Long-term use of mechanical ventilation contributes to the deterioration of human diaphragm muscle

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A new study by University of Pennsylvania School of Medicine shows, for the first time in humans, that ventilators combined with diaphragm disuse contributes to muscle atrophy in the diaphragm in as little as eighteen hours. Muscle atrophy in the diaphragm is a major contributor of why patients who have undergone prolonged mechanical ventilation often have difficulty breathing after being removed from the ventilator.

The report, published in the March 27th edition of the *New England Journal of Medicine*, measured a greater than 50 percent decline in muscle fibers in the diaphragm. In addition, the study measured the proteins that play a key role in the muscle-wasting chemical cascade. By intervening in this pathway, the research suggests, a new pharmacological approach to safely and quickly wean patients off ventilators could be developed.

Sanford Levine, PhD, Professor of Thoracic Surgery and co-director of the Respiratory Muscle Research Laboratory, led a team that conducted 22 biopsies on both deceased and living patients. Fourteen brain-dead organ donors, aged 18 to 58, comprised the case study with each having undergone between 18 and 69 hours of mechanical ventilation. The eight-member control group each received less than three hours.

Levine said both groups were demographically and statistically similar except for the time each had spent on mechanical ventilation. Biopsy

results on the other hand were different.

Compared to the control group, the diaphragms of the 14 case study members revealed:

-- 23 percent lower levels of the free-radical fighting antioxidant, glutathione

-- 154 percent more Caspase-3, a calcium-dependant “executioner” enzyme that degrades protein molecules and is responsible for programmed cell deaths

-- Muscle-wasting Atrogin-1 genes at a ratio of 200:1 over MBD4 housekeeper genes that maintain healthy cells

-- MURF-1 nucleotides that attack myofiber proteins at a ratio of 590:1 over housekeeper genes

“From our observations, we conclude that these (biopsy differences) could only be attributed to marked atrophy caused by a combination of complete diaphragm inactivity and mechanical ventilation,” Levine said.

“Disuse atrophy of human diaphragm myofibers could be a major contributor to the weaning problems that occur in some of our patients,” Levine said. “Therefore, we believe fiber atrophy of the magnitude noted in our case diaphragms could have clinical significance.”

Source: University of Pennsylvania

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