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LUNG ALERT

Inhaled cyclosporine may increase survival after lung transplantation

▲ Iacono AT, Johnson BA, Grgurich WF, *et al*. A randomized trial of inhaled cyclosporine in lung-transplant recipients. *N Engl J Med* 2006;**354**:141–50

In this single centre, randomised, double blind, placebo controlled trial, inhaled cyclosporine 300 mg or placebo was given in addition to conventional immunosuppression for 3 days a week for the first 2 years after lung transplantation. The trial included 58 recipients of a single or bilateral lung transplant. The primary end point was the rate of histological acute rejection, with secondary end points including chronic rejection free survival and mortality.

There was no difference in the primary end point with rates of acute rejection similar in the cyclosporine and placebo groups (0.44 (95% CI 0.31 to 0.62) episodes per patient per year in the cyclosporine group and 0.46 (95% CI 0.33 to 0.64) per patient per year in the placebo group). Secondary end points did show improvement with inhaled cyclosporine. There were only three deaths in the treatment arm compared with 14 in the placebo group (relative risk of death 0.20, 95% CI 0.06 to 0.70; $p = 0.01$), showing that overall survival was improved. Chronic rejection free survival as determined by spirometric and histological analysis also showed improvement. The risk of nephrotoxic effects and opportunistic infection were similar in both groups.

This study shows that, although there was no difference in acute rejection, inhaled cyclosporine improved survival and extended periods of chronic rejection free survival. These results are surprising as previous studies have linked repeated episodes of acute rejection with chronic rejection. The authors propose that, as chronic rejection begins in the airways as bronchiolitis obliterans, inhaled treatment may have a greater effect than in acute rejection where the pathology is mainly vasculitic. Further experience is needed to confirm the magnitude and durability of these results.

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