Blood flow restriction by low compressive force prevents disuse muscular weakness

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Abstract

Repetitive blood flow restriction prevents muscular atrophy and weakness induced by chronic unloading. However, it was unclear which external compressive force for blood flow restriction was optimal to prevent muscular dysfunction. The present study was intended to investigate the effects of repeated muscle blood flow restriction at low pressure on muscular weakness induced by immobilization without weight bearing. Using casts, the left ankles of 11 healthy males were immobilized for 2 weeks. Subjects were instructed to walk using crutches with no weight bearing during the period. Subjects were divided randomly into two groups: a restriction of blood flow (RBF) group (application of external compressive force of 50 mm Hg) and a control (CON) group (no intervention). We measured changes in the muscle strength of the knee extensor–flexor and ankle plantar flexor. The percent changes in knee extensor torque at 60 °/s under eccentric contraction in the RBF group were significantly smaller than in the CON group (−12.5 ± 10.7% and −30.1 ± 10.9%, p < 0.05). The percent changes in knee flexor torque when performing an eccentric contraction at 60 °/s, an isometric contraction, or a concentric contraction at both 60 and 300 °/s in the RBF group were significantly smaller than those in the CON group (p < 0.05). In conclusion, our results show that repetitive restriction of blood flow with 50 mm Hg cuff pressure to the lower extremity reduces muscular weakness induced by chronic unloading.

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1. Introduction

Chronic unloading resulting from space flight, 1–4 bed rest, 5–9 and immobilization 10–13 induces muscular atrophy and reduces muscle strength. It has been demonstrated that resistance training prevents disuse muscle atrophy. 14–16 We showed in an earlier study that repetitive blood flow restriction during a 2-week immobilization and non-weight bearing period prevents muscle weakness and atrophy. 16 The preventative effects were more pronounced than those achieved through isometric training and the results of that study suggest that blood flow restriction, like resistance training, has a preventive effect against muscle atrophy and weakness induced by disuse.

It remains unclear how blood flow restriction prevents muscle dysfunction induced by chronic unloading. The effect of resistance training was ameliorated when it was combined with blood flow restriction. 17–20 Therefore, it is hypothesized that the intramuscular accumulation of phosphate metabolites and hydrogen ions influence the hypertrophic effects of continuous muscle contraction. 21 Data obtained from our earlier study 16 suggest that blood flow restriction with 200 mm Hg cuff pressure prevents disuse muscle atrophy. Based on those results, it is hypothesized that intramuscular metabolic changes induced by ischemia prevent muscle atrophy induced by chronic unloading. 16 Furthermore, the previous study 22 showed that the effects of resistance exercise with blood flow restriction, even the application of lower cuff pressure...
(50 mm Hg), significantly increased muscle strength. Therefore, it is assumed that repetitive blood flow restriction per se (without any exercise) with 50 mm Hg cuff pressure prevents disuse atrophy. The present study was designed to investigate the effects of repeated muscle blood flow restriction at low pressure (50 mm Hg) on muscular weakness induced by immobilization and non-weight bearing.

2. Methods

Subjects were 11 healthy untrained males without a history of injuries to the lower extremities or serious medical complaints. This study was approved by the Human Ethics Committee of Juntendo University. Prior to the experiment, the purpose of the study, contents, experimental protocol, possible risk involved, and management or security offered if an accident occurs were fully explained to these subjects. Their consent in writing was obtained.

We investigated the effect of blood flow restriction by application of external compressive forces of 50 mm Hg on muscular weakness. For each subject, we measured muscle strength and the circumference of the lower extremity at baseline (before intervention). The muscle strength of the lower extremities was measured as the torque of the knee and ankle joints performing an isokinetic contraction. Details of these measurements are described in the Measurement of muscle strength section.

To determine changes in the volume of thigh and leg muscles, we measured the circumference of the thigh region at 10 and 15 cm above the upper border of the patella (thigh 10 and 15) and the maximum circumference of the leg using a tape while the subject was standing (n = 5 in the RBF group, n = 6 in the CON group). The measurements of each region were performed three times and the average values were used for analysis.

For 2 weeks after all measurements, to induce muscular weakness, the left ankle joint of subjects was fixated at the neutral position (ankle joint angle = 0°) using a cast. Subjects were required to use crutches to move without weight bearing. Subjects were then divided randomly into two groups: subjects who received repetitive blood flow restriction with compressive force of 50 mm Hg (RBF group, n = 5, age: 22.8 ± 0.8 year, height: 174.2 ± 5.9 cm, weight: 68.0 ± 3.7 kg) and subjects for whom blood flow was not restricted (control group, CON group, n = 6, age: 22.8 ± 1.2 year, height: 174.8 ± 3.9 cm, weight: 70.3 ± 5.0 kg). During the 2-week period, blood flow to the lower left extremity was restricted by compressing the proximal end of the thigh using a tourniquet (77 mm width, 770 mm length, MIZUHO Co. Ltd., Tokyo) in subjects of the RBF group. A set consisted of 5 min of applied blood flow restriction followed by 3 min of rest (release of compression); each subject underwent five sets twice a day (morning and afternoon) for 14 days. Our preliminary data demonstrated that compared with the control (before compression), the pulse wave velocity (PWV) measured with the second derivative plethysmograph (Fukuda Denshi Co. Ltd., Tokyo) during the application of external compression of 50, 100, 200 and 300 mm Hg was reduced to 90.0 ± 23.1, 80.9 ± 26.4, 64.2 ± 26.3, 2.6 ± 7.3%, respectively (n = 8). At the end of the 2-week period, muscle strength was measured again.

The knee extensor–flexor torque under isokinetic and isometric contraction and the ankle plantar flexor torques under isokinetic contraction were measured quantitatively using an apparatus that determines isokinetic muscle strength (System 3 Dynamometer; Biodex Medical Systems, Shirley, NY).

To determine the knee extensor–flexor torque, subjects were seated; the measured femoral region and upper part of the subject were constrained using 1–3 belts. The subject extended and flexed the knee joints 3 or 5 times at an angular speed of 60, 180, or 300°/s using a concentric contraction (CC60, CC180, and CC300), and at angular speeds of 60 and 180°/s using an eccentric contraction (EC60 and EC180). Isometric contractions were performed with the knee joint flexed at an angle of 60° (IM). The subject continued extending or flexing the knee joints for 5 s with a 10-s break between knee extension and flexion. Following determination of the ankle plantar flexor torque, the subject lay in a supine position and the measurement limbs were fastened with a belt. The subject then extended and flexed the ankle joints three times at CC60, CC120, EC60, and EC120.

All data were expressed as mean ± SD. Differences in muscle strength at each angular speed and contraction pattern, and circumference, before and after the intervention were statistically analyzed using a paired t-test in the RBF and CON groups respectively. In addition, percent changes calculated from the muscle strength and circumference before and after the intervention were tested using an unpaired t-test between the RBF and CON groups. All p values less than 0.05 were inferred as demonstrating a statistically significant difference.

3. Results

Table 1 shows the knee extensor–flexor muscle strength before and after 2 weeks of immobilization without weight bearing. Almost all muscle strength values had decreased significantly in the CON after the protocol, while several muscle strength values in the RBF group showed no significant protection against such changes in muscle strength for both the knee extensor and flexor muscles. The percent changes in knee extensor torque showed significant differences in EC60 and knee flexor torques in EC60, IM, CC60, and CC300. Fig. 1 shows that the percent changes in knee extensor torque at EC60 in the RBF group were significantly smaller than in the CON group (−12.5 ± 10.7% and −30.1 ± 10.9%, p = 0.025). Fig. 2 portrays that the percentage changes in knee flexor torques at EC60, IM, CC60 and CC300 in the RBF group were significantly smaller than those in the CON group: EC60 (−3.5 ± 4.7% and −18.9 ± 9.6%, p = 0.0095),
Knee extensor–flexor torques at baseline and after a 2-week immobilization and non-weight bearing period combined with blood flow restriction (RBF) and no intervention (CON).

<table>
<thead>
<tr>
<th>Group</th>
<th>EC180 (N m)</th>
<th>EC60 (N m)</th>
<th>IM (N m)</th>
<th>CC60 (N m)</th>
<th>CC180 (N m)</th>
<th>CC300 (N m)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pre</td>
<td>255.7 ± 65.7</td>
<td>185.7</td>
<td>125.4</td>
<td>224.2</td>
<td>156.8</td>
<td>172.3</td>
</tr>
<tr>
<td>Post</td>
<td>185.7 ± 26.8</td>
<td>128.6 ± 28.5</td>
<td>138.5</td>
<td>188.5 ± 24.4</td>
<td>193.3 ± 23.9</td>
<td>172.3 ± 24.0</td>
</tr>
</tbody>
</table>
| Data are mean ± SD. *p < 0.05, **p < 0.01, ***p < 0.001.

In the RBF group, the muscle strength value in CC60 had decreased significantly after the protocol: thigh 10 (pre: 122.6 ± 79.9 N m and post: 110.8 ± 79.9 N m, p = 0.004), CC60 (pre: 57.2 ± 16.1 cm and post: 47.2 ± 15.5 cm, p = 0.020). In the RBF group, the muscle strength value in CC60 had decreased significantly after the protocol: EC120 (pre: 122.6 ± 27.3 N m and post: 104.1 ± 28.7 N m, p = 0.032), EC60 (pre: 133.1 ± 27.0 N m and post: 110.8 ± 18.5 N m, p = 0.004), CC60 (pre: 79.9 ± 18.3 N m and post: 59.5 ± 18.1 N m, p = 0.008) and CC120 (pre: 57.2 ± 10.2 N m and post: 44.7 ± 13.7 N m, p = 0.005). In the RBF group, the muscle strength value in CC60 had decreased significantly after the protocol: (pre: 87.2 ± 15.5 N m and post: 68.0 ± 16.5 N m, p = 0.005), but RBF partially protected against such changes in muscle strength. Specifically, the percentage change in ankle plantar flexor torque at EC60 in the RBF group was significantly less than that of the CON group (−0.2 ± 12.1% and −16.1 ± 6.3%, p = 0.020).

All circumferences of the lower extremities had decreased significantly in the CON group after the protocol: thigh 10 (pre: 48.5 ± 2.8 cm and post: 47.2 ± 2.7 cm, p = 0.013), thigh 15 (pre: 52.6 ± 3.5 cm and post: 51.1 ± 2.9 cm, p = 0.012) and leg (pre: 38.5 ± 2.0 and post: 37.5 ± 2.1, p = 0.007).

In the RBF group, the circumferences in thigh 15 and leg had decreased significantly after the protocol: thigh 10 (pre:
48.2 ± 1.0 cm and post: 47.2 ± 1.2 cm, \( p = 0.051 \), thigh 15 (pre: 52.3 ± 1.2 cm and post: 51.5 ± 1.6 cm, \( p = 0.045 \)) and leg (pre: 37.5 ± 1.5 cm and post: 36.8 ± 1.6 cm, \( p = 0.005 \)). In addition, the differences between the RBF and CON groups were not significant for all percent changes of circumference.

4. Discussion

The main finding of this study is that repeated muscle blood flow restriction at low pressure (50 mm Hg) mitigated muscular weakness induced by immobilization and non-weight bearing. This result suggests that mild blood flow restriction, achieved by 50 mm Hg cuff pressure, has a mild preventive effect on muscular atrophy and weakness induced by chronic unloading.

We observed partial reduction of muscle weakness by blood flow restriction with low cuff pressure (50 mm Hg). Comparison with data from our previous report shows that a 50 mm Hg cuff pressure program has a milder effect on muscle weakness induced by chronic unloading than the 200 mm Hg cuff pressure program. Our previous study using the same weight-bearing protocol described that less than a 5% decrease of muscle strength was observed in the 200 mm Hg cuff pressure group, although 10–25% reduction was observed in the control group. In the present study, 50 mm Hg cuff pressure had a preventive effect against the knee flexor muscle strength decrease, in agreement with the results of our previous study, but only a slight effect was observed in the knee extensor muscle strength (Fig. 1). The PWV data suggest that 50 mm Hg cuff pressure has a smaller effect on arterial blood flow than 200 mm Hg cuff pressure. Therefore, the level of blood flow restriction might be an important factor to prevent muscle weakness by repetitive blood flow restriction, especially in the knee extensor muscle.

It remains unclear how blood flow restriction with 50 mm Hg cuff pressure prevents muscle weakness induced by chronic unloading. It has been reported that hemodynamic responses to the blood flow restriction were less observed in a 50 mm Hg cuff pressure compared with 200 mm Hg cuff pressure. Because 50 mm Hg is lower than the arterial blood pressure, but higher than the venous blood pressure, 50 mm Hg cuff pressure might induce venous congestion in lower extremities. This congestion might have some roles to diminish muscle dysfunction. It has been reported that the accumulation of intramuscular phosphate metabolites and hydrogen ions influence the hypertrophic effects of continuous muscle contraction. Consequently, blood flow restriction with 50 mm Hg cuff pressure might prevent muscle weakness through those underlying mechanisms. In addition, the different effects of 50 mm Hg cuff pressure and 200 mm Hg cuff pressure programs are also explained by this hypothesis because the PWV data suggest that 50 mm Hg cuff pressure had less effect on arterial blood flow than 200 mm Hg cuff pressure. Further studies are necessary to clarify the underlying mechanisms of the effects of blood flow restriction.

Results of this study did not clarify whether muscular atrophy was prevented by blood flow restriction. We only measured the respective circumferences of thigh and leg and the data suggest that the circumferences of those muscles were significantly but similarly decreased in both groups. Therefore, it seems that a low cuff pressure program, in contrast to the high pressure program, might not be effective for preventing muscle atrophy induced by chronic unloading. Interestingly, muscle weakness was predominantly prevented in knee flexor muscles, which suggests that a muscle specific effect can occur by blood flow restriction, thereby necessitating direct measurement (CT or MRI) to measure muscle atrophy more precisely. In addition, it has been reported that the maximum force production is directly dependent on muscle cross-sectional area. It is also generally known that neuromuscular coordination plays an intimate role in the expression of muscle strength. These factors might contribute to the inconsistent results between muscle weakness and atrophy in the present study.

5. Conclusion

The repetitive restriction of blood flow with 50 mm Hg cuff pressure to the lower extremity partially prevents muscular weakness induced by chronic unloading. Further investigation is necessary to clarify the underlying mechanisms of the anti-atrophic effects of blood flow restriction.

Practical implications

- Blood flow restriction is a potential measures to prevent muscle atrophy and weakness induced by chronic unloading such as that which occurs as bed rest and cast immobilization.
- Blood flow restriction may also be used as a medical treatment in the rehabilitation of sports injury.
- The positive effect of blood flow restriction on the muscle weakness depends on the external compressive force.

References

17. Abe T, Kearns CF, Sato Y. Muscle size and strength are increased following walk training with restricted venous blood flow from the leg muscle, Kaatsu-walk training. *J Appl Physiol* 2006;100(5):1460–6.