Most patients in a small trial survived after a single dose of mesenchymal stem cells

 by Nancy Walsh *Senior Staff Writer, MedPage Today*

DENVER -- A single intravenous dose of allogeneic bone marrow-derived mesenchymal stem cells as a treatment for acute respiratory distress syndrome (ARDS) showed promise in a phase I trial, a researcher reported here.

Among nine patients with ARDS who had the treatment, the three who received the highest dose, 10 million cells/kg predicted body weight, all survived and had decreases in lung injury scores, according to [Michael A. Matthay, MD](http://profiles.ucsf.edu/michael.matthay), of the University of California San Francisco. Four of the other six assigned to lower doses also survived.

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Markers of inflammation and endothelial/epithelial injury decreased between baseline and day three, and there were no serious adverse events considered to be associated with the stem cell treatment, she reported at the [annual meeting of the American Thoracic Society.](http://conference.thoracic.org/2015/)

There are no effective pharmacologic therapies for ARDS and mortality remains high.

"However, [preclinical studies](http://www.ncbi.nlm.nih.gov/pubmed/25830837) have suggested that allogeneic mesenchymal stem cell treatment may decrease lung injury and improve survival, possibly through paracrine release of anti-inflammatory cytokines and keratinocyte growth factor, repair of the injured alveolar epithelium, and interestingly, the treatment has antimicrobial and antiapoptotic properties," he said.

With the primary goal of testing the safety of a single intravenous dose, between August 2013 and January 2014, Wilson and colleagues conducted the [STem cells for ARDS Treatment (START) trial](http://stemcellsards.ucsf.edu/), a multicenter, open-label, dose-escalating study in patients with moderate-to-severe ARDS.

Secondary endpoints included standard respiratory and systemic endpoints, 1- and 2-month mortality, and effects on biomarkers of inflammation and tissue injury.

Patients had to have a ratio of arterial oxygen partial pressure to fractional inspired oxygen (PaO2/FiO2) below 200 mm Hg treated with at least 8 cm H2O positive end-expiratory pressure, and were enrolled within 96 hours of ARDS onset.

Exclusion criteria included liver disease, recent cancer treatment, age under 18 years, and moribund status.

The first three patients received a low-dose infusion of 1 million cells/kg predicted body weight, the second three received an intermediate dose of 5 million cells/kg predicted body weight, and the final three were given the high-dose treatment.

The treatment was given over the course of an hour, and a physician was present at the patient's bedside during the infusion and for 6 hours thereafter. The main concern was the possibility of infusion-associated adverse events such as hemodynamic instability and increased need for vasopressor treatment.

In the low-dose group, one patient age 28 with preeclampsia as the cause of ARDS survived after 5 days of mechanical ventilation, as did one age 59 with aspiration after 11 days of ventilation.

In the intermediate-dose group, one patient age 67 with aspiration survived after 7 days of ventilation as did another age 46 with aspiration after 3 days of ventilation.

In the high-dose group, one 52-year old patient with pneumonia and an APACHE III score (a predictor of in-hospital mortality) of 121 was mechanically ventilated for 3 days and lung injury scores decreased from 2.75 to 1.33. The patient was alive at day seven.

A second patient age 55 with biliary sepsis and an APACHE III score of 127 was ventilated for 9 days and lung injury scores declined from 3.5 to 2. This patient was alive at day 14.

The third patient was 38 and had pneumonia with an APACHE III score of 68. After 17 days of mechanical ventilation, lung injury scores fell from 2.33 to 1.33, and the patient was alive at day 25.

The changes in lung injury scores were numerically lower, though not significantly so. No trends in changes in vital signs were observed.

Two out of the nine patients died before being discharged from the hospital, for an inpatient mortality rate of 22%.

"Based on these results, we have begun a phase II component of the study using the highest dose of mesenchymal stem cells," he said. That trial is being conducted at the University of California San Francisco, San Francisco General Hospital, Massachusetts General Hospital, and the University of Pittsburgh Medical Center.

An audience member asked if even the high-dose treatment might have been underdosing, because only 60% of the stem cells are considered viable after being thawed.

"The dose is an educated guess based on our mouse and sheep studies," Matthay replied.