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MUSCLES STARVE IN THE ABSENCE OF VITAMIN D, STUDY OF MICE FINDS

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Crucial link: Without vitamin D, muscles continued to make glycogen, but could not convert it to glucose, as Dr. Aneeshkumar (right) explains. | Photo Credit: iStockphoto

Skeletal muscles normally brim with energy, yet they starve in the absence of Vitamin D, says recent research led by Aneeshkumar A. G. of National Institute of Immunology, New Delhi. This research demonstrates that glycogen stored in the skeletal muscles is not converted into a usable form of energy without Vitamin D.

Usually, the glucose absorbed from the food is converted into glycogen and stored in the skeletal muscle. This stored energy reserve is used by muscles to produce energy after the food consumed is digested. However, in the absence of vitamin D, the skeletal muscle is starved of energy, decreasing muscle mass.

Vitamin D deficiency is often associated with rickets. In rickets, the bone tissue does not correctly mineralise calcium and phosphorus, leading to softening of bones resulting in skeletal deformities. However, we are becoming aware that vitamin D works more as a hormone than and is involved in a host of biochemical reactions. It is key to maintaining metabolic functions, immune system, bone health and plays a crucial role in depression, mood swings, anxiety and sleep quality.

As part of the normal metabolic process, proteins produced in our body degrade, and in due course, new proteins are made to replace them. Usually, when the protein degradation exceeds protein synthesis, skeletal muscle atrophy or simply a decrease in muscle mass occurs.

"We wanted to find out the molecular nature of muscle dysfunction in the absence of vitamin D. We started with the hypothesis that the root cause is metabolic dysfunction. We used a mouse model which does not have a vitamin D receptor:[VDR] a protein that binds to vitamin D and switches several genes on or off to test our hypotheses," says Dr. Aneeshkumar.

Typically, the protein synthesis is high when the digestion of the food is taking place and is slower during the post-absorptive state when the digestion is completed. "In order to examine if the protein degradation and subsequent muscle wasting occur primarily during the absorptive or post-absorptive phase, we compared the protein synthesis during both the phases. In control mice, the levels were as expected. Nevertheless, in mice lacking VDR after the weaning stage of growth, the protein synthesis was impaired during the post-absorptive stage," explains Dr. Aneeshkumar, and adds, "without the vitamin D receptor there was a general increase in protein degradation and a decrease in post-absorptive protein synthesis."

Initially, scientists suspected that the absence of VDR is preventing the synthesis of glycogen from the food. "We checked whether the energy deprivation in skeletal muscles is associated with differences in glycogen levels," says Dr. Aneeshkumar. To their surprise, VDR knockout mice had higher glycogen levels than the control ones. "We found that the glycogen synthase, the key enzyme that converts glucose into glycogen, was having a field day without the inhibitory enzymes active". More and more glycogen was being produced and stored in the skeletal muscle.

Nevertheless, the glycogen phosphorylase, an enzyme that converts glycogen to glucose when energy is needed, was significantly lower. "As a result, while muscle continued to make glycogen, none of it could be converted back to glucose resulting in energy deficiency," explains Dr. Aneeshkumar. Even with abundant glycogen present, the skeletal muscle could not extract the energy in the absence of vitamin D.

"From this research, we think we have found the molecular mechanism by which the vitamin D deficiency leads to muscle wasting. Without vitamin D, glycogen storage cannot be utilised for glucose production. When the glycogen storage does not give energy, particularly in a post-absorb state, the skeletal muscle draws more glucose from the blood. This leads to a systemic energy shortage. When there is systemic lack of energy, like during hunger, the protein degradation in muscle is triggered leading to muscle wasting," explains Dr. Aneeshkumar. "Although our study is in mice, we think this mechanism is broadly applicable in humans as well," he said.

(T.V. Venkateswaran is a scientist with Vigyan Prasar and is a science communicator.)

Fortification will increase serum ferritin without changing haemoglobin level

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