Pulmonary arterial hypertension (PAH) is a progressive disease characterized by progressive elevation of pulmonary vascular resistance and pulmonary artery pressure (PAP), which leads to right heart failure and death. Survival of patients with PAH is closely related to right ventricular (RV) function [1,2]. Eisenmenger syndrome (ES) represents PAH with a non-restrictive intracardiac or extracardiac communication and cyanosis. Although ES has a better prognosis than that of other causes of PAH, ES is also associated with substantial morbidity and mortality [3].

Treatment of ES with PAH-targeted drugs

PAH-targeted drugs including prostanooids, endothelin receptor antagonists (ERAs), phosphodiesterase type-5 inhibitors, and a soluble guanylate cyclase stimulator have become available in the past two decades. Advanced therapy with those pulmonary vasodilators has become part of the standard treatment, but there have been only a few studies providing guidance for the use of PAH-targeted drugs in patients with ES. One randomized clinical trial (RCT) revealed that bosentan, an ERA, has beneficial effects on exercise capacity and quality of life [4], and it is recommended for WHO-FC III patients with ES [5]. However, its effect on mortality remains uncertain. Observational studies revealed that ambrisentan [6], an ERA, and phosphodiesterase type-5 inhibitors including sildenafil [7] and tadalafil [8] show favorable functional and hemodynamic effects in patients with PAH associated with congenital heart disease (CHD) and ES.

As far as prostanoids are concerned, intravenous epoprostenol improves hemodynamics and quality of life in patients with PAH associated with CHD according to a single center, single-arm trial [9]. In this issue of Journal of Cardiology, Chon et al. report the results of a prospective, multicenter, single-arm trial of effects of inhaled iloprost treatment [10]. This study shows that long-term (48 weeks) iloprost treatment improves echocardiographic parameters of RV function in patients with ES.

Estimated mean PAP and systolic PAP significantly reduced after iloprost treatment in the study. These results indicate that reduction of pressure overload contributes to improvement in RV function in ES. As is the case in patients with idiopathic PAH, normalization of pressure overload after lung transplantation leads to prompt recovery of RV function [11]. Furthermore, Matsubara et al. reported that sufficient reduction of pressure overload by PAH-targeted drugs improves not only hemodynamic parameters but also prognosis [12–14]. Sufficient reduction of pressure overload by PAH-targeted drugs may lead to improvement in prognosis in patients with ES. Further studies are needed to clarify this point.

Future perspective

RCTs are needed to reveal the effects of PAH-targeted drugs including iloprost on mortality in patients with ES. Furthermore, additional clinical trials are needed to establish the efficacy and safety of combination therapy with PAH-targeted drugs aimed at sufficient reduction of pressure overload in patients with ES.

Conflicts of interest

None.

References


