The Utility of a Small Animal Grip Strength Measurement Device as a Model for Exercise-Induced Muscle damage

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Introduction

Exercise-induced muscle damage (EIMD) is characterized by structural damage to muscle tissue resulting from high-intensity exercise or unaccustomed physical activities. This phenomenon induces significant alterations in the ultrastructure of muscles and leads to elevated levels of various biochemical markers. Specifically, increased levels of creatine kinase (CK) and myoglobin concentrations are characteristically observed. Additionally, inflammatory cell infiltration occurs at the site of damage, and necrosis is observed in some muscle fibers.

Muscle damage induced by exercise is particularly pronounced during eccentric contractions. This contraction modality is known to cause more severe muscle damage compared to concentric contractions. While delayed onset muscle soreness (DOMS) occurs under similar exercise conditions, the precise causal relationship between DOMS and EIMD remains an active area of research.

The physiological response to muscle damage includes the release of inflammatory cytokines such as TNF-α and IL-1β. Furthermore, oxidative stress is closely associated with muscle damage. During exercise, oxygen demand increases, leading to elevated production of reactive oxygen species (ROS). When the production of ROS exceeds the processing capacity of the body's antioxidant defense system, oxidative stress occurs.

In animal studies, various muscle damage models have been established, including treadmill running, electrical stimulation, and injection of toxins or drugs. However, further verification is needed to determine whether these models accurately reflect exercise-induced muscle damage in humans. Therefore, the purpose of this study is to evaluate the utility of a small animal grip strength measurement device as a model for exercise-induced muscle damage.

Methods

Thirty-four male C57BL/6NcrSlc mice were housed under controlled conditions with a 12-hour light/dark cycle. The mice were divided into four groups based on post-exercise time points: three experimental groups scheduled for dissection at 48 hours, 96 hours, and 168 hours post-exercise, and a control group that received no exercise intervention.

The exercise loading protocol used a novel method using a forelimb grip strength device. Specifically, the protocol involved pulling the mouse's tail 50 times at a 60Hz rhythm, with grip strength data recorded using Toriemon USB software.

Plasma biochemical parameters measured included AST, ALT, CK, UA, BUN, CRE, LDH, and ALD. RT-qPCR analysis was performed to examine the expression of inflammation-related genes, including TNF-α, IL-1β, and IL-6. Additionally, oxidative stress was evaluated using three distinct measurements: BAP test (biological antioxidant potential), d-ROMs test (oxidative stress), and OXY-adsorbent test (total antioxidant capacity).

For data analysis, one-way analysis of variance (ANOVA) was employed as the primary statistical method, with Tukey's post-hoc test utilized for detailed examination of inter-group differences. Statistical significance was defined as $P<0.05$, while $P<0.1$ was considered to indicate a trend toward significance.

Results

Grip strength was evaluated at three time points: 48 hours, 96 hours, and 168 hours post-exercise. Among muscle damage markers,

aldolase showed a significant increase at 48 hours post-exercise ($P<0.01$), while the values of CK, LDH, AST elevated in the group that was dissected 48 hours after exercise, but no significant differences were observed.

Gene expression analysis in the triceps brachii revealed no significant changes in inflammation-related genes, and IL-10 was not detected. Regarding oxidative stress-related factors, NF-kB showed a significance trend ($P<0.1$), while Keap1 and Nrf-2 remained unchanged.

In plasma oxidative stress parameters, BAP demonstrated a significant decrease at 168 hours, showing particularly low values compared to both the control group ($P<0.01$) and the 96-hour group ($P<0.05$). Additionally, d-ROMs exhibited a significant trend at 96 hours ($P<0.1$), whereas OXY showed no significant changes.

Discussion

In the muscle damage markers, aldolase (ALD) showed elevation at 48 and 96 hours post-exercise, while no significant changes were observed in CK or LDH levels. The earlier release of ALD into the bloodstream may be attributed to its smaller molecular weight (40 kDa) compared to CK (80-82 kDa).

Regarding inflammatory markers, the triceps brachii showed no significant changes in the expression of TNF-α, IL-1β, and IL-6. This suggests that resistance exercise, unlike endurance exercise, is associated with lower inflammatory mediator activity.

Regarding oxidative stress, plasma d-ROMs and NF-kB exhibited significant trends. However, no significant changes were observed in the expression of Nrf2 and KEAP1. Given that d-ROMs observed a trend toward significance at 96 h, oxidative stress reached its highest level, and as a result of the antioxidant response, antioxidant substances were depleted in the 168 h group, leading to a decrease in BAP.

The study concludes that this grip strength exercise model may induce exercise-induced muscle damage through oxidative stress pathways. Furthermore, it suggests that adjusting exercise intensity could potentially elicit antioxidant stress indicators (BAP, OXY).

Conclusion

Plasma samples collected from mice after exercise showed an increase in aldolase (ALD) levels and a significant trend toward elevated oxidative stress.

This grip strength exercise model may induce exercise-induced muscle damage by oxidative stress.