Levosimendan shows respiratory benefits in patients with ALS

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Video Abstract

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Abstract

A new clinical trial suggests levosimendan could improve respiratory function in patients with amyotrophic lateral sclerosis. ALS is an adult-onset neurodegenerative disease that results in progressive weakness. Those affected by the disease typically die within three to four years of diagnosis due to respiratory failure commonly resulting from weakening of the diaphragm. Prior studies indicate that levosimendan – a calcium sensitizer on the market since 2000 for the treatment of acute worsening of severe heart failure – can also boost the force and efficiency with which the diaphragm contracts. This prompted researchers to investigate whether levosimendan is clinically beneficial to those with ALS. The phase 2 trial used a randomized, double-blind, placebo-controlled, crossover design to evaluate the efficacy and safety of oral levosimendan in 66 patients with ALS. The patients received three 14-day periods of treatment in random order: twice-daily dosing with 1 mg levosimendan, 1 mg levosimendan taken in the morning followed by a placebo in the evening, or twice-daily dosing of placebo. Open-label follow-up was offered starting with 1 mg levosimendan in the morning for 2 weeks, followed by an increase to 1 mg twice daily if tolerated. The primary endpoint was slow vital capacity in the sitting position. Although this endpoint was not met, post hoc analysis indicated significant and dosedependent treatment effects between levosimendan and placebo in supine slow vital capacity after a 14-day treatment period. This observation has important implications, as diaphragmatic performance is more dramatically reduced by lying versus sitting, and the first clinical signs of respiratory insufficiency in ALS often appear during sleeping or when lying down. It's possible that upright vital capacity might not reveal abnormalities that are noticeable in the supine position. Headache and increased heart rate were more common with levosimendan than placebo and showed a dose-dependent increase in frequency, although most patients tolerated levosimendan well and no significant differences between the treatments were observed for other adverse events. The trial provides the first clinical evidence that levosimendan may improve respiratory function in patients with ALS. While encouraging, larger and longer studies are needed to confirm the results.