Pulmonary hypertension: Emerging therapies and challenges.

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Introduction

Pulmonary hypertension (PH) is a complex and progressive condition characterized by elevated pressure in the pulmonary arteries, leading to significant morbidity and mortality. The condition can arise idiopathically or secondary to other diseases, such as heart failure, chronic lung diseases, or connective tissue disorders. Despite advancements in understanding its pathophysiology, PH remains a challenging condition to treat effectively. This article explores the emerging therapies and challenges associated with managing pulmonary hypertension [1].

Pulmonary hypertension is classified into five groups by the World Health Organization (WHO) based on its underlying etiology. These include pulmonary arterial hypertension (PAH), PH due to left heart disease, PH due to lung diseases or hypoxia, chronic thromboembolic pulmonary hypertension (CTEPH), and PH with unclear multifactorial mechanisms. The pathophysiology involves complex mechanisms, including endothelial dysfunction, vascular remodeling, and increased pulmonary vascular resistance, which ultimately lead to right ventricular overload and failure [2].

Current treatment strategies for PH are primarily tailored to the specific classification and underlying cause. For PAH, targeted therapies include endothelin receptor antagonists (ERAs), phosphodiesterase-5 inhibitors (PDE5is), and prostacyclin analogs. These agents work by targeting specific pathways involved in the disease—such as the nitric oxide, endothelin, and prostacyclin pathways—to reduce pulmonary vascular resistance and improve symptoms [3].

For CTEPH, pulmonary endarterectomy remains the gold standard treatment. However, for patients ineligible for surgery, medical therapies like riociguat, a soluble guanylate cyclase (sGC) stimulator, have proven effective. Meanwhile, PH associated with left heart disease or lung diseases often focuses on managing the underlying condition, as targeted PH therapies may be less effective or even harmful in these populations [4].

Recent years have witnessed significant progress in developing novel therapies for PH. Sotatercept, a first-in-class activin receptor type IIA-Fc fusion protein, has shown promise in clinical trials by targeting the transforming growth factor-beta (TGF-β) signaling pathway. Early studies suggest it improves hemodynamics and exercise capacity in PAH patients [5].

Another area of interest is the use of inhaled vasodilators, such as treprostinil, which provide targeted delivery to the pulmonary vasculature while minimizing systemic side effects. Additionally, therapies aimed at modulating immune responses and fibrosis pathways are under investigation, given their potential roles in vascular remodelling [6].

Despite these advances, several challenges persist in the management of PH. Early diagnosis remains a critical issue, as symptoms like dyspnea and fatigue are often nonspecific and mistaken for other conditions. Consequently, many patients are diagnosed at advanced stages when the disease has already caused significant cardiac damage [7].

The heterogeneity of PH further complicates treatment. While targeted therapies have revolutionized PAH management, their efficacy in other PH groups remains limited. For example, PH due to left heart disease or lung diseases often does not respond well to PAH-specific treatments, highlighting the need for tailored approaches [8].

The high cost of PH therapies poses another challenge, particularly in low- and middle-income countries. These therapies often require lifelong administration, adding to the financial burden on patients and healthcare systems. Furthermore, the chronic nature of PH significantly impacts patients' quality of life, with many experiencing limitations in daily activities, emotional distress, and frequent hospitalizations [9].

Effective management of PH often requires a multidisciplinary approach involving cardiologists, pulmonologists, and specialized PH centers. This approach ensures comprehensive care, including accurate diagnosis, individualized treatment plans, and access to advanced therapies and clinical trials. Patient education and support groups also play a vital role in improving outcomes and adherence to treatment [10].

Conclusion

Pulmonary hypertension remains a formidable medical challenge, but recent advancements in understanding its pathophysiology and developing novel therapies offer hope for improved outcomes. While significant progress has been made, addressing the challenges of early diagnosis, treatment heterogeneity, and economic burden requires continued research and innovation. By adopting a multidisciplinary and patient-centered approach, the medical community can work towards overcoming these hurdles and providing better care for individuals living with PH.

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