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Editorial

Udenafil as a Therapeutic Option for Pulmonary Arterial Hypertension

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▸ See the article "Acute Hemodynamic Changes after Single Administration of Udenafil in Pulmonary Arterial Hypertension: a Phase IIa Study" in volume 49 on page 353.

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Pulmonary arterial hypertension (PAH) is a life-threatening condition, with reported survival rates as 85% and 60% at 1 year and 3 years, respectively.[1] With an improved understanding of the pathophysiologic mechanism of PAH, several effective drugs targeting endothelin, nitric oxide, or prostacyclin pathway of pulmonary vasculature have been developed and widely used in the treatment of PAH.[2][3]

By the inhibition of the cyclic guanosine monophosphate (cGMP) which degrades enzyme phosphodiesterase type 5 (PDE-5), PDE-5 inhibitors results in the vasodilation of pulmonary arterial trees through nitric oxide/cGMP pathway. Three PDE-5 inhibitors (sildenafil, tadalafil, and vardenafil) which are approved for erectile dysfunction were also introduced and recommended in the current guideline for the treatment of PAH.[2] The clinical efficacy and safety of these drugs have been investigated in large number of experimental and clinical studies.

Udenafil (Zydena®) is a currently developed PDE-5 inhibitor, and the clinical efficacy and safety of udenafil on the erectile dysfunction, cardiac hypertrophy, portal hypertension, and heart failure with reduced ejection fraction have been validated in clinical trials.[4-7] Udenafil, theoretically, would be beneficial in treating PAH as demonstrated in other PDE-5 inhibitors such as sildenafil and tadalafil, but the hemodynamic effects of udenafil never been evaluated in patients with PAH.

In this issue of *Korean Circulation Journal*, Chang et al.[8] reported an important pilot study regarding the acute hemodynamic changes after single administration of udenafil with each dosage of 50 and 100 mg in patients with PAH. Cardiac and pulmonary vascular hemodynamic changes were evaluated by the comprehensive right heart catheterization in this study. This is a well-designed and first clinical trial demonstrating the clinical efficacy and safety of udenafil in PAH patients. According to this study, udenafil produced the most favorable hemodynamic benefits when 50 mg was administrated as a single dose, with rarely documented adverse events. As the results are comparable to that of sildenafil and tadalafil, udenafil might be suggested as an alternative PDE-5 inhibitor in the treatment of PAH. Impressively, these responses lasted at least 4 hours, which means udenafil has the longest duration of action among other approved PDE5-inhibitos.

Combination therapy on the different signaling pathway may offer favorable clinical outcomes, especially for the patients with ongoing or worsening of dyspnea despite initial monotherapy. Sildenafil showed better prognosis when used with epoprostenol, and tadalafil had better outcome when used with bosentan.[9][10] In the study by Chang et al.,[8] similarly, 72% of the study population were already being treated with endothelin receptor antagonists, which is supportive for the use of udenafil as a combination therapy. To be a useful alternative of the approved PED-5 inhibitors in PAH, further larger studies will have to be addressed to demonstrate whether these favorable hemodynamic effects of udenafil in PAH may be associated with the improved clinical outcomes or not.

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