Recommendations for treatment of inherited lung disease are unjustified

July 6 2010

An expensive treatment recommended for a genetic disorder called alpha-1 antitrypsin deficiency has no proven clinical benefit, according to a systematic review by Cochrane Researchers. The disorder causes chronic lung disease and the review concludes that considering the lack of evidence for its benefits, and possible adverse effects, the treatment should not be recommended.

Alpha-1 antitrypsin deficiency affects less than one in 1,600 people. Those who inherit the disorder have low levels of the protein alpha-1 antitrypsin, also called alpha-1 proteinase inhibitor, which protects the tissue of the lungs from destruction by the body's own white blood cells. At a relatively young age, this can result in symptoms of emphysema, including shortness of breath and wheezing. The aim of alpha-1 antitrypsin replacement therapy is to give the patient back the protective protein they are missing. This should limit damage to lungs and, ultimately, prevent early death. The protein is extracted from blood donated by healthy volunteers.

The researchers reviewed data from two trials involving a total of 140 people with the disorder, all of whom were at a high genetic risk of developing chronic lung disease. In one trial, patients were given intravenous alpha-1 antitrypsin or a placebo every four weeks for three years and in the other, the protein or a placebo was given weekly for a minimum of two years. There was no difference between treatment and control groups in terms of exacerbations of lung disease, or quality of life. Combining the results from the trials, the review authors found no

evidence of a clinically important effect on lung function; indeed the results suggested modest harm, or at best no effect. In contrast, the treatment might cause a reduction in the deterioration of lung appearance on CT scan, but it is not clear whether this is a clinically meaningful difference.

Based on this evidence, the researchers say the treatment, which costs up to $150,000 a year in the US, cannot be recommended. "The drug has not shown any clinical benefit, is extremely costly and has important adverse effects," said lead researcher Peter Gøtzsche of the Nordic Cochrane Center at Rigshospitalet in Copenhagen, Denmark. "In view of the lack of evidence and high cost of treatment, treating alpha-1 antitrypsin deficiency by replacement therapy cannot be recommended."

Neither of the trials included in the review reported mortality data and the researchers point out that adverse events were not well reported. In previous studies, a small proportion of patients suffered allergic reactions and breathing difficulties following treatment.

The researchers say recommendations by the American Thoracic Society and European Respiratory Society that promote alpha-1 antitrypsin replacement are misguided. "Both societies recommend augmentation therapy for patients with breathing problems related to alfa-1 antitrypsin deficiency. In our opinion, these recommendations are not reasonable," said Gøtzsche.

Provided by Wiley