

## EDITORIAL

# Idiopathic Pulmonary Hypertension

Idiopathic pulmonary hypertension is not a very rare disease. It is quite common in cardiology and respiratory medicine practice in our country. Most of the cases are diagnosed very late and come to specialist in very advanced stages of the disease. Some of the patients are presenting so late when only palliative therapy is possible. It is very important to diagnose the condition early and start appropriate management to alter the progression otherwise it will end with right ventricular failure (RVF) and death of the patient.<sup>1</sup>

The first reported case of pulmonary hypertension was described in 1891 by a German physician called Ernst von Romberg, who at autopsy, showed thickening of the pulmonary artery but no heart or lung disease that might have caused the condition.

Several studies have suggested that pulmonary vascular reactivity to vasodilators is lost as concentric medial hypertrophy leads to intimal fibrosis and plexiform lesions. Therefore, various strategies have been developed for the evaluation of acute pulmonary vascular reactivity. One of the most important is hemodynamic testing and different drugs are used for this purpose e.g. Nitric oxide (NO), adenosine, prostacyclin, acetylcholine. Responders are defined as reduction of pulmonary vascular resistance >20% and reduction of mean pulmonary arterial pressure >20% and Nonresponders are those with no significant change of PVR. "Nonresponders" are candidates for continuous intravenous prostacyclin therapy as a bridging therapy until transplantation is done.<sup>2,3</sup>

From the therapeutic standpoint, the treatment of pulmonary hypertension remains challenging and rapidly changing. The currently available disease-specific therapies have made significant changes in the disease natural history. Six medical therapies have been approved that target 3 different pathways: the prostacyclin pathway, the nitric oxide pathway, and the endothelin pathway. Prostacyclin is the first and probably most potent specific therapy. It is produced predominantly by endothelial cells and it is a potent vasodilator of all vascular beds.<sup>4</sup> Intravenous epoprostenol for the treatment of idiopathic pulmonary arterial hypertension was approved by the FDA and considered as a landmark in the treatment stages of pulmonary arterial hypertension. Inhaled prostacyclin

analogue, Iloprost, was also approved by FDA. Phosphodiesterases-5 inhibitors are the second group of therapy that deal primarily with nitric oxide pathway and selectively inhibit cGMP-specific phosphodiesterases and so augment the pulmonary vascular response to endogenous or inhaled nitric oxide.<sup>5-8</sup> Sildenafil citrate, an oral phosphodiesterase type-5 inhibitor, was approved by the FDA. The third group of disease-specific therapy is the Endothelin receptors antagonist (ERA). Two distinct types of endothelin-receptor have been identified, ETA and ETB. Activation of ETA receptors facilitates vasoconstriction and proliferation of vascular smooth-muscle cells,<sup>9</sup> while ETB receptors activation are thought to be principally involved in the clearance of endothelin, particularly in the vascular beds of the lung and kidney leading to vasodilation and nitric oxide release. Bosentan, an endothelin ETA/ETB receptor antagonist, was the first oral therapy approved for the treatment of pulmonary arterial hypertension, the oral Endothelin receptors antagonist selective ERA ambrisentan and sitaxsentan was approved recently.<sup>9</sup>

Now the question is, how far benefit we achieved by these new agents. We did not achieve even the partial benefit. Most of these agents are not manufactured by our pharmaceutical companies and the cost of imported medicine is very high which can not be afforded by our majority of population. So it is necessary that we should have a national registry to find out the prevalence of the disease and we should formulate a national guideline according to our resources. In this way we may be able to help our patients better.

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