Some members of the paromyxoviridae (PV) family, such as respiratory syncytial virus (RSV), parainfluenza virus (PIV) and human metapneumovirus (hMPV), are increasingly being recognized as pathogenic to lung transplant recipients. The spectrum of disease may vary from mild upper respiratory tract infection to severe pneumonia requiring mechanical ventilation. Some of these infections have been implicated in allograft rejection. Diagnosis may be performed by rapid antigen testing and PCR, which for RSV has a sensitivity and specificity > 90%.¹ Few systematic studies are available for treatment of PV infections in lung transplant recipients and published case series are limited to small numbers. The limited evidence supports the use of ribavirin; however, the most appropriate route of administration and dose is not clearly established. Oral, intravenous and inhalation routes have been used with variable success.

Fuehner and colleagues from Hannover (Germany) recently published their single center experience using oral ribavirin in lung and lung-heart transplant recipients with PV infections.² The primary clinical endpoint was new onset of bronchiolitis obliterans syndrome (BOS) within 6 months of PV infection. Secondary endpoints were time to recovery of FEV1, incidence of acute rejection, BOS progression, and survival or graft loss after 6 months. Viral detection was performed from nasopharyngeal swabs by PCR only if bronchoalveolar lavage (BAL) was not feasible or isolated symptoms of upper respiratory tract infections were present. Direct immunofluorescence antigen testing was the primary detection method for BAL samples followed by PCR testing for negative samples from patients with a clinical history suggestive of infection. A total of 38 patients were treated with ribavirin (15-20mg/kg/day in two divided doses for 14 days) and increased prednisolone (ribavirin (R) group), whilst 29 patients with contraindications for ribavirin treatment (i.e. renal failure, anemia, leucopenia or known intolerance to ribavirin) received supportive treatment including increased prednisolone (0.5mg/kg/day) if symptomatic (non-ribavirin (NR) group). RSV was the most common PV detected (>63%) followed by PIV (>25%) and hMPV. In 10 patients ribavirin was stopped (due to hemolysis (n=5), renal failure (n=4) and nausea (n=1. Median FEV1 dropped by 20% and 18% from baseline for the R and NR groups, respectively. In 84% of the R group and 59% of the NR group graft function recovered within 30 days (P= 0.02). New onset BOS developed within 6 months in 5% of the R group versus 24% of the NR group (P=0.02). The authors conclude that treatment with oral ribavirin seems to be associated with earlier recovery of graft function and prevention of BOS.

To date, this is the largest prospective study of oral ribavirin published for lung-/heart transplant recipients using a comparison group without ribavirin. Both groups also received an increased prednisolone dose. The selection criteria for inclusion into the ribavirin group were lack of contra-indications for ribavirin rather than a random allocation of subjects potentially eligible for such a treatment. This allocation may have introduced a selection
bias, which somewhat limits the conclusions that can be drawn from the study. Nevertheless, this prospective trial provides the strongest evidence thus far supporting the use of oral ribavirin in PV infections and suggests beneficial effects concerning lung function recovery and a reduced incidence of BOS. It also provides some indication regarding dose and duration and draws attention to known adverse events. Close monitoring is advisable to allow for drug discontinuation to prevent hemolytic anemia or kidney failure. Oral ribavirin is considerably less expensive and easier to use than the aerosolized form, which factors may be decisive in case of equal efficacy. Randomized studies comparing various application routes are needed to clarify this question.

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References: