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Treatment Approaches for Pulmonary Hypertension in Kyphoscoliosis Related Alveolar Hypoventilation

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Abstract

Pulmonary hypertension is a lethal complication of kyphoscoliosis. It develops in the presence of alveolar hypoventilation, similar to other diseases with alveolar hypoventilation such as obstructive sleep apnea and obesity hypoventilation syndrome. Extrapolating from the treatment of other diseases with alveolar hypoventilation, treatment of pulmonary hypertension related to kyphoscoliosis should be aimed at resting the respiratory muscle and restoring respiratory drive by using nocturnal noninvasive positive pressure ventilation. Supplemental oxygen therapy in addition to nocturnal noninvasive positive pressure ventilation might be effective for reducing the hypoxic vasoconstriction of the pulmonary artery. Even with the use of nocturnal noninvasive positive pressure ventilation and oxygen therapy, pulmonary hypertension develops in patients with kyphoscoliosis. In such cases, pulmonary artery hypertension-approved vasoactive drug can be a candidate therapy. Experiences on the treatment of pulmonary hypertension in patients with kyphoscoliosis must be accumulated.

Keywords: Alveolar hypoventilation; Kyphoscoliosis; Non-Invasive Positive Pressure Ventilation (NIPPV); Phosphodiesterase type 5 inhibitor; Pulmonary hypertension

Introduction

Kyphoscoliosis can be complicated by Pulmonary Hypertension (PH) and/or right heart failure in the presence of alveolar hypoventilation. PH has been recognized as a lethal complication of kyphoscoliosis that can shorten patients' lives across age groups [1]. However, we have only few opportunities to encounter a patient with kyphoscoliosis in a single center in modern times and thus have little recognition about PH complicating kyphoscoliosis. Furthermore, even if we encounter a kyphoscoliotic patient with PH, no guidance or guidelines are available for reference.

Recently, we have reported the successful outcome of a yearlong treatment of PH in a patient with kyphoscoliosis-related alveolar hypoventilation who had undergone Non-Invasive Positive Pressure Ventilation (NIPPV) [2]. This review summarizes the current concept and possible treatment option for PH in kyphoscoliosis-related alveolar hypoventilation, which we have obtained through our experience with the present case.

PH due to Respiratory Disorders

PH related to kyphoscoliosis is classified into PH group 3 or PH due to lung diseases and/or hypoxia, in the recent guidelines [3]. Group 3 PH includes the following 7 disease categories: (a) Chronic Obstructive Pulmonary Disease (COPD), (b) Interstitial Lung Disease (ILD), (c) Other pulmonary diseases with mixed restrictive and obstructive patterns, (d) sleep-disordered breathing, (e) alveolar hypoventilation disorders, (f) chronic exposure to high altitude, and (g) developmental lung diseases. Although this group of PH develops in relation to disorders of the respiratory systems, the pathophysiology involved in each disease category differs and can be roughly categorized as follows: (a) PH develops in lung disease, in which chronic remodelling in the lung tissue may affect PH development, and (b) PH with no or minimal lung disease develops in hypoxia or alveolar hypoventilation. For lung disease-related PH such as COPD-and ILD-related PH, treatment with Pulmonary Artery Hypertension (PAH)-approved vasoactive drugs is not recommended because they may increase the blood flow to the diseased area in the lung, which is ineffective in gas exchange, and worsen hypoxemia [3]. Treatment of the underlying lung disease is the only coping strategy for PH in lung diseases. Guidelines recommend treating only patients with mild lung disease and severe PH as a PAH-phenotype disease with PAH drugs.

The most common diseases that develop PH other than COPD and ILD in this group may be Obstructive Sleep Apnea (OSA) and Obesity Hypoventilation Syndrome (OHS), in which hypoxia and/or alveolar hypoventilation is thought to play a major role in the development of PH and the involvement of lung disease in the development of PH is minimal. Persons with an apnea/hypopnea index of ≥ 5 times per hour with the symptoms related to OSA are diagnosed as having OSA, and those with daytime PaCO2 of>45 mmHg and body mass index of>30 kg/m^2 are diagnosed as having OHS. OSA and OHS overlap, and most OHS cases develop as a continuum of OSA. In the adult population, the incidence of OSA ranges from 3% to 7% in males and from 2% to 5% in females. Of the patients with OSA, 8.5% to 22% have OHS [4]. Cohort studies showed a high prevalence rates of PH in OSA and OHS, which are 17% and 58%, respectively [5,6]. These results indicate a large number of patients with PH in this disease group. In these diseases, decreased respiratory drive during Rapid-Eye Movement (REM) sleep induces alveolar hypoventilation and hypoxemia. The main cause of PH is hypoxic vasoconstriction of the pulmonary artery induced by prolonged alveolar hypoventilation and hypoxemia. In OSA, other factors such as increased venous return induced by increased intrathoracic negative pressure during occlusion of the upper airway and endothelial dysfunction are thought to be involved in the

development of PH [4]. In some patients with OHS, restriction of the chest wall and diaphragm movement by obesity itself induces hypoxemia, without the episode of apnea during sleep. As coexistence of heart disease is common in these diseases, some patients have the factor of group 2 PH, or PH due to left heart disease [7].

The treatments of OSA and OHS, which are aimed at restoring nocturnal breathing and recovering respiratory drive, are the mainstay treatments for PH related to OSA and OHS. Continuous Positive Airway Pressure (CPAP), the most fundamental treatment of OSA, has been proven to decrease pulmonary artery pressure in patients with OSA [8]. In patients with OHS, bariatric surgery has been reported to decrease pulmonary artery pressure [9]. Although the treatments for OSA and OHS have been proven to decrease pulmonary artery pressure, PH still exists in some patients with OSA and OHS even after treatment with CPAP and other supportive therapy [7]. Comorbid PH worsens the prognosis of these diseases [10]. Thus, the strategy for the next step of treatment for PH in these diseases is needed, and treatment with PAH-approved vasoactive drugs seems convincing because ventilation-perfusion imbalance in the lung, which is the reason to avert the use of PAH-approved vasoactive drugs in lung disease-related PH, might be minimal in these diseases. However, the use of PAH-approved vasoactive drugs in these diseases has not been reported yet.

PH in Kyphoscoliosis

In a registry study of paediatric PH, only 2 patients with kyphoscoliosis were registered among 357 patients with confirmed PH, 52 of who had group 3 PH [11]. In a similar registry study of adult PH, none of the 1,344 patients with PH had kyphoscoliosis [12]. This may be due to the small number of patients with confirmed PH who were diagnosed using right heart catheterization among the patients with kyphoscoliosis and, of course, the small number of patients with kyphoscoliosis. Thus, it is difficult to discuss about PH in kyphoscoliosis as a single entity. However, the mechanisms of the development of PH in alveolar hypoventilation and hypoxemia may be common in diseases with alveolar hypoventilation. Load on the respiratory muscle is increased because the motion of the rib cage and diaphragm is anatomically limited in patients with kyphoscoliosis. Chronic fatigue of the respiratory muscle induces hypoventilation particularly in REM sleep. The alveolar hypoventilation during sleep increases PaCO2 and deranges the respiratory drive from the brain, which prolongs the duration of alveolar hypoventilation. This mechanism has been proven by nocturnal use of Non-Invasive Positive Pressure Ventilation (NIPPV), which improves daytime PaO2, PaCO2, and respiratory muscle performance, in patients with kyphoscoliosis [13-15].

Evidence concerning the effect of treatment on the prognosis of patients with kyphoscoliosis and PH is scarce. The basic concept of the treatment of PH related to kyphoscoliosis might be the same as that of the treatments of OSA and OHS, which is to normalize breathing particularly during sleep and improve respiratory drive. Nocturnal use of NIPPV, which assists ventilation during sleep, seems more suitable than CPAP, which is aimed at opening the upper respiratory tract during sleep, for patients with kyphoscoliosis. Oxygen therapy, in addition to NIPPV, might be effective because the main cause of PH might be hypoxic vasoconstriction of the pulmonary artery [16]. Oxygen therapy alone might be rather harmful, because it does not aid for attaining respiratory muscle rest but decrease respiratory drive [16]. Even with the use of NIPPV, PH develops in patients with kyphoscoliosis, like in OSA and OHS [14]. For this condition, PAH-approved vasoactive drugs may be used, although no case of using PAH-approved vasoactive drug has been reported, except for the present case in a patient with severe kyphoscoliosis who was still active in his work 3 years after the initiation of oxygen therapy and phosphodiesterase 5 inhibitor, with>10 years of nocturnal NIPPV [2]. The normal lung structure has been reported to be maintained except for microatelectasis induced by distortion and shortening of the thoracic cage; thus, the ventilation-perfusion imbalance will be minimal in the lungs of patients with kyphoscoliosis [17]. Therefore, deterioration of hypoxemia should not occur with the use of PAH-approved vasoactive drugs in patients with kyphoscoliosis.

Conclusion

Historically, it is a well-established fact that patients with PH in kyphoscoliosis have poor prognosis. PH develops in the presence of alveolar hypoventilation, similarly as other diseases with alveolar hypoventilation, such as OSA and OHS. Nocturnal NIPPV and supplemental oxygen therapy might be effective for the treatment of kyphoscoliosis-related PH. Furthermore, PH develops even after the initiation of these treatments. In this case, PAH-approved vasoactive drugs can be candidate therapies. We have reported the case of a patient with PH who responded well to a phosphodiesterase 5 inhibitor. PH that develops in patients with kyphoscoliosis could be treatable. Thus, it is important not to overlook the signs of PH in patients with kyphoscoliosis. Accumulating cases of kyphoscoliosis that are diagnosed with right heart catheterization and treated has been difficult. A prospective registry study is appropriate for establishing the treatment for kyphoscoliosis-related alveolar hypoventilation and PH, rather than the usual method of establishing guidelines for various diseases, such as in randomized controlled studies.

References

1. Bergofsky EH, Turino GM, Fishman AP (1959) Cardiorespiratory failure in kyphoscoliosis. Medicine 38: 263-318.
2. Okada S, Sugawara A, Yamagata S, Takeuchi S, Watanuki Z (2018) Pulmonary hypertension and its response to treatment in a patient with kyphosis-related alveolar hypoventilation. Intern Med 57: 1003-1006.
3. Galiè N, Humbert M, Vachiery JL, Gibbs S, Lang I, et al. (2016) 2015 ESC/ERS guidelines for the diagnosis and treatment of pulmonary hypertension: The joint task force for the diagnosis and treatment of pulmonary hypertension of the European Society of Cardiology (ESC) and the European Respiratory Society (ERS): Endorsed by: Association for European Paediatric and Congenital Cardiology (AEPC), International Society for Heart and Lung Transplantation (ISHLT). Eur Heart J 37: 67-119.
4. Piper A (2016) Obesity hypoventilation syndrome: Weighing in on therapy options. Chest 149: 856-868.
5. Chaouat A, Weitzenblum E, Krieger J, Oswald M, Kessler R (1996) Pulmonary hemodynamics in the obstructive sleep apnea syndrome: Results in 220 consecutive patients. Chest 109: 380-386.
6. Kessler R, Chaouat A, Schinkewitch P, Faller M, Casel S, et al. (2001) The obesity-hypoventilation syndrome revisited: A prospective study of 34 consecutive cases. Chest 120: 369-376.
7. Kauppert CA, Dvorak I, Kollert F, Heinemanna F, Jörres RA, et al. (2013) Pulmonary hypertension in obesity-hypoventilation syndrome. Respir Med 107: 2061-2070.
8. Arias MA, García-Río F, Alonso-Fernández A, Martínez I, Villamor J (2006) Pulmonary hypertension in obstructive sleep apnoea: Effects of

continuous positive airway pressure: A randomized, controlled cross-over study. Eur Heart J 27: 1106-1113.

9. Sugerman HJ, Baron PL, Fairman RP, Evans CR, Vetrovec GW (1988) Hemodynamic dysfunction in obesity hypoventilation syndrome and the effects of treatment with surgically induced weight loss. Ann Surg 207: 604-613.
10. Minai OA, Ricaurte B, Kaw R, Hammel J, Mansour M, et al. (2009) Frequency and impact of pulmonary hypertension in patients with obstructive sleep apnea syndrome. Am J Cardiol 104: 1300-1306.
11. Berger RMF, Beghetti M, Humpl T, Raskob GE, Ivy DD, et al. (2012) Clinical features of paediatric pulmonary hypertension: A registry study. Lancet 379: 537-546.
12. Hurdman J, Condliffe R, Elliot CA Davies C, Hill C, et al. (2012) ASPIRE registry: Assessing the spectrum of pulmonary hypertension identified at a REferral centre. Eur Respir J 39: 945-955.
13. Sawicka EH, Branthwaite MA (1987) Respiration during sleep in kyphoscoliosis. Thorax 42:801-808.
14. Smith IE, Laroche CM, Jamieson SA, Shneerson JM (1996) Kyphosis secondary to tuberculosis osteomyelitis as a cause of ventilatory failure: Clinical features, mechanisms and management. Chest 110: 1105-1110.
15. Nauffal D, Domènech R, Martínez García MA, Compte L, Macián V, et al. (2002) Noninvasive positive pressure home ventilation in restrictive disorders: Outcome and impact on health-related quality of life. Respir Med 96: 777-783.
16. Buyse B, Meersseman W, Demedts M (2003) Treatment of chronic respiratory failure in kyphoscoliosis: Oxygen or ventilation? Eur Respir J 22: 525-528.
17. Turino GM, Goldring RM, Fishman AP (1965) Cor pulmonale in musculoskeletal abnormalities of the thorax. Bull N Y Acad Med 41: 959-980.