote growth (Takarada *et al.*, 2000a; Reeves *et al.*, 2006; Wilkinson *et al.*, 2006; Widdowson *et al.*, 2009; Abe *et al.*, 2012; Schroeder *et al.*, 2013). According to the findings of the current study, LI-5% BFR resulted in enhancement of hormonal responses. The increase in plasma GH concentration was greater in the HI and LI-5% BFR groups than in the CG and LI groups.

Performance of high-intensity resistance exercise can result in acute changes in GH and IGF-1 plasma levels. Changes in the resting levels of GH and IGF-1 after short-term training have also been reported (Kraemer & Ratamess, 2005). In a previous study, performance of LI-BFR exercise training resulted in extensive, acute increases in levels of plasma GH (Takarada *et al.*, 2004), which led the authors to speculate that GH may play a part in the muscle hypertrophy observed after this type of training. However, the evidence for a role for GH in exercise-induced muscle hypertrophy is limited.

In terms of this study, there were increases in GH and IGF-1 after HI and LI-5% BFR training. Therefore, it can be speculated that stimulated secretion of GH may play a part in the observed effects of LI-BFR exercise training on muscular hypertrophy.

CONCLUSION

Using portable elastic belts to reduce arm and thigh circumferences by 5% was effective in improving GH, IGF-1 and muscle strength in middle-aged women. In particular, LI-5% BFR resulted in similar increases in GH and IGF-1 levels compared with traditional high-intensity resistance exercise. It was demonstrated that using LI-5% BFR resulted in similar improvements in muscle strength compared with traditional high-intensity resistance exercise.

These findings have potential implications for exercise specialists who prescribe exercises to improve muscle strength and hypertrophy. In addition, low intensity of resistance exercise with blood flow restriction with portable cuffs has potential application for rehabilitation training programmes for athletes and the elderly. Finally, improvements in muscle strength with low intensity resistance exercise training could also be advantageous during various sport activities.

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