The role of calcium in skeletal muscle cell damage induced by exercise or anoxia

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This PhD dissertation was accepted by the Faculty of Health Sciences, University of Aarhus, and defended on the 29th of June 2007.

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Dan Med Bull 2007;54:245

ABSTRACT

The aims of the PhD studies (Institute of Physiology and Biophysics and Institute of Sport Science, University of Aarhus) were to elucidate the role of calcium overload in eliciting membrane damage in both isolated rat muscles and in human skeletal muscle.

Isolated rat EDL muscles were exposed to electrical stimulation and/or anoxia. Calcium influx, accumulation of calcium, and release of enzymes were measured. The effect of extracellular concentration of calcium on membrane damage was investigated as well. Contraction in fast-twitch muscles was blocked (pharmacologically) to separate the effects of mechanical stress from those of calcium overload. Finally, the role of reduced energy levels of the muscle cells in the development of membrane damage was investigated.

In human studies we investigated the effects of long distance running and eccentric exercise on muscle calcium content, strength loss, enzyme release, soreness and T2 relaxation times (by MRI technique). Finally, calcium content was measured in ischemic muscle samples from amputated human legs.

Excitation of isolated skeletal muscles induces an immediate increase in calcium influx and accumulation, which is followed by a delayed release of intracellular enzymes. The degree of damage depends on the extracellular concentration of calcium, the duration of stimulation and the degree of hypoxia. Passive stretch alone does not cause considerably membrane damage. In contrast, the level of ATP in the cells seems to be of importance to whether or not the increased calcium influx leads to membrane damage.

Long distance running leads to accumulation of calcium, strength loss and loss of intracellular enzymes in humans. Eccentric exercise leads to strength loss, soreness and loss of intracellular enzymes. Moreover the T2 relaxation time increases in the eccentric working muscles. Muscle damage seems to be more pronounced in women than in men. Finally, ischemic muscles from amputated legs seem to have an increased content of calcium.

Several pathological conditions are known to involve loss of cellular calcium homeostasis eventually leading to muscle cell damage. Among these are sepsis, rhabdomyolysis, muscular dystrophy, atherosclerosis, and cardiac and respiratory failure. In several of these conditions muscles are exposed to ischemia and many of these patients experience muscle soreness and loss of strength.