

Heart drug offers possible treatment for patients facing respiratory failure

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Treatment with the calcium-sensitizing drug levosimendan may be effective in improving muscle function in patients with respiratory muscle weakness, which often accompanies chronic diseases such as chronic obstructive pulmonary disease (COPD) and congestive heart failure, according to researchers in the Netherlands, who studied the effects of the drug on healthy volunteers. The drug, which is normally prescribed in patients with acute heart failure, increases the sensitivity of muscle tissue to calcium, improving the muscle's ability to contract.

The findings were published online ahead of the print edition of the American Thoracic Society's [American Journal of Respiratory and Critical Care Medicine](#).

"We found that the calcium sensitizer levosimendan improves the mechanical efficiency of the human diaphragm, suggesting a new, therapeutic approach to improve respiratory muscle function in patients with respiratory failure," said Leo Heunks, M.D. PhD, who is a pulmonary and critical care physician at Radboud University Nijmegen Medical Centre in Nijmegen, the Netherlands.

"Respiratory muscle weakness frequently occurs in patients with chronic diseases, and also in critically ill patients on the ventilator, making breathing more difficult and causing more severe illness and even death," Dr. Heunks added. "To date, there is no specific drug treatment available to improve respiratory muscle function in patients with respiratory muscle failure."

Calcium is a necessary element in [muscle contraction](#), and calcium sensitizers like levosimendan improve muscle tissue's ability to contract by making them especially sensitive to the effects of calcium. In vitro studies have demonstrated calcium sensitizers improve the function of the respiratory muscles, and results of animal studies have shown calcium sensitivity is reduced in specific chronic illness settings. A recent in vitro study of diaphragm muscle tissue taken from COPD patients showed levosimendan enhanced the ability of those tissues to contract.

Based on the results of those studies, the researchers in this study hoped to determine whether levosimendan would improve the ability of the diaphragm muscle to contract in healthy volunteers, Dr. Heunks explained.

The researchers enrolled 30 healthy volunteers and randomized them to receive either levosimendan or placebo. Each volunteer performed two identical breathing exercises, one before receiving levosimendan or placebo and one afterward. During each exercise, the researchers used a specialized catheter to measure the nervous system's stimulation of the respiratory muscles and the amount of force those muscles used in forced exhalation. Magnetic nerve stimulation was used to evaluate the movements of the diaphragm before and after the exercise period, and heart rate, blood pressure, exhaled carbon dioxide and blood oxygen levels were continuously measured.

At the end of their study, the researchers found subjects in the placebo group had a 9-percent loss of muscle contraction following the exercises, while those in the levosimendan group had no loss of contraction. In addition, the mechanical efficiency of the diaphragm during the exercises improved by 21 percent in the levosimendan group compared to the placebo group, meaning subjects treated with levosimendan needed less effort than those treated with placebo to achieve the same

amount of muscle force in the diaphragm.

"On average, the breathing exercises in subjects receiving placebo resulted in significant reductions in diaphragm muscle contractions, while the group receiving levosimendan had no significant decrease in contractions," Dr. Heunks said. "Essentially, levosimendan prevents the development of muscle fatigue of the respiratory muscles."

Dr. Heunks noted that while these results indicate calcium sensitizers like levosimendan may provide an effective therapeutic option for chronically ill patients with respiratory muscle weakness or patients using mechanical ventilation, larger studies are necessary to confirm these results and determine the optimal dose.

"The dose of levosimendan used in this current study was derived from earlier studies in healthy subjects, demonstrating limited side effects," he said. "Future studies should evaluate the effects of lower doses of levosimendan on respiratory [muscle function](#) in humans, to ensure patients can be effectively treated with as little risk for side effects or complications as possible."

Provided by American Thoracic Society

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