Rapid increase in plasma growth hormone after low-intensity resistance exercise with vascular occlusion

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It has been generally known that heavy resistance exercise has a potent effect in promoting increases in size and strength of skeletal muscle. This effect has been believed to be specific to the intensity of exercise, in such a way that an intensity >65% of 1 repetition maximum (1 RM) is required for gaining a substantial effect (16).

The precise mechanisms underlying such an intensity specificity of resistance exercise remain unclear and may involve combinations of multiple factors, i.e., mechanical stress, neuromotor control, metabolic demands, and endocrine activities. Among these factors, secretions of some anabolic hormones have been clearly shown to depend on the prescription of exercise used and are regarded as important in promoting muscular hypertrophy. Kraemer et al. (11–13) have shown that high-intensity exercises for large muscle groups (~80% 1 RM, 10 repetitions × 6 sets), done with an inrequent reperfusion may produce reactive oxygen species (ROS) and cause considerable tissue damage.

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METHODS

Subjects. Six young male athletes aged 20–22 yr volunteered for the study. Their physical characteristics were height, 173.8 ± 6.7 (SD) cm, and weight, 79.4 ± 8.7 kg. They were previously informed about the experimental procedure to be utilized as well as the purpose of the study, and their informed consent was obtained. The study was approved by the Ethical Committee for Human Experiments, University of Tokyo.

Experimental design and exercise protocol. The subjects performed bilateral knee extension exercise in seated position with an isotonic leg extension machine. The range of joint motion was from 0 to 90° (expressed as 0° at full extension). Throughout the session of exercise lasting for ∼10 min, both sides of their thighs were pressure occluded at the proximal ends by means of specially designed tourniquets (width, 33 mm; length, 800 mm), and the pressure was released immediately after the exercise session. The mean pressure given by the tourniquet was 214 ± 7.7 (SE) mmHg. The exercise session consisted of five sets of exercise at a mean intensity of ∼20% of the weight that could just be lifted once throughout the complete range of movement (1 RM), with a short interset rest period (30 s). In each set of exercise, the subjects repeated the movements until exhaustion. The mean repetition per set was 14.4 ± 1.6. The mean intensity and repetitions for each set are shown in Table 1. Two sessions were made as pre-experimental practice. For the control experiment, the same subjects performed the exercise without occlusion at the same intensity (∼20% 1 RM) and quantity as those for the exercise with occlusion. Here, each subject repeated the movement so as to match completely the intensity and the number of repetitions for each set with those in the exercise with occlusion. The sessions for experimental and control experiments were separated by 1 wk. The subjects were instructed to raise and lower the weight for ∼1 s at an approximately constant velocity. All of the exercise sessions were preceded by a 10-min warm-up on a bicycle ergometer at ∼50% of the maximum heart rate and stretching of the major muscle groups subjected to the exercise.

Blood sampling. Venous blood samples (20 ml for each point of measurement) were obtained from the subjects seated in a slightly reclined position through an indwelling cannula in a superficial arm vein. All of the blood sampling was conducted at the same time of the day to reduce the effects of any diurnal variations on the hormonal concentrations. A resting blood sample was obtained after a 20-min equilibration period. The exercise session started 5 min after the resting blood sample was drawn. After the exercise sessions, the occlusion was released and blood samples were obtained at 0 (immediately after exercise), 15, 45, and 90 min, and at 24 h. All blood samples were processed and stored at −20°C until analysis. The subjects were refrained from ingesting alcohol and caffeine for 24 h and performing any strenuous exercise for 48 h before the experimental exercise session.

Biochemical analyses. Plasma concentrations of La, GH, NE, IL-6, and LP were measured with spectrophotometry for lactate dehydrogenase-coupled enzymatic system (1), radioimmunoassay (2), high-performance liquid chromatography (34), chemiluminescent enzyme immunoassay (26), and spectrofluorimetry for the reaction product of malondialdehyde and thiobarbituric acid (31), respectively. Plasma activity of CPK was measured with spectrophotometry for NADPH formed by hexokinase and D-glucose-6-phosphate-dehydrogenase-coupled enzymic system.

Electromyogram recording. Electromyogram (EMG) signals were recorded from vastus lateralis muscle. Bipolar surface electrodes (5 mm in diameter) were placed over the bellies of muscles with a constant interelectrode distance of 30 mm. The EMG signals were amplified and fed into full-wave rectifier through both low (time constant, 0.03 s) and high (1-kHz)-cut filters, analog-to-digital converted, and stored in a Macintosh 8100/100 computer. The rectified EMG signals during force generation were integrated (EMG) with respect to time and used as an indicator of muscle-fiber recruitment during the exercise movement (3).

RESULTS

Plasma concentrations of La, GH, and NE. Figure 1 shows plasma concentrations of La, GH, and NE measured before and after the exercises. All of the concentrations dramatically increased after the exercise with occlusion, whereas they did not change a great deal after the exercise without occlusion done at the same intensity and volume as that with occlusion. The concentrations appeared to reach a peak immediately after exercise (0 min) for La and NE, and 15 min after exercise for GH, thereafter returning rapidly toward their resting level in an exponential fashion. It should be noted that the concentration of GH increased up to 40 µg/l, a concentration ∼290 times as high as that before exercise. This magnitude of increase in GH concentration was larger by a factor of ∼1.7 than that reported by Kraemer et al. (13) for high-intensity resistance exercise with a short rest period (typical bodybuilding routine), indicating that the exercise with occlusion can provoke strong endocrine responses even at an extremely low intensity. In addition, the time course of changes in concentrations of NE and GH appeared to be closely similar to that of La.

Plasma concentrations of IL-6 and LP and activity of CPK. Figure 2 shows plasma concentrations of IL-6 and LP and plasma activity of CPK measured before and after the exercises. The concentration of IL-6 gradually increased up to ∼1 pg/ml within 60 min after the exercise with occlusion and was maintained at a slightly higher level than in control (exercise without occlusion) even 24 h after exercise. IL-6 has been shown to be one of the early inflammatory cytokines, which are produced in the early stages of exercise-induced muscular damage (19). Indeed, the plasma concentration of IL-6

<table>
<thead>
<tr>
<th>Set 1</th>
<th>Set 2</th>
<th>Set 3</th>
<th>Set 4</th>
<th>Set 5</th>
<th>Mean</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intensity, %1 RM</td>
<td>33.2 ± 1.6</td>
<td>28.2 ± 2.1</td>
<td>20.9 ± 0.7</td>
<td>18.0 ± 1.9</td>
<td>15.5 ± 2.0</td>
</tr>
<tr>
<td>Repetitions</td>
<td>20.0 ± 1.8</td>
<td>12.2 ± 1.7</td>
<td>11.3 ± 1.5</td>
<td>15.2 ± 1.4</td>
<td>13.2 ± 1.1</td>
</tr>
</tbody>
</table>

Table 1. Intensity and repetitions for each set of exercise with occlusion

Values are means ± SE; n = 6 subjects. In control experiment, each subject performed exercise without occlusion at the same intensity and repetitions for each set. 1 RM, 1 repetition maximum.
has been shown to increase gradually after strenuous eccentric exercises and exceed 4 pg/ml within 90 min (9). The present exercise with occlusion gave rise to a similar change in IL-6 concentration, although the concentration measured 90 min after the exercise was less than one-quarter of that reported for eccentric exercise. Because the mechanical stress was expected to be so small in the present exercise, such an inflammatory response was thought to be caused by productions of ROS on reperfusion subsequent to an occluded, hypoxic state. However, both the concentration of LP and the activity of CPK did not show a significant difference from those after the exercise without occlusion.
considerably. However, slight elevation of plasma IL-6 and oxidative stress (LP concentration) did not increase plasma markers for muscular damage (CPK activity) be associated with serious tissue damage, because both for gaining muscular size (13). Such an effect would not magnitude than that reported to occur after the typical in plasma GH concentration was much greater in low intensity, causes enhanced muscular electrical activity and endocrine responses. Notably, the increase of resistance exercise aiming the muscular hypertrophy in both humans and rats (8, 14, 27). Therefore, the present results have shown that circulating GH stimulates synthesis and secretion of IGF-I within the muscle, which then acts on the muscle itself to promote growth (6, 10, 28). Although whether administrations of exogenous GH and IGF-I stimulate the muscular growth in adult humans (4, 5, 24, 30, 32, 33) has been controversial, combinations of GH application and exercise stimuli have been shown to evoke interactive, positive effects in potentiating muscular hypertrophy in both humans and rats (8, 14, 27). Therefore, the present results imply the intramuscular condition to be satisfied during resistance exercise aiming the muscular hypertrophy: acute hypoxia and accumulation of metabolites.

In a practical view, long-term exercise training on the basis of the present methodology would be potentially useful for subjects to whom heavy resistance training cannot be applied. Indeed, we observed in elderly women that low-intensity exercise with vascular occlusion for elbow flexors caused marked muscular hypertrophy and a concomitant increase in strength (unpublished observations). In addition, periodical applications of an occlusion-reperfusion stimulus effectively prevented postoperative immobilization-induced atrophy of lower limb muscles after the reconstruction of the anterior cruciate ligament (25). Although the possibility of serious tissue damage was excluded, further studies are required on fine microdamage in blood vessels and subtle changes in blood flow, both of which may stimulate thrombosis.

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REFERENCES


