Editorial

Pulmonary Arterial Hypertension and Novel Therapeutic Interventions-Present and Future

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Pulmonary hypertension (PH) is a rare and fatal disease characterized by elevated mean pulmonary arterial pressure, dyspnea initially while exercising, fatigue, dizziness or fainting, chest pressure or pain, edema of the ankles and legs, ascites, cyanosis, and increased heart rate. If left untreated, it results in right heart ventricular failure and ultimately death. Current treatment of PH is pulmonary hypertension targeted drugs. Long-term survival of patients with PH is still suboptimal. This thematic issue addresses the new developments in the pathogenesis of PH and novel treatment modalities. The following are the highlights of this thematic issue.

Prasad, K., discusses the incidence of various types of PH and its pathology. His main focus is on the role of advanced glycation end products (AGEs), its cell-bound receptor (RAGE), and soluble RAGE (sRAGE) in the pathogenesis of PH. The mechanisms of AGE-RAGE-induced PH have been discussed in detail. He has coined the term AGE-RAGE stress which, if high, produces PH. Based on the available data, he has suggested that reduction in consumption and formation of AGE, suppression of RAGE expression, blockage of RAGE ligand binding, elevation of sRAGE levels, and antioxidants may be novel therapeutic targets for prevention, regression, and slowing of the progression of PH.

Ishak Gabra, N.B., et al, in this review deals with the definition, diagnosis and management of pulmonary arterial hypertension (PAH) including most recent advances and future directions. Etiology and classification of PAH have been described. Management of PAH with medications targeted at specific pathway of pathogenesis of PAH has been discussed. The treatment strategies are paired with lifestyle changes and tailored to average metrics that are used to prognosticate and measure the severity of patients with PAH. Combination therapy with separate signaling

pathway affecting pathology of PAH is rapidly growing. This type of treatment has additive effects with low toxicity. Currently there is a search for treating PAH through targeting various vasoactive peptides, inhibition of cell proliferation, induction of apoptosis, and mitochondrial modulation of angiogenesis.

Booth, D., has shown that there is a current shift in the combination therapy of pulmonary artery hypertension (PAH). Monotherapy includes phosphodiesterase-5 inhibitors, endothelin receptor antagonists, and prostanoids. Despite promising improvement in the hemodynamics, monotherapy has limited and unsatisfactory clinical benefits, and long-term poor prognosis. He has discussed numerous clinical trials of combination therapy. Combination therapy has a better outcome compared with monotherapy because of possible additive and synergic effects in a combination therapy. The data suggests that there is a progressive shift in the study design using longer event driven trials comparing the upfront and sequential combination therapy on clinical worsening outcome. Combination therapy significantly reduced the risk of clinical worsening compared with monotherapy.

Tak, T., et al, have described in detail the pathophysiology and diagnostic measures of pulmonary embolism-induced pulmonary hypertension. Using patient presentation, clinical suspicion and various scoring systems, a definite diagnosis may be made and appropriate treatment can be instituted. Pulmonary embolism rule out criteria have been pointed out. Treatment such as oxygenation, stabilization of patients, anticoagulant, thrombolysis, surgical embolectomy and circulatory mechanical support have been discussed. Future direction in the management of pulmonary embolism has also been addressed.

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Tyagi, S. and Batra, V., focus on the drugs that reduce the vascular tone. They specially stress the NO-sGC-cGMP related agonists, PDEs inhibitors, prostacyclin analogues, and endothelin receptor antagonists for the treatment of PH. They also stress on the genetics, antioxidants, immunosuppressants, and stem cells for the treatment of PH.

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