KAATSU-WALK TRAINING

Increases serum bone-specific alkaline phosphatase in young men

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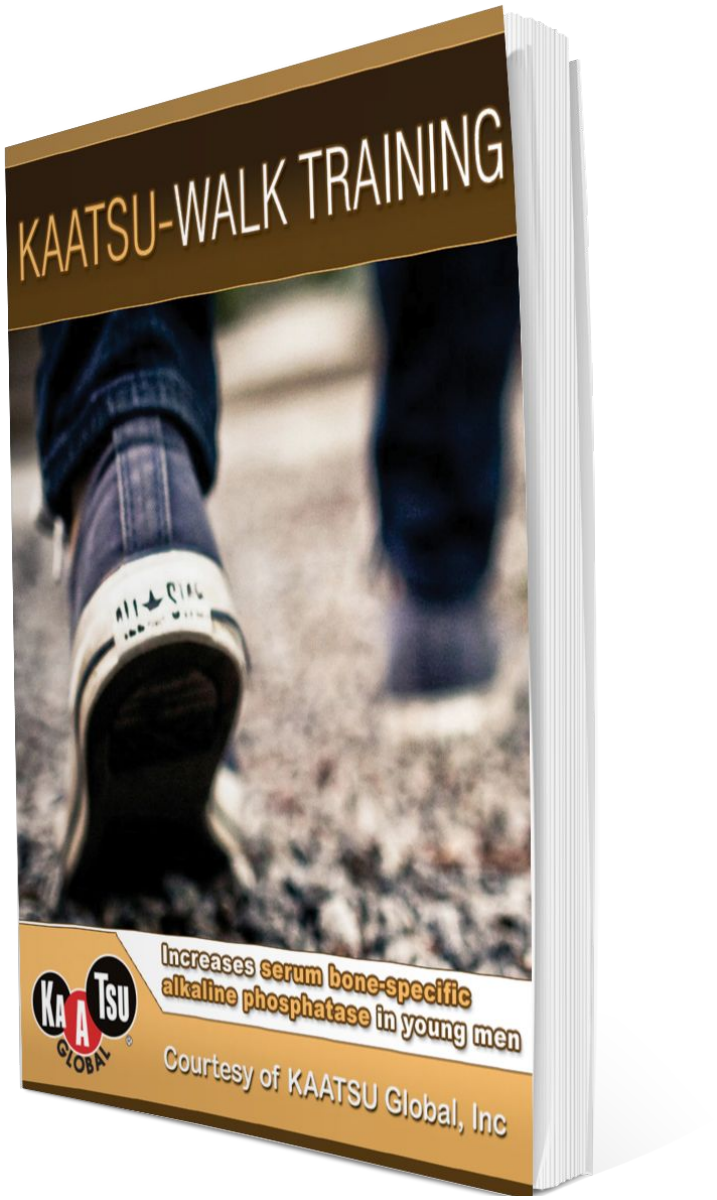

CASE REPORT

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Previous research has shown that high intensity resistance training causes increases in bone density and increases in serum measures of bone turnover like bone-specific alkaline phosphatase (BAP). Medium intensity or low intensity training (like walking) does not result in these changes. However, low intensity training with blood flow restriction (KAATSU) has shown promise in bone and muscle rehabilitation settings. We hypothesized that there would be increases in serum BAP following low intensity KAATSU walk training. Healthy men walked on a treadmill twice per day (at least 4 hours between sessions) for 3 weeks with (KAATSU; n=9) or without (Control; n=9) blood flow occlusion pressure belts on their thighs. After three weeks of training, the KAATSU group experienced significant increases in MRI-measured muscle CSA ($P<0.01$), 1-RM muscle strength ($P<0.01$), and serum BAP levels ($P<0.05$). Percent change in BAP was 10.8% for the KAATSU-walk and 0.3% for the Control-walk. There was no significant change in serum IGF-1 for either group. We conclude that 3 weeks KAATSU walk training increases BAP, a serum marker of bone turnover.

Key words: bone metabolic marker, KAATSU-walk training, muscle hypertrophy

INTRODUCTION

Osteoblasts are a type of cell responsible for deposition of the protein matrix of bone. The protein matrix of bone is where calcium salts (particularly phosphates) are deposited. Osteoblasts are rich in alkaline phosphatase [Watts, 1999]. Bone-specific alkaline phosphatase (BAP) is a tetrameric glycoprotein found on the membrane of the osteoblast cell. Although the function of BAP is not fully understood, BAP levels are considered to reflect osteoblastic activity and can therefore be used as a marker of bone formation [Gundberg, 2000].

Because high impact and/or high-intensity physical activity such as jumping or resistive exercise has beneficial effects on bone mass and strength [Bemben et al., 2004; Creighton et al., 2001; Taaffe et al., 1997], BAP activity may be stimulated by high intensity physical activity. Previous published studies reported that serum BAP level increased after a single bout of high intensity physical exercise [Rudberg et al., 2000; Wallace et al., 2000]. Also, following 4 months of high intensity (75% of 1-RM) resistance training, resting serum BAP is increased [Tajima et al., 2000]. However, there is no significant change in serum BAP after a single bout of moderate intensity (50-75% of 10 repetition maximum) resistance exercise [Whipple et al., 2004]. Finally, low intensity exercise like walking also results in no significant change in bone mineral density [Welsh et al., 1997]. The differing results between those studies may be explained, in part, by the intensity of resistance exercise.

Low-intensity (20% of 1-RM) resistance training combined with restriction of muscular venous blood flow (KAATSU) via a special cuff can increase skeletal muscle volume and strength in men and women [Abe et al., 2005; Takarada et al., 2000a]. Also, in a study of patients who underwent reconstruction of the anterior cruciate ligament, KAATSU cuff use alone decreased the CSA of the thigh muscle extensors and flexors by only ~9% each, while CSA of the control groups' (no KAATSU) thigh muscle extensors and flexors decreased by 21 and 11%, respectively [Takarada et al., 2000b]. Interestingly, several clinical studies reported that femoral head avascular necrosis or bone atrophy was improved following KAATSU resistance training [Inoue et al., 2002; Odagiri 2004]. Therefore, we hypothesized that an increase in resting serum BAP level could occur following KAATSU resistance training. Thus the purpose of this case study was to investigate the chronic effect of 3 weeks of twice-daily walk training combined with KAATSU on resting serum BAP level in young men.

METHODS

Subjects

Eighteen healthy young men [mean (SD) age, 21.3 (2.8) yrs; height, 174 (5) cm; body mass, 64.8 (5.3) kg] volunteered to participate in the study . All subjects led active lives, with 8 of 18 participating in regular aerobic exercise. However, none of the

subjects had participated in a regular resistance exercise program for at least one year prior to the start of the study. The subjects were randomly divided into two training groups: a walk-training with restricted venous blood flow from the leg muscles (KAATSU-walk, n=9) group and a walk-training without restricted leg muscle blood flow (Control-walk, n=9) group. All subjects were informed of the procedures, risks, and benefits, and signed an informed consent document before participation. The Tokyo Metropolitan University Ethics Committee for Human Experiments approved the study.

Training protocol and blood sampling

The subjects in both KAATSU-walk and Control-walk groups participated in three weeks of supervised walk-training. Training was conducted twice per day (morning and afternoon sessions, with at least 4 hours between sessions), six days per week for 3 weeks. Following a warm up, the subjects performed walking (50 m/min for five 2 min bouts, with 1 min of rest between bouts) on a motor-driven treadmill. Subjects in the KAATSU-walk group wore a pressure belt (Kaatsu-Master, Tokyo, Japan) on each leg during training. On the first day of the training, the belt pressure was 160 mmHg, and the pressure was increased 10 mmHg each day until a final cuff pressure of 230 mmHg was reached. The restriction pressure of 160-230 mmHg was selected for the occlusive stimulus as this pressure has been suggested to restrict venous blood flow and cause pooling of blood in capacitance vessels distal to the belt, and ultimately restricts arterial blood flow [Takarada et al. 2000a]. The estimated coefficient of variation (CV) of this pressure measurement was 2.2%. The restriction of muscular blood flow was maintained for the entire exercise session, including the 1 min rest periods. Subject leg blood flow was restricted for about 15 min at each exercise session. The belt pressure was released immediately upon completion of the session. The Control-walk group performed the same exercise at the same treadmill speed but without the pressure belt.

One-RM strength measurements

One week prior to training, the subjects were familiarized with strength testing equipment. Proper lifting technique was demonstrated for the leg press and leg curl exercises and all subjects performed practice lifts prior to attempting maximal effort lifts. Maximum dynamic strength (1-RM) was assessed prior to (baseline) and 3 days after the final training (post-testing) for each exercise. After warming up, the load was set at 80% of the predicted 1-RM. Following each successful lift the load was increased by ~5% until the subject failed to lift the load through the entire range of motion. A test was considered valid only when the subject used proper form and completed the entire lift in a controlled manner without assistance. On average, five trials were required to complete a 1-RM test. Approximately 2-3 min of rest was allotted between each attempt to ensure recovery.

MRI-measured muscle CSA and volume

Magnetic resonance imaging (MRI) images were captured using a General Electric Signa 1.5 Tesla scanner (Milwaukee, Wisconsin, USA). A T1-weighted, spin-echo, axial plane sequence was performed with a 1500-millisecond repetition time and a 17-millisecond echo time. Subjects rested quietly in the magnet bore in a supine position with their legs extended. Contiguous transverse images with 1.0-cm slice thickness (0 cm interslice gap) were obtained at mid-point of the thigh for each subject. The MRI scan was segmented into four components (skeletal muscle, subcutaneous adipose tissue, bone, and residual tissue) by a highly trained analyst, and then traced. For each slice, the skeletal muscle tissue CSA was digitized and calculated using NIH image software. The estimated CV of this measurement was 2.1% [Abe et al. 2003]. The average value of the right and left sides of the body was used. This measurement was completed prior to (baseline) and 3 days after the final training (post-testing).

Hormonal analyses

Resting venous blood was drawn from each subject at baseline (pre-testing) and 3 days after the final training (post-testing). All blood samples were obtained at the same time of day (9:00-10:00 AM) following an overnight fast (12-13 hours). The subjects were counseled to refrain from ingesting alcohol and caffeine for 24 hours prior to blood collection and not to perform any strenuous exercise. Serum BAP activity and IGF-1 were measured at S.R.L. Inc. (Tokyo) by the use of commercially available enzyme immunoassay (OSTEOLINKS-BAP, Sumitomo Seiyaku Biomedical Co., Osaka) and radioimmunoassay (Daiichi Radioisotope Laboratory, Chiba).

Statistical Analyses

Results are expressed as means and standard deviations (SD) for all variables. Statistical analyses were performed by a two-way analysis of variance (ANOVA) with repeated measures [Group (Kaatsu-walk and Control-walk) x Time (pre- and post-testing)]. Post-hoc testing was performed by a Fisher's least significant differences test. Baseline differences between two groups and percentage changes between baseline and post-testing were evaluated with a one-way ANOVA. The relationship between serum BAP activity and circulating IGF-1

Table 1. Percent changes in strength, muscle CSA and blood parameters following 3 weeks of walk training combined with (KAATSU) and without (Control) restriction of leg muscle blood flow.

	Leg press 1-RM	Thigh muscle CSA	Bone-specific ALP	IGF-1
Control	1.3 ± 3.8	-0.6 ± 2.9	0.3 ± 8.9	-0.2 ± 14.7
KAATSU	7.5 ± 6.2 *	5.8 ± 3.8 †	10.8 ± 0.6 *	3.5 ± 15.0

CSA, cross-sectional area; ALP, alkaline phosphatase; IGF-1, insulin-like growth factor-1
*P<0.05, †P<0.01 Control vs. KAATSU

concentrations was assessed using Pearson's product-moment correlation coefficient. Statistical significance was set at $P < 0.05$.

RESULTS

There were no statistically significant differences in 1-RM strength, mid-thigh muscle CSA and blood parameters between KAATSU-walk and Control-walk groups at baseline. Significant group x time interactions were observed for mid-thigh muscle CSA ($P = 0.001$) and leg press 1-RM strength ($P = 0.029$). Post-hoc analyses indicated that KAATSU-walk experienced significant increases ($P<0.01$) in muscle CSA and strength after training. Percent changes in 1-RM strength and muscle CSA were 7.5% (baseline 95 ± 16 kg, post-testing 102 ± 15 kg) and 5.8% (baseline 123.0 ± 17.6 cm^2, post-testing 129.7 ± 15.9 cm^2), respectively in the KAATSU-walk and 1.3% (baseline 107 ± 20 kg, post-testing 108 ± 18 kg) and -0.6% (baseline 127.9 ± 19.2 cm^2, post-testing 127.1 ± 19.5 cm^2), respectively in the Control-walk (Table 1). A significant group x time interaction was observed for BAP ($P = 0.049$). Post hoc analyses indicated that KAATSU-walk experienced greater increases in BAP compared with Control-walk after the training ($P<0.05$, Figure 1). Percent change in BAP was 10.8% for the KAATSU-walk and 0.3% for the Control-walk (Table 1). There was no change ($P>0.05$) in IGF-1 between pre- and post-testing in both groups (KAATSU-walk: baseline 292 ± 89 ng/ml, post-testing 297 ± 72 ng/ml; Control-walk: baseline 288 ± 73 ng/ml, post-testing 289 ± 80 ng/ml). Although there was no significant correlation between percent changes in BAP and IGF-1 ($r = 0.44$, $P = 0.078$), a clear trend was noted.

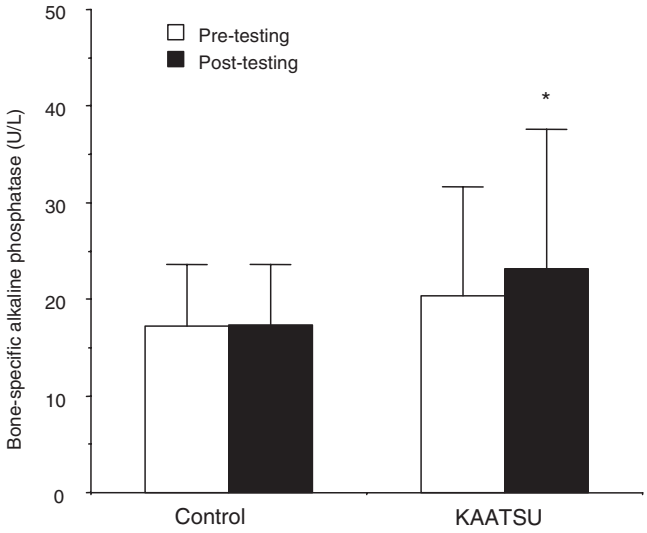

Figure 1. Bone-specific alkaline phosphatase responses following 3 weeks of walk training combined with (KAATSU) and without (Control) restriction of leg muscle blood flow. *P<0.05 pre- vs. post-testing

DISCUSSION

Previous cross-sectional [Creighton et al., 2001; Matsumoto et al., 1997] and longitudinal [Kerr et al., 1996; Walker et al., 2000] studies have reported that bone remodeling is influenced by physical activity. High-intensity resistance training has been shown to increase bone metabolic makers such as bone-specific alkaline phosphatase (BAP) and increase bone mass [Tajima et al., 2000]. BAP has a role in the mineralization of newly formed bone, although the function is not fully understood [Watts, 1999]. Previous results suggest that the it is the high mechanical stress to the bone as a result of high intensity training that causes the changes in bone density, size and metabolic makers. Low intensity exercise training, on the other hand, has previously not been shown to increase bone mass or remodeling [Cavanaugh and Cann, 1988; Kerr et al., 1996; Shinaki et al., 1996]. It is assumed that the low intensity loads do not create enough strain to induce changes in bone mass or remodeling.

The major finding of the present study was that 3 weeks of twice-daily KAATSU-walk training

increased serum BAP in young men. Our results are similar to previous studies that detected an increase in serum BAP activity within the first month after the beginning of high intensity resistance training [Fujimura et al., 1997]. Thus, the increases in circulating BAP probably indicate increased bone remodeling secondary to low-intensity KAATSU exercise training. This means that, in some cases, the high mechanical stress on the bone via high intensity training may not be the only necessary signal to begin bone remodeling. We are therefore the first to show certain types of low intensity training (walking with a special cuff) can increase serum markers of bone turnover.

A single bout of low-intensity KAATSU resistance exercise stimulates growth hormone (GH) secretion [Takarada et al., 2000c]. We have also shown that serum GH concentration increases after acute KAATSU-walk exercise [Abe et al. 2005b], and that serum IGF-1 increases after low intensity KAATSU resistance training [Abe et al., 2005a]. It is believed that GH and IGF-1 stimulate bone turnover and result in long term augmentation of bone mass and strength. Although the correlations did not reach statistical significance (P=0.078), the percent change in BAP following KAATSU-walk training tended to follow the changes in serum IGF-1. Perhaps the non-significant increase (trend) we saw in IGF-1 response to KAATSU-walk training was enough to then elicit a BAP response. It may also be conceivable that BAP increased in response to some other as yet undiscovered signal induced by KAATSU-walk training. For instance, extracellular fluid flow has been implicated in formation of bone in a rat model [Chambers et al., 1993; Hillam et al., 1995]. It is likely that there are extracellular fluid shifts during KAATSU exercise training because of the large external pressures used in the cuff. In fact, estimated thigh muscle size and hematocrit are increased after a single bout of KAATSU-walk, but not Control-walk (data not shown).

In conclusion, resting levels of serum BAP (a bone formation marker) increased following KAATSU-walk training. Therefore low-intensity exercise combined with KAATSU can influence bone metabolic markers.

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References

Abe T, Kearns CF, Fukunaga T (2003) Sex differences in whole body skeletal muscle mass measured by magnetic resonance imaging and its distribution in young Japanese adults. Br J Sports Med **37**: 436-440.

Abe T, Yasuda T, Midorikawa T, Sato Y, Kearns CF, Inoue K, Koizumi K, Ishii N (2005a) Skeletal muscle size and circulating IGF-1 are increased after two weeks of twice daily KAATSU resistance training. Int J KAATSU Training Res **1**: 6-12.

Abe T, Sato Y, Kearns CF, Yoshitomi A (2005b) Acute hormonal responses to restriction of leg muscle blood flow during walking (Abstract). Med Sci Sports Exerc **37**: S108.

Ashizawa N, Ouchi G, Fujimura R, Yoshida Y, Tokuyama K, Suzuki M (1998) Effects of a single bout of resistance exercise on calcium and bone metabolism in untrained young males. Calcif Tissue Int **62**: 104-108.

Bemben DA, Buchanan TD, Bemben MG, Kenhans AW (2004) Influence of type of mechanical loading, menstrual status, and training season on bone density in young women athletes. J Strength Cond Res **18**: 220-226.

Cavanaugh DJ, Cann CE (1988) Brisk walking does not stop bone loss in postmenopausal women. Bone **9**: 201-204.

Chambers TJ, Evans M, Gardner TN, Turner SA, Chow JW (1993) Induction of bone formation in rat trail vertebrae by mechanical loading. Bone Miner **20**: 167-178.

Creighton DL, Morgan AL, Boardley D, Brolinson PG (2001) Weight-bearing exercise and markers of bone turnover in female athletes. J Appl Physiol **90**: 565-570.

Fujimura R, Ashizawa N, Watanabe M, Mukai N, Amagai H, Fukubayashi T, Hayashi K, Tokuyama K, Suzuki M (1997) Effect of resistance exercise training on bone formation and resorption in young male subjects assessed by biomarkers of bone metabolism. J Bone Miner Res **12**: 656-662.

Gundberg CM (2000) Biochemical markers of bone formation. Clin Lab Med **20**: 489-501.

Hillam RA, Skerry TM (1995) Inhibition of bone resorption and stimulation of formation by mechanical loading of the modeling rat ulna in vivo. J Bone Miner Res **10**: 683-689.

Inoue K, Sato Y, Ishii N (2002) Application to rehabilitation of pressure muscle training method. J Jpn So Clin Sports Med **10**: 395-403.

Kerr D, Morton A, Dick I, Prince R (1996) Exercise effects on bone mass in postmenopausal women are site-specific and load-dependent. J Bone Miner Res **11**: 218-224.

Matsumoto T, Nakagawa S, Nishida S, Hirota R (1997) Bone density and bone metabolic markers in active collegiate athletes: findings in long-distance runners, judoists, and swimmers. Int J Sports Med **18**: 408-412.

Odagiri K (2004) Effectiveness of KAATSU rehabilitation in several patents. J Clin Sports Med **21**: 253-257.

Sinaki M, Wahner HW, Bergstralh EJ, Hodgson SF, Offord KP, Squires RW, Swee RG, Kao PC (1996) Three-year controlled, randomized trial of the effect of dose-specified loading and strengthening exercises on bone mineral density of spine and femur in nonathletic, physically active women. Bone **19**: 233-244.

Taaffe DR, Robinson TL, Snow CM, Marcus R (1997) High-impact exercise promotes bone gain in well-trained female athletes. J Bone Miner Res **12**: 255-260.

Tajima O, Ashizawa N, Ishii T, Amagai H, Mashimo T, Liu LJ, Saitoh S, Tokuyama K, Suzuki M (2000) Interaction of the effects between vitamin D receptor polymorphism and exercise training on bone metabolism. J Appl Physiol **88**: 1271-1276.

Takarada Y, Takazawa H, Sato Y, Takebayashi S, Tanaka Y, Ishii N (2000a) Effects of resistance exercise combined with moderate vascular occlusion on muscular function in humans. J Appl Physiol **88**: 2097-

2106.
Takarada Y, Takazawa H, Ishii N (2000b) Applications of vascular occlusion diminish disuse atrophy of knee extensor muscles. Med Sci Sports Exerc **32**: 2035-2039.
Takarada Y, Nakamura Y, Aruga S, Onda T, Miyazaki S, Ishii N (2000c) Rapid increase in plasma growth hormone after low-intensity resistance exercise with vascular occlusion. J Appl Physiol **88**: 61-65.
Watts NB (1999) Clinical utility of biochemical markers of bone remodeling. Clin Chem **45**:1359-1368.
Whipple TJ, Le BH, Demers LM, Chinchilli VM, Petit MA, Sharkey N, Williams NI (2004) Acute effects of moderate intensity resistance exercise on bone cell activity. Int J Sports Med **25**: 496-501.

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