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Letter to the Editor

Potential Influence of Exercise-Induced Rhabdomyolysis by Branched-Chain Amino Acid Supplementation

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Dear Editor-in-Chief

Among the many nutritional supplements, the branched-chain amino acids (BCAA) valine, isoleucine, and leucine are widely used to improve physical performance. However, the studies to define thresholds for adverse effect have not yet been performed or reviewed in human participants. Aside from these concerns, many studies have shown the positive effects of BCAA intake, such as with the noted decreased muscle enzyme release (1), reduced skeletal muscle damage following high intensity exercise (2), and reduced protein degradation seen in subjects (3).

In contrast, it is significant to state that BCAA intake could potentially have a negative impact. Excessive intake of BCAA may be neurotoxic and might increase the risk of amyotrophic lateral sclerosis, which is known as a motor neuron disease (4). Especially, with high levels of BCAA there is the chance of an induce reduction of serotonin and catecholamine synthesis in the brain (5), indicating an imbalance in the primary motor cortex excitability and inhibitory.

In view of this, rhabdomyolysis is a severe muscle damage condition that could be caused by abnormal ATP/ADP ratio controlling (6) via accumulation of intracellular Ca^{2+} under combined intake of alcohol and drugs (7), and/or can come as a result of performing high intensity exercise (8). As a consequence, rhabdomyolysis may be caused by various factors, however, to our knowledge, there have been no reported cases of BCAA intake.

In the present study, we report a case of rhabdomyolysis caused by the first BCAA intake. In this case, a 34-year-old man regularly performed aerobic and resistance exercises for more than two years. In fact, it is remembered that even on the day of rhabdomyolysis, there were no special changes such as temperature, humidity, and exercise intensity in the subject's routine. In addition, it was noted that the study subject's fatigue after his usual exercise was similar to that which was experienced on other regular exercise days. One difference noted on the day of the incident is that he drank 30 g of BCAA in 200 ml of water. The symptoms he felt about 30-40 hours after exercising were that he noticed coffee-colored urine, an unusually severe muscle pain, and he did experience an unusual swelling of the legs. He visited the hospital and underwent a blood chemistry examination test. His aspartate transaminase, alanine transaminase, and alkaline phosphate were 943 IU/L, 521 IU/L, and 286 IU/L, respectively. In

biomarkers for muscle damage including creatine kinase, lactate dehydrogenase, and myoglobin were confirmed by 19,843 IU/L, 2654 IU/L, ands 624.7 ng/ml, respectively. Therefore, based on the test results, he was finally diagnosed as rhabdomyolysis by the physician who reviewed the subjects test results.

This case highlights that BCAA intake may be a potential risk factor for the development of the symptoms associated with rhabdomyolysis in humans.

It is also important to realize, that BCAA intake could not be considered the sole trigger for rhabdomyolysis. However, some studies may predict the possibility of BCAA-induced rhabdomyolysis. Circulating high dose BCAA augmented the production of mitochondrial reactive oxygen species (9). It can be responsible for the subsequent increase in mitochondria dysfunction in humans (10). Moreover, high levels of BCAA selectively disrupt pyruvate utilization of mitochondria under ischemia-reperfusion injury in heart, indicating BCAA intake may inhibit ATP synthesis, leading to increased intracellular Ca^{2+} levels, and subsequently triggering the activation of mechanisms for the onset of rhabdomyolysis. In addition, because the recommended range of BCAA based on scientific evidence is unclear, studies on concentrations that may cause other prolific side effects will be necessary.

Conflicts of interest

The authors declare that there is no conflict of interest.

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