N-Acetyl Cysteine Attenuates the Sarcopenia and Muscle Apoptosis Induced by Chronic Liver Disease

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Abstract

Background: Sarcopenia is characterized by the loss of muscle mass and strength (muscle atrophy) because of aging or chronic diseases, such as chronic liver disease (CLD). Different mechanisms are involved in skeletal muscle atrophy, including decreased muscle fibre diameter and myosin heavy chain levels and increased ubiquitin–proteasome pathway activity, oxidative stress and myonuclear apoptosis. We recently found that all these mechanisms, except myonuclear apoptosis, which was not evaluated in the previous study, were involved in muscle atrophy associated with hepatotoxin 5-diethoxycarbonyl-1,4-dihydrocollidine (DDC)-induced CLD.

Objective: In the present study, we evaluated the involvement of myonuclear apoptosis in CLD-associated sarcopenia and the effect of N-acetyl cysteine (NAC) treatment on muscle strength and apoptosis, using a DDC-supplemented diet-fed mouse model.

Methods: Four-month-old male C57BL6 mice were fed with a standard or DDCsupplemented diet for six weeks in the absence or presence of NAC treatment.

Results: Our results showed that NAC attenuated the decrease in muscle fibre diameter and muscle strength associated with CLD-induced muscle wasting in gastrocnemius (GA) muscle of DDC-supplemented diet-fed mice. In addition, in GA muscle of the mice fed with DDC-supplemented diet-induced CLD showed increased

myonuclear apoptosis compared with the GA muscle of the control diet-fed mice, as evidenced by increased apoptotic nuclei number, caspase-8 and caspase-9 expression, enzymatic activity of caspase-3 and BAX/BCL-2 ratio. NAC treatment inhibited all the mechanisms associated with myonuclear apoptosis in the GA muscle.

Conclusion: To our knowledge, this is the first study which reports the redox regulation of muscle strength and myonuclear apoptosis in CLD-induced sarcopenia.