RELEVANCE BETWEEN EXERCISE-INDUCED SKELETAL MUSCLE INJURY AND SKELETAL MUSCLE CELL APOPTOSIS

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ABSTRACT

It is essential to understand the relation between bone cell apoptosis and exercise-induced skeletal muscle injury in order to achieve an effective prevention treatment for exercise-induced bone crisis injury. Therefore, this paper reveals the clinical datas on retrospective analysis of skeletal muscle cell apoptosis of 1000 patients with micro exercise-induced skeletal muscle injury. The results obtained demonstrated a close correlation between physiological environment, micro exercise-induced skeletal muscle injury due to sports and skeletal muscle cell apoptosis. Hence, study on relevance between micro exercise-induced skeletal muscle injury and skeletal muscle cell apoptosis is of important significance for prevention and treatment of exercise-induced injury.

***Keywords**: Micro Exercise-Induced Skeletal Muscle Injury, Skeletal Muscle Cell Apoptosis, Relevance.*

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Introduction

Skeletal muscle belongs to striated muscle, which is mainly distributed in the extremities (see Figure 1). As the power organ of body movement system, it performs contractile activity under the control of nervous system so that the body has a variety of sports. Changes in skeletal muscle nuclei directly affect morphology and physiological function of skeletal muscle[1-3].

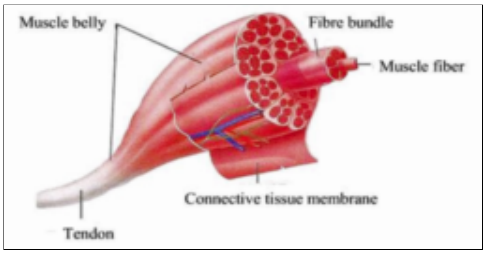

Figure 1: Skeletal muscle (Picture source: [2]Yu Xinkai, Chao Weiwei, Zuo Qun. Research Progress in Ultrastructural Changes of Exercise-Induced Skeletal Muscle Injury. Progress of Anatomical Sciences, 2013, 03: 298-302).

There are approximately 600 skeletal muscles with different shapes in human body (see Figure 2). Growing age, long-term physical exercise and various muscle-related activities causes unpredictable degrees of impact on skeletal muscle structures and functions[4].

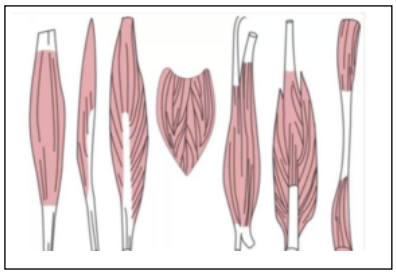

Figure 2: Different forms of human skeletal muscle ([10] Li Chen, Lv Chenxi, Wu Lei. Protective Effect of Taishan Ganoderma Lucidum on Micro Skeletal Muscle Injury after Repetitive Movement. Journal of Taishan Medical College, 2014, 08: 711-716).

Related studies have shown that, prolong excessive muscle exercise might lead to skeletal

muscle injuries. Nevertheless, pragmatic endurance training would improve skeletal muscle structure and function in various degree[5-6].

Exercise-induced skeletal muscle injury is the most common cause of injury that can be categorized into acute and chronic type of injuries[7]. Micro exercise-induced skeletal muscle injury is different from general muscle damage and inflammation of human body, which refers to a normal physiological response after intensive load of muscle. Micro exercise-induced skeletal muscle injury can occur during aggressive training which is mainly expressed by muscle pain, increased muscle volume, reduced angle of motion, decreased muscle strength and so on[8-10].

The most frequent feature is delayed muscular soreness which generally occurs within 12-24 hours after exercise and lasts for about seven days. Delayed muscular soreness can cause reduced muscle operational capability and contractility. Athletes will clearly feel this change in living and training process, thereby generating intense discomfort. But this injury is a reversible, repairable damage. Athlete behavior restriction is temporary. After a period of physical adjustment and recovery, patients' bone function will be restored. Also, appropriate adjustment can be made according to patients' condition. In recent years, lots of research been done on exercise-induced skeletal muscle injury that impart different conclusions. Cell apoptosis is a morphological concept of programmed cell death, an initiative dying process that maintains homeostasis after the cells received signals or subjects to stimulation factor[11].

In this paper, in-depth research on correlation between micro exercise-induced skeletal muscle injury and skeletal muscle cell apoptosis was conducted with the hope of providing better prevention technique for exercise-induced skeletal muscle injury.

Materials and Methods

General Information

For this study, 1000 athletes with micro skeletal muscle injury during sports or training between March 2012-March 2016 were selected. Among the athletes,524 were male and 476 were female; aged between 14 to 23 years, with the average age of 17.8 ± 2.1 years.

Analysis Method

Conduct retrospective study based on patients' clinical data with the focus on relevance between the extent of patient's skeletal muscle injury, pain, pain time and skeletal muscle cell apoptosis. Specific methods include morphological observation utilizing electron microscope, terminal deoxynucleotidyl transferase dUTP nick end labeling (TUNEL), gel electrophoresis for DNA fragment detection and flow cytometry.

In addition, investigation by clinical researchers on domestic and foreign clinical datas for the past 10 yearsconcluded the relevance between skeletal muscle cell apoptosis and skeletal muscle tissue injury.

Discussion

First of all, a significant correlation between physiological environment of micro exercise-induced skeletal muscle injury and cell apoptosis was noted, which can be explained based on three aspects

• It is known that the disorder within cytoplasm may cause apoptosis. Under physiological conditions, intracytoplasmic calcium concentration is about 10-7 mol/L while extracellular calcium concentration is around 10-3 mol/L. In normal circumstance, cells conserve such huge concentration gradient through a series of transport mechanisms so that intracellular low calcium could be maintained.

When faced with appropriate stimulation, cells could instantly improve intracellular calcium ion concentration, partially or on the whole through multiple ways. Substantial increase in intracytoplasmic calcium concentration can trigger a series of physiological & biochemical reactions. For instance, by activation of proteases such as calpain and nuclear scaffold protease, death-associated protein kinase, transglutaminase apoptosis related genes and ribozyme as well as cell apoptosis could be mediated.

Apoptosis may be caused by DNA breakage due to activation of endonuclease after the calcium transport system, convey calcium ions into nucleus. Therefore, increased calcium ion concentration is necessary for most cell apoptosis. In the process of apoptosis within mammal cells, activation of aspartate-specific cysteine protease family plays a key role. Cysteine protease is synthesized and stored in normal cells in inactive precursor form.

Subsequently, apoptotic signal may then lead to cell damage and cell apoptosis.

• The second point highlights on the increased calcium concentration in mitochondria (Figure 3) that may cause cell apoptosis.

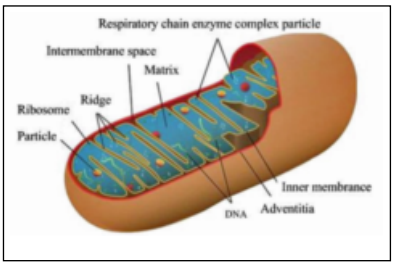

Figure 3: Mitochondria (Picture source: [17] Qu Honglin, Wang Yong. Stem Cells and Exercise-Induced Skeletal Muscle Cell Apoptosis. Chinese Journal of Tissue Engineering Research, 2010, 06: 1088-1091).

Mitochondria play a decisive role in cell apoptosis or necrosis. Under normal physiological condition, combination of mitochondria and calcium ions would provide adequate strength for the muscle's activities. Mitochondrial calcium ion transport is influenced by voltage-dependent anion channel (VDAC) on the outer mitochondrial membrane. VDAC is a 31 kDa protein that presents in mitochondrial outer membrane can form hydrophilic voltage-gated channel on the membrane. Through interaction with calcium ions, energy, glutamic acid NADH and different proteins, it transports anions, cations, ATP and other metabolites in and out of mitochondria. This regulates mitochondrial outer membrane permeability, controls mitochondrial function and thus plays an important role in maintaining mitochondrial and cell activity[12, 13].

It regulates mitochondria-mediated cell death in two main ways. First, it acts as major component of mitochondrial permeability transition pore to regulate cell apoptosis. Besides that, it also interacts with Bcl-2 family protein to regulate cell apoptosis. This leads to anti-apoptotic factor that promotes VDAC closure while pro-apoptotic factor favours the opening of VDAC channels. Consequently, exercise increases mitochondrial calcium transport capacity in skeletal muscle cells and mitochondrial calcium concentration, causes change in VDAC, which thereafter affects mitochondrial membrane potential and results in cell apoptosis.

• The third characteristics are the reduction of calcium concentration in endoplasmic reticulum that may instigate cell apoptosis. Endoplasmic reticulum is the main place for intracellular protein synthesis, post-translational modification, folding, as well as the location for calcium reservation and calcium signal transduction. It is believed that intracellular calcium homeostasis is conserved through endoplasmic reticulum. Accordingly after exercise, the transport capacity of inner-sarcoplasmic reticulum calcium ion begins to decrease/ Meanwhile, both the capacity of calcium release channel and calcium pump uptake decreases as well. As the centrifugal movement causes large amounts of calcium being released by sarcoplasmic reticulum and this lowers the endoplasmic calcium. subsequently leading to cell apoptosis. Besides, increase of cytosolic calcium ion in micro exercise-induced skeletal muscle injury, excess of mitochondrial calcium and reduced endoplasmic reticulum calcium also prompts cell apoptosis.

Secondly, study on related literature concludes significant relationship between free radicals in micro skeletal muscle injury and cell apoptosis. The studies revealed that increased free radical and mitochondrial free radical may cause cell apoptosis.

In addition, it been reported that heat shock proteins also play a role in skeletal muscle injury and cell apoptosis. Heat shock proteins are synthesized proteins due to stimuli reflect after biological suffering from physical, chemical, and mental stress in the environment[14, 15]. Heat shock proteins are closely related with cell apoptosis. In particular, HSP70, HSP27 exert protective effect on cell apoptosis activated by heat shock, oxidative stress, ionizing radiation, which inhibit stress-activated protein kinase and apoptosis genes[16].

Energy metabolic disorder theory in micro exercise-induced skeletal muscle injury claims that during muscle contraction, inner-muscle cell energy depletion and accumulation of metabolites have an impact on muscle fiber function and working ability of the entire muscle, which is an important reason for micro exercise-induced skeletal muscle injury. Depletion of energy substances also plays an important role in cell apoptosis. Moreover, there is great correlation between possible mechanism of ischemia-reperfusion with delayed muscle soreness and cell apoptosis[17].

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