

Anti-clotting agent does not improve outcomes of patients with severe pneumonia

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Use of the blood clot-inhibiting medication tifacogin does not appear to improve outcomes of patients with severe community-acquired pneumonia (sCAP), according to a study conducted by researchers from North and South America, Europe, Asia and Africa. The drug had shown some potential benefit in the sCAP subgroup of an earlier trial involving sepsis patients.

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

"Administration of tifacogin showed no treatment benefit in this large population of patients with severe CAP," said Richard Wunderink, MD, professor of pulmonary and critical care medicine at Northwestern University's Feinberg School of Medicine. "This result was consistent across a range of disease severity indices."

In the U.S., community-acquired pneumonia (CAP) is the eighth leading cause of death, with a death rate of 18.8/100,000. The number of individuals hospitalized with CAP annually is expected to increase up to 1 million in 2020, with similar trends in many other countries due to the disproportionate growth of the elderly population. Globally, [intensive care unit](#) mortality in patients admitted with sCAP is about 30%.

In most sCAP patients, the blood clotting system is activated as part of the response to infection, in some cases interfering with circulation and

leading to multiple organ failure. Researchers hope reducing this excess clotting through use of anticoagulants in individuals with sCAP may prevent [organ failure](#).

Tifacogin acts by blocking activated tissue factor, an essential for clot formation. In a prior trial of sepsis patients, tifacogin had shown some benefit for patients in that trial who had CAP. Based on those results, Dr. Wunderink said researchers involved in this study, dubbed CAPTIVATE (Community-Acquired Pneumonia Tifacogin Intravenous Administration Trial for Efficacy), aimed to assess the efficacy and safety of tifacogin as adjunct therapy in sCAP.

"CAP remains the most common cause of death from infection," Dr. Wunderink said. "Anti-clotting therapies are sought to complement the antimicrobial treatment and supportive care measures that are currently used for sCAP patients."

In this study, researchers enrolled 2,138 sCAP patients from 188 centers from 2005 to 2008, randomizing them to receive tifacogin or placebo intravenously for four days. Although two doses of tifacogin (0.025 mg/kg/h and 0.075 mg/kg/h) were initially included in the study, the higher dose was dropped early on when no benefit was demonstrated.

At the end of the study although tifacogin did show an effect on clotting measures in the blood, the researchers found mortality rates and the incidence of adverse events were similar in both the tifacogin and placebo groups.

Dr. Wunderink said the study's negative results could be due to several factors.

"The coagulation and inflammatory responses may have been irreversibly activated before tifacogin was administered, or specific

processes that occur during CAP may have blunted the effect of the drug," he said. "However, the most logical explanation is that tissue factor activation, while important, may not be a critical step in the pathogenesis of sCAP mortality."

Although the study showed no benefit associated with the use of tifacogin in sCAP patients, Dr. Wunderink said it clearly demonstrates the need for additional research to improve sCAP mortality rates.

"CAPTIVATE represents the largest clinical trial of severe CAP performed to date," Dr. Wunderink said. "The design and execution of the study demonstrates that a more homogeneous population with a single source of infection, rather than a more generic sepsis population, can be defined, which will be of benefit for future studies.

"Although the primary end-point was not achieved, this study demonstrates the persistent unmet need for further interventions to improve mortality of sCAP and the feasibility of those studies," he added.

Provided by American Thoracic Society

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