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Year Book of MEDICINE 2020

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Interstitial Lung Disease

ARTICLE 1

Effect of pulmonary rehabilitation (PR) program in patients with interstitial lung disease (ILD)–Indian scenario

Devani P, Pinto N, Jain P, Prabhudesai P, Pandey A. Effect of Pulmonary Rehabilitation (PR) Program in Patients with Interstitial Lung Disease (ILD)–Indian scenario.

J Assoc Physicians India. 2019;67:28-33.

Abstract

Introduction: Interstitial lung diseases (ILDs) are group of disorders wherein due to varied etiologies, interstitium goes into progressive inflammation or fibrosis. Although the awareness has improved but, the therapy is still facing challenges. Pulmonary rehabilitation (PR) is a worthy modality, which not only supports but also imparts evident benefits in these patients.

Materials and methods: The study is a retrospective observational study conducted over a period of 2 years at "pulmonary rehabilitation center", a private clinic setup on patients with different restrictive lung diseases such as ILDs, neuromuscular disorders, and postsurgical patients. A total of 100 patients were enrolled, out of which 21 patients were lost to follow-up. The study population included 34% males and 66% females with a mean age of 56.3 ± 14.2 years. Around 24 patients required oxygen support (where SpO_2 <90% at baseline). Outcome measures were assessed in these patients at the time of enrollment into the program (0 week) and at the end of the program (8 weeks). Effect of PR program was then analyzed with appropriate statistical methods.

Results: Overall, statistically significant benefits were noted in 6-minute walk distance (6MWD), muscle strength, dyspnea, and quality of life with 8 weeks. The mean 6 MWTD was 297.9 m pre-PR, which improved to 359.7 m at the completion of 8 weeks post PR. Mean difference was 61.8 m, which was found to be statistically significant (p value < 0.001). Improvement in muscle strength of different upper and lower limb muscle groups were noted. Also, significant improvement in comprehensive score of chronic respiratory diseases questionnaire (CRDQ) scores was documented. Statistically significant improvement was found in the dyspnea, fatigue, and emotional components. However, mastery components did not show statistically significant change.

Conclusion: Pulmonary rehabilitation has proven to be a very useful modality in the management of restrictive lung diseases, especially with the known limitations of pharmacological options to treat this disabling chronic lung diseases, even with those with evident type I respiratory failure at the beginning.

"Nothing is to be found that can substitute for exercise in any way....Exercise is only one of the components of rehabilitation."

COMMENT

Pulmonary rehabilitation (PR) is a supervised and structured program that involves a multidisciplinary approach in the management of certain chronic lung conditions. PR consists of

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exercise training and breathing techniques, health education, nutrition and psychological supports. PR is beneficial in that it helps to decrease the symptoms (dyspnea and fatigue) as well as to improve quality of life and exercise tolerance. In addition, it causes reduction of healthcare utilization (particularly bed-days) and increase in physical activity. Benefits of PR in cases of chronic obstructive pulmonary disease (COPD) have been shown in several studies in the past; therefore, PR constitutes an essential component of its management.

Unlike in case of COPD, there is much less experience with PR in patients with chronic interstitial lung diseases (ILDs) who suffer from progressive breathlessness and respiratory disability. Nonetheless, the limited data from a few studies support its role to improve both short-term and long-term outcomes in these patients. In a Cochrane Library Systematic Data Review, the authors found low-to-moderate quality of evidence in favor of PR as safe for patients with ILD causing improvements in functional exercise capacity, dyspnea, and quality of life.[1] But, there was little evidence regarding longer-term benefits.

There are very few reports from India on PR in different diseases. It is generally considered as a labor-intensive and time-consuming method of management. The authors of this study analyzed their retrospective data of 100 patients with restrictive lung disease seen in a 2-year period. Final data were available in only 79 patients since 21 were lost to follow-up. After 8 weeks of PR, there was significant improvement in 6-minute walk distance (6MWD), muscle strength, and quality of life. The authors also report improvement of symptoms such as dyspnea, fatigue, and emotional components.

The present study included patients with restrictive diseases such as neuromuscular disorders and postsurgical patients with generally healthy lungs. These disorders do not necessarily behave like parenchymal ILD with progressive fibrosis. Therefore, the benefit cannot be directly applied to different kinds of ILDs. Importantly, however, the authors have taken a step toward the institution of a regular program of PR in patients with different diseases. Such a step should significantly help in the development of similar programs in other chronic pulmonary disorders.

Key Messages

- ***Pulmonary rehabilitation caused significant improvement in 6-minute walk distance (6MWD), muscle strength, and quality of life in patients with restrictive lung disease.***
- ***Pulmonary rehabilitation also causes symptomatic improvement of dyspnea, fatigue, and emotional components.***

ARTICLE 2

The natural history of progressive fibrosing interstitial lung diseases

Kolb M, Vašáková M. The natural history of progressive fibrosing interstitial lung diseases.
Respir Res. 2019;20:57.

Abstract

A proportion of patients with certain types of interstitial lung disease (ILD), including chronic hypersensitivity pneumonitis and ILDs associated with autoimmune diseases, develop a progressive fibrosing phenotype that shows similarities in clinical course to idiopathic pulmonary fibrosis (IPF). Irrespective of the clinical diagnosis, these progressive fibrosing ILDs show commonalities in the underlying pathogenetic mechanisms that drive a self-sustaining process of pulmonary fibrosis. The natural history of progressive fibrosing ILDs is characterized by decline in lung function, worsening of symptoms and health-related quality of life, and early mortality. Greater impairment in forced vital capacity (FVC) or diffusion capacity

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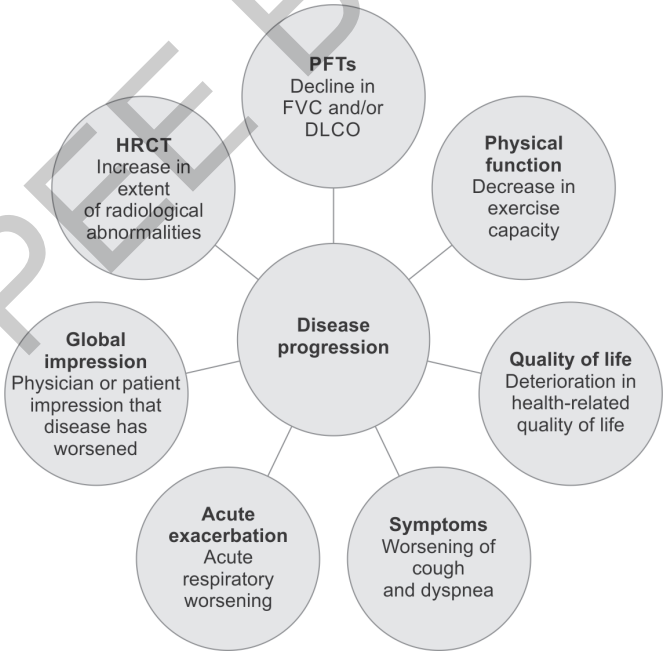
of the lungs for carbon monoxide and a greater extent of fibrotic changes on a computed tomography scan are predictors of mortality in patients with fibrosing ILDs. However, the course of these diseases is heterogenous and cannot accurately be predicted for an individual patient. Data from ongoing clinical trials and patient registries will provide a better understanding of the clinical course and impact of progressive fibrosing ILDs.

"All pulmonary fibrosis is not idiopathic pulmonary fibrosis (IPF)."

COMMENT

After nearly 2 decades of characterizing idiopathic interstitial pneumonias into distinct histopathological entities and determining specific treatment protocols for these subtypes, we are beginning to understand that up to 40% of interstitial lung diseases (ILDs) with histological features other than usual interstitial pneumonia (UIP) can evolve into the so-called "progressive fibrosing ILDs (PF-ILD), whose disease behavior mirrors that of UIP. Some ILDs known to progress thus include connective tissue disease-related ILDs (rheumatoid arthritis, systemic sclerosis, and polymyositis/dermatomyositis), chronic sarcoidosis, chronic hypersensitivity pneumonitis, idiopathic nonspecific interstitial pneumonia, and some unclassifiable ILDs. The possible pathogenetic mechanisms contributing to PF-ILD include recurrent epithelial and vascular injury resulting in an unregulated fibroblast migration and proliferation, and fibrosis.

In this review, Kolb and Vasakova have reviewed literature pertaining to the natural history of PF-ILDs. The authors discuss various physiological indicators, serum biomarkers, and genetic variations in PF-ILD and their relation to rate of disease progression and mortality (**Fig. 1**).



(DLCO: diffusing capacity of the lungs for carbon monoxide; FVC: forced vital capacity; HRCT: high-resolution computed tomography; PFT: pulmonary function test)

FIG. 1: Factors affecting progression of various nonidiopathic pulmonary fibrosis interstitial lung diseases (IPF ILDs).
Courtesy: Adapted from the article under discussion.

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Most of the studies reviewed in this article pertain to individual categories of ILD and thus the statistical figures are heterogenous. However, a common theme that emerges is that a poorer pulmonary function at diagnosis [forced vital capacity (FVC) and diffusing capacity of the lungs for carbon monoxide (DLCO)], increased rate of decline of FVC (>10%) and DLCO, a greater degree of fibrosis on CT, and propensity for exacerbations characterizes this subset of patients and determines mortality. Besides, serum biomarkers of progression to fibrosis such as KL-6 (Kerbs von den Lungen-6 protein), Matrix metalloproteinase-7, surfactant protein-D and serum collagen degradation products are being evaluated as prognostic indicators. Certain genetic changes reported in idiopathic pulmonary fibrosis (IPF) such as the *MUCB* single nucleotide polymorphisms and short telomere length have been reported with rheumatoid arthritis-related interstitial lung disease (RA-ILD) and chronic hypersensitivity pneumonitis respectively.

This review summarizes the available diverse literature on PF-ILD and drives home the point that initial histological radiological characterization does not predict progression of non-UIP ILD and that identification of indicators of progression is important at diagnosis and during follow-up. There is also an emerging indication for the use of antifibrotic agents in the subset of patients who evolve to PF-ILD.

FURTHER READING

1. Collins BF, Raghu G. Eur Respir Rev. 2019;28(153):190022.
2. Cottin V, Wollin L, Fischer A, Quaresma M, Stowasser S, Harari S. Fibrosing interstitial lung diseases: knowns and unknowns. Eur Respir Rev. 2019;28:180100.

Key Messages

- ***Although histopathological and radiological characterization of ILD can help prognostication, emerging evidence indicates that many categories of non-UIP ILD can progress to the fibrosing phenotype.***
- ***It is very important to assess disease progression using spirometric, radiological, and possibly serological markers during follow-up for early identification of progression to PF-ILD.***

ARTICLE 3

Clinical effectiveness of antifibrotic medications for idiopathic pulmonary fibrosis

Dempsey TM, Sangaralingham LR, Yao X, Sanghavi D, Shah ND, Limper AH. Clinical effectiveness of antifibrotic medications for idiopathic pulmonary fibrosis.
Am J Respir Crit Care Med. 2019;200:168-74.

Abstract

Rationale: Since their approval, there has been no real-world or randomized trial evidence evaluating the effect of the antifibrotic medications pirfenidone and nintedanib on clinically important outcomes such as mortality and hospitalizations.

Objectives: To evaluate the clinical effectiveness of the antifibrotic medications pirfenidone and nintedanib in patients with idiopathic pulmonary fibrosis (IPF).

Methods: Using a large US insurance database, we identified 8,098 patients with IPF between October 1, 2014 and March 1, 2018. A one-to-one propensity score-matched cohort was created to compare patients treated with antifibrotic medications (n = 1,255) with those not on treatment (n = 1,255). The primary

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outcome was all-cause mortality. The secondary outcome was acute hospitalizations. Subgroup analyses were performed to evaluate mortality differences by drug.

Measurements and main results: The use of antifibrotic medications was associated with a decreased risk of all-cause mortality [hazard ratio (HR) 0.77; 95% confidence interval (CI) 0.62–0.98; p value = 0.034]. However, this association was present only through the first 2 years of treatment. There was also a decrease in acute hospitalizations in the treated cohort (HR 0.70; 95% CI 0.61–0.80; p value < 0.001). There was no significant difference in all-cause mortality between patients receiving pirfenidone and those on nintedanib (HR 1.14; 95% CI 0.79–1.65; p = 0.471).

Conclusions: Among patients with IPF, antifibrotic agents may be associated with a lower risk of all-cause mortality and hospitalization compared with no treatment. Future research should test the hypothesis that these treatments reduce early, but not long-term, mortality as demonstrated in our study.

"Antifibrotics in IPF: Does it buy time?"

COMMENT

Idiopathic pulmonary fibrosis (IPF) is a progressive and irreversible lung disease with a median survival of 3–5 years. In this article, the authors have attempted to unravel an unanswered aspect in treatment of IPF; namely, the mortality benefit and reduction in hospitalization among patients treated with pirfenidone or nintedanib. A retrospective cohort was built from a large private insurance database from 2014 to 2018; propensity score-matching yielded 1,255 pairs of patients with IPF who were treated or untreated.

All-cause mortality was reduced both in the pirfenidone and nintedanib group with hazard ratio (HR) of 0.77; hospitalization was also reduced by 30% in the treated group. Pirfenidone showed better mortality benefit than nintedanib, although this was statistically insignificant. Nevertheless, nintedanib reduced the risk of acute exacerbation. However, the mortality benefit with either antifibrotic did not extend beyond 2 years of therapy.

This study adds a silver lining to patients diagnosed with a progressive and fatal disease, for whom no treatment existed or was harmful, prior to the advent of antifibrotics. Prior CAPACITY (Clinical Studies Assessing Pirfenidone in IPF: Research of Efficacy and Safety Outcomes) and ASCEND (Assessment of Pirfenidone to Confirm Efficacy and Safety in IPF) studies, evaluating pirfenidone, have shown reduction in risk of death or disease progression by 38%. The INPULSIS-1 and -2 studies have also proven fall in forced vital capacity (FVC) of 125 mL/year in patients treated with nintedanib as opposed to 236 mL/year in untreated patients.

Although unmeasured confounders could account for some of the observed effect in this type of observational study, newer evidences, such as the INSIGHTS-IPF (INvestigating SIGnificant Health TrendS in Idiopathic Pulmonary Fibrosis) registry from Germany and the French National Health System claim data, also support the benefits from treatment with antifibrotics. Many trials such as INJOURNEY^{TM} have explored the safety and tolerability of combined therapy with pirfenidone and nintedanib.

The important aspect of reduced mortality and acute exacerbations addressed by the antifibrotics are proven in a clinical setting in this study. This finding raises pertinent questions for further research pathways as shown in **Figure 1**. Large multicentric randomized controlled trials (RCTs) with multiple collaborators and funding are needed to address these issues.

FURTHER READING

1. Behr J, Prasse A, Wirtz H, Koschel D, Pittrow D, Held M, et al. Survival and course of lung function in the presence or absence of antifibrotic treatment in patients with idiopathic pulmonary fibrosis: long-term results of the INSIGHTS-IPF registry. Eur Respir J. 2020:1902279. [online ahead of print].
2. Torrisi SE, Pavone M, Vancheri A, Vancheri C. When to start and when to stop antifibrotic therapies. Eur Respir Rev. 2017;26:170053.

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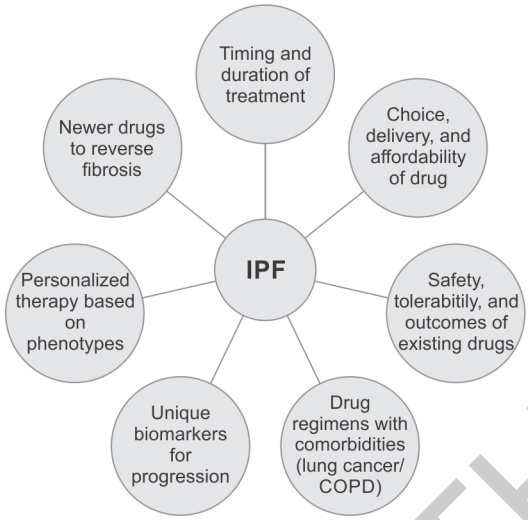

(COPD: chronic obstructive pulmonary disease)

FIG. 1: Future directions in idiopathic pulmonary fibrosis (IPF) management.

Key Message

- ***The antifibrotics, either pirfenidone or nintedanib, used in treatment for IPF reduce the risk of all-cause mortality and acute hospitalizations.***

ARTICLE 4

Nintedanib in progressive fibrosing interstitial lung diseases

Flaherty KR, Wells AU, Cottin V, Devaraj A, Walsh SLF, Inoue Y, et al. Nintedanib in progressive fibrosing interstitial lung diseases. ***N Engl J Med. 2019;381:1718-27.***

Abstract*

Background: Nintedanib, an intracellular inhibitor of tyrosine kinases, is known to slow down the progression of lung fibrosis. Although its efficacy has been shown in idiopathic pulmonary fibrosis (IPF), it is not known if shows the same effect across a broad range of fibrosing lung diseases.

Methods: A double-blind, placebo-controlled, randomized phase 3 trial was conducted in 15 countries in which patients with fibrosing lung disease affecting >10% of lung volume on high-resolution computed tomography (CT) received either nintedanib at a dose of 150 mg twice daily or placebo. All the patients met criteria for progression of interstitial lung disease in the past 24 months despite treatment and had a forced vital capacity (FVC) of at least 45% of the predicted value and a diffusing capacity of the lung for carbon monoxide ranging from 30 to 80% of the predicted value. Stratified randomization according to the fibrotic pattern [a pattern of usual interstitial pneumonia (UIP) or other fibrotic patterns] on high-resolution CT was done. The annual rate of decline in the FVC assessed over a 52-week period was the primary outcome which was observed in the overall population and patients with a UIP-like fibrotic pattern.

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Results: A total of 663 patients were treated. In the overall population, the adjusted rate of decline in the FVC was –80.8 mL/year and –187.8 mL/year with nintedanib and placebo, respectively. The between-group difference was 107.0 mL/year [95% confidence interval (CI) 65.4–148.5; p < 0.001). In patients with a UIP-like fibrotic pattern, the adjusted rate of decline in the FVC was –82.9 mL/year and –211.1 mL/year with nintedanib and placebo, respectively. Here, the between-group difference was 128.2 mL (95% CI 70.8–185.6; p < 0.001). Diarrhea was reported in 66.9% and 23.9% of patients treated with nintedanib and placebo, respectively. Also, nintedanib group was more commonly associated with abnormalities on liver-function testing.

Conclusion: Nintedanibin is associated with lower annual rate of decline in FVC of patients with progressive fibrosing interstitial lung diseases, as compared to placebo. Diarrhea was a common adverse event. *Redrafted abstract

"The person who takes medicine must recover twice, once from the disease and once from the medicine."

—William Osler

COMMENT

Treatment of interstitial lung disease (ILD) has undergone a sea change in the last decade with the addition of new antifibrotics such as pirfenidone and nintedanib while older combinations of medicines such as N-acetyl cysteine and immunosuppressant combinations becoming discredited.[2] However, most of the newer studies have targeted patients suffering from idiopathic pulmonary fibrosis (IPF), while other ILDs were mostly ignored.

A new paradigm in the treatment of ILDs has been the description of the phenotype of "progressive fibrosing ILDs (PF-ILD)". Conceptually, it suggests that all ILDs, regardless of cause, enter a final common phase characterized by progressive fibrosis and respiratory failure with common pathophysiological mechanisms of progression. At this stage, the individual aspects of the ILD are diluted down and symptoms are mainly due to progressive fibrosis. Therefore, treatment with antifibrotic medication should be effective in any ILD which has reached this phase.[3] One of the main trials in this area was the SENSCIS™ (The Safety and Efficacy of Nintedanib in SystemIc Sclerosis) trial, in which patients with systemic sclerosis associated ILD were treated with nintedanib and showed a favorable outcome.[4]

The INBUILD trial builds on the aforementioned concept where patients diagnosed to have PF-ILD were treated for nintedanib for 1 year. It was a multicenter, double-blind, placebo-controlled, phase 3 randomized control trial. A total of 663 patients were randomized to either placebo (n = 331) or nintedanib (n = 332) 150 mg twice a day daily for 1 year. The inclusion criteria for the study population included patients who, in the past 2 years, had (i) a relative decline in the FVC of at least 10% of the predicted value, or (ii) a relative decline in the FVC of 5% to <10% of the predicted value and worsening of respiratory symptoms or an increased extent of fibrosis on high-resolution CT, or (iii) worsening of respiratory symptoms and an increased extent of fibrosis on high-resolution CT. Patients were allowed to take immunosuppressant medications for up to 4 weeks before start of trial by were excluded if they had taken nintedanib or pirfenidone previously. The study included mild-to-moderate patients of ILD.

The results were studied in four groups—placebo group, treatment effect in patients with usual interstitial pneumonia (UIP) pattern on CT, treatment effect in patients with non-UIP pattern, and in the overall population. The primary study endpoint was the rate of decline of forced vital capacity (FVC) at 1 year while the secondary endpoints were the change in K-BILD score (a respiratory questionnaire for quality of life), acute exacerbation, and death rates. It was found that use of nintedanib for 1 year led to a reduction of the decline of FVC in the treatment group as compared to the placebo groups. The difference in the overall population was –80.8 mL/year with

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nintedanib and –187.8 mL/year with placebo, while in patients with a UIP-like fibrotic pattern it was –82.9 mL/year with nintedanib and –211.1 mL/year with placebo, for a difference of 128.2 mL. In patients with a non-UIP-like fibrotic pattern it was –79.0 mL/year in the nintedanib group and –154.2 mL/year in the placebo group (between-group difference, 75.3 mL). The hazard ratios for acute exacerbations and death were also better with nintedanib. Adverse effects were on expected lines with diarrhea and liver function test abnormalities being associated with nintedanib use.

This trial is the first study to show usefulness of nintedanib in non-IPF-ILDs with a progressive fibrosing phenotype. The place of nintedanib in these patients would be probably after the initial, nonfibrotic phase of illness which has not responded to conventional treatment. The results are significant and if the reduction of the rate of decline of FVC persists with use beyond 1 year it would translate to a significant benefit over time. However, we have to wait for long-term data to trickle in before making any conclusion. For the time being, it can be said that a new weapon has been added to the armamentarium!

Key Message

- ***Nintedanib is also useful for non-IPF patients who show a progressing fibrosing phenotype.***

Airway Disease

ARTICLE 5

Association of indoor air pollution with allergic respiratory diseases in paediatric population residing in national capital region

Kumar R, Singh K, Nagar JK, Mavi AK, Kumar M, Kumar D. Association of indoor air pollution with allergic respiratory diseases in paediatric population residing in national capital region.
Indian J Chest Dis Allied Sci. 2019;61:181-97.

Abstract

Background: World Health Organization (WHO) has observed that around seven million people died every year globally due to indoor air pollution. The purpose of this study is to evaluate the effect of indoor air pollution on respiratory health [bronchial asthma (BA) and/or allergic rhinitis (AR)] in a pediatric population in the National Capital Region (NCR) of Delhi, India.

Methods: A cross-sectional study to assess the factors responsible for respiratory diseases (BA and/or AR) in homes in rural areas of National Capital Region (NCR), India, was done. Around 61 households where at least one child who had symptoms of BA/AR (case households; Group A) and another 61 households with children without any symptom of BA/AR (Group B) were selected for the study. A standard questionnaire was used to collect the information about the health status of children and pollution levels in these homes.

Results: A total of 95 (43.8%) children in Group A households were found to have history of allergic respiratory diseases (n = 43–BA, n = 19–AR) while 33 children had both BA and AR. There was a statistically significant difference in the 24-hour particulate matter concentration (24 h) PM2.5 (p = 0.01) and 6-hour concentration of PM10 (p = 0.02) in Group A households as compared to Group B households. The 6-hour concentration of PM2.5 and PM1 and 12-hour concentration of volatile organic compounds (VOCs) was found to be higher in households of Group A. Group A households also had a higher number of smokers and usage of kerosene oil for lighting of lamps.

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Conclusions: Tobacco smoking, use of kerosene oil for lighting and combustion of solid fuel for cooking results in an increased level of particulate matter, and VOCs in indoor air are the major contributing factors for respiratory illness in the pediatric population.

"Respiratory disease is the index of air we breathe—more so in children."

COMMENT

Most people, particularly the children, spend 12–18 hours every day in their homes. This is about half to two-thirds of their daily indoor time. Therefore, the indoor air is far more important for health. Indoor air pollution (IAP) these days is better referred to as household air pollution (HAP) because of the continuous exchange of indoor and outdoor air. World-over, HAP is an important issue in being responsible for adverse health effects for both children and adults. The list of diseases caused by IAP or HAP is rather large. In particular, the burden of cardiorespiratory illnesses caused and/or aggravated by exposure to HAP is quite significant.[5] There is proven association of HAP with presence of general respiratory symptoms, infections, and chronic obstructive pulmonary disease. There is also some evidence to suggest its relationship with exacerbations of asthma necessitating increased healthcare utilization. But, there is ambiguity whether HAP is also responsible for an increased prevalence of respiratory allergies including allergic rhinitis (AR) and bronchial asthma (BA).

Kumar and colleagues in this paper have studied the factors responsible for IAP in homes in rural areas of National Capital Region (NCR). They selected 61 households with presence of at least one child with history of respiratory diseases (BA and/or AR) and 61 households with children without any symptom of BA/AR. They found higher 6-hour concentrations of particulate matter (PM2.5 and PM1) and 12-hour concentration of volatile organic compounds (VOCs) in households with presence of children with respiratory allergies. The number of smokers and usage of kerosene oil for lighting of lamps was also higher in these households. The evidence suggests a causal relationship of indoor pollutants with AR and asthma.

The study is rather small for an epidemiological interpretation. But, the authors have measured and compared the concentrations of particulate pollutants and VOCs in households with and without children suffering from nasobronchial allergies. They have convincingly shown a higher prevalence of respiratory allergies in households with higher levels of HAP. This is a significant addition to our existing knowledge about the possible adverse effects of IAP or HAP on respiratory disease. Both AR and BA are responsible for an enormous morbidity. This is particularly so in children in whom it is responsible for ill health, school absenteeism, and poor development of lung function. The observations raise the need to study the subject in larger samples among different populations.

Key Messages

- ***Households with children suffering from nasobronchial allergies had higher concentrations of indoor air-pollutants.***
- ***Increased levels of particulate matter and VOCs in indoor air are the major contributing factors for respiratory illness in the pediatric population.***

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ARTICLE 6

Diffusing capacity of carbon monoxide in assessment of COPD

Balasubramanian A, MacIntyre NR, Henderson RJ, Jensen RL, Kinney G, Stringer WW, et al. Diffusing capacity of carbon monoxide in assessment of COPD.
Chest. 2019;156:1111-9.

Abstract

Background: Diffusing capacity of the lung for carbon monoxide (DLCO) is inconsistently obtained in patients with chronic obstructive pulmonary disease (COPD), and the added benefit of DLCO testing beyond that of more common tools is unknown.

Objective: The goal of this study was to determine whether lower DLCO is associated with increased COPD morbidity independent of emphysema assessed via spirometry and CT imaging.

Methods: Data for 1,806 participants with COPD from the genetic epidemiology of COPD (COPDgene) study 5-year visit were analyzed including pulmonary function testing, quality of life (QoL), symptoms, exercise performance, and exacerbation rates. DLCO% predicted was primarily analyzed as a continuous variable and additionally categorized into four groups: (1) DLCO and forced expiratory volume in 1 second (FEV1) >50%; (2) only DLCO ≤50%; (3) only FEV1 ≤50%; and (4) both ≤50% predicted. Outcomes were modeled by using multivariable linear and negative binomial regression including emphysema and FEV1% predicted among other confounders.

Results: In multivariable analyses, every 10% predicted decrease in DLCO was associated with symptoms and QoL [COPD assessment test: 0.53 ($p < 0.001$); St George's respiratory questionnaire: 1.67 ($p < 0.001$); Medical Outcomes Study Short Form 36 Physical Function: –0.89 ($p < 0.001$)], exercise performance (6-minute walk distance: –45.35 feet; $p < 0.001$), and severe exacerbation rate (rate ratio: 1.14; $p < 0.001$). When categorized, severe impairment in DLCO alone, FEV1 alone, or both DLCO and FEV1 were associated with significantly worse morbidity compared with the reference group ($p < 0.05$ for all outcomes).

Conclusions: Impairment in DLCO was associated with increased COPD symptoms, reduced exercise performance, and severe exacerbation risk even after accounting for spirometry and CT evidence of emphysema. These findings suggest that DLCO should be considered for inclusion in future multidimensional tools assessing COPD.

Trial registration: ClinicalTrials.gov NCT00608764.

"The missing link in chronic obstructive pulmonary disease (COPD) profiling?"

COMMENT

Chronic obstructive pulmonary disease (COPD) has been conventionally diagnosed with a combination of pertinent clinical history and spirometry. With the expansion of knowledge on diverse disease behavior, multidimensional profiling of COPD is becoming the norm with spirometry, effort tolerance, and quality of life (QoL) measures being included as part of the standard workup for COPD. Although serum biomarkers and additional pulmonary function measurements are being studied as indicators of disease progression and frequent exacerbations, they have not found widespread use in COPD phenotype profiling (**Fig. 1**).

Among the pulmonary function parameters, diffusing capacity of the lung for carbon monoxide (DLCO) is a sparingly used modality to prognosticate COPD except in the context of patients with emphysema, where impaired DLCO has been demonstrated and has been postulated

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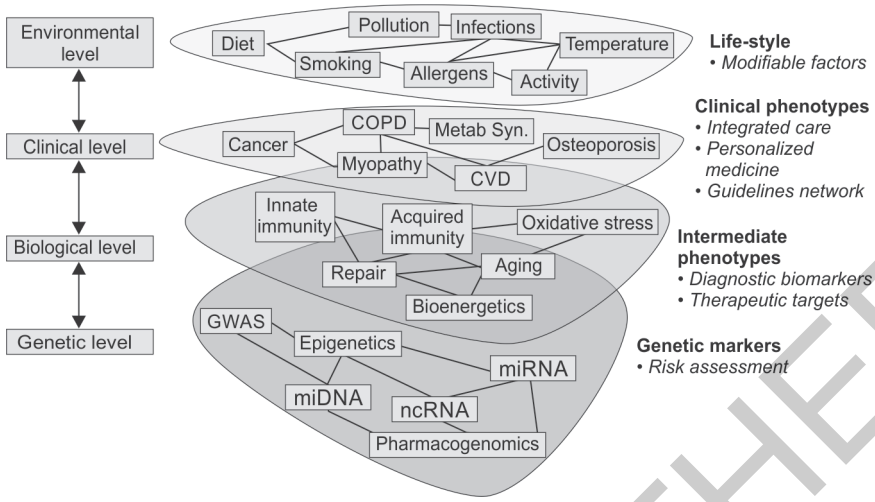

(CVD: cardiovascular disease; GWAS: genome-wide association studies; miDNA: mitochondrial deoxyribonucleic acid; miRNA: micro ribonucleic acid; ncRNA: noncoding ribonucleic acid)

FIG. 1: A model for phenotypes and endotypes in chronic obstructive pulmonary disease (COPD).
Source: Adapted from Agusti A, Vestbo J. Current controversies and future perspectives in chronic obstructive pulmonary disease. Am J Respir Crit Care Med. 2011;184:507-13.

to result from destruction of the airspace and capillary membrane. However, the association of impaired DLCO with QoL and exacerbations independent of emphysema has not been studied.

In this study, Balasubramaniam et al. have hypothesized that DLCO, independent of forced expiratory volume in 1 second (FEV1) and quantitative CT measures of emphysema, is associated with worse COPD morbidity. They classified 1,806 patients from the COPDgene cohort into four subgroups based on FEV1 and DLCO (DLCO and FEV1 >50%, only DLCO <50%, only FEV1 <50%, and both <50% predicted) and analyzed the association between isolated and combined impairment of these parameters with morbidity indicators such as symptoms, QoL, exercise performance, and exacerbations. On multivariate analysis, they found that a lower predicted DLCO alone was associated with increased COPD morbidity, independent of FEV1 values and the presence of emphysema on quantitative CT.

This study raises the interesting possibility of including DLCO as a standard of care test in the initial assessment as well as follow-up of patients with COPD as it can be used as a predictor of worsening symptoms, effort tolerance, and development of acute exacerbations. An improvement in DLCO can also be used as a predictor of the efficacy of pulmonary rehabilitation.

FURTHER READING

1. Boutou AK, Shrikrishna D, Tanner RJ, Smith C, Kelly JL, Ward SP, et al. Lung function indices for predicting mortality in COPD. Eur Respir J. 2013;42(3):616-25.
2. Nambu A, Zach J, Schroeder J, Jin GY, Kim SS, Kim YI, et al. Relationships between diffusing capacity for carbon monoxide (DLCO), and quantitative computed tomography measurements and visual assessment for chronic obstructive pulmonary disease. Eur J Radiol. 2015;84(5):980-5.

Key Messages

- ***As precision medicine is being increasingly employed in the management of chronic respiratory diseases, sparingly used diagnostic tests have come to the forefront as markers of disease severity and progression.***
- ***Diffusing capacity of the lung for carbon monoxide is one among these tests, which can be used at baseline and at follow-up to assess progression as well as response to treatment.***

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ARTICLE 7

Low and high blood eosinophil counts as biomarkers in hospitalized acute exacerbations of COPD

MacDonald MI, Osadnik CR, Bulfin L, Hamza K, Leong P, Wong A, et al. Low and high blood eosinophil counts as biomarkers in hospitalized acute exacerbations of COPD.
Chest. 2019;156:92-100.

Abstract

Background: Characterizing acute exacerbations of chronic obstructive pulmonary disease (AECOPD) and individualizing therapy is challenging. Key exacerbation therapies include antibiotics and systemic corticosteroids. Blood eosinophils, when either low or high, may offer a simple and inexpensive distinction to predict beneficial responses to these therapies.

Methods: We conducted derivation (n = 242) and validation (n = 99) cohort studies of patients hospitalized for AECOPD. Patients who received oral corticosteroids before emergency department (ED) presentation were excluded. The derivation cohort was identified by individual case file review. The validation cohort was prospectively recruited during hospital admission. Exacerbations were grouped according to blood eosinophil count as low (<50/μL), normal (50–150/μL), or high (>150/μL). Exacerbations were classified as being associated with infection if either virus testing was positive or C-reactive protein was ≥20 mg/L. Associations of eosinophil groups with infection, hospital length of stay, and 12-month survival were compared using appropriate statistical methods.

Results: There were no significant differences in baseline characteristics between patients with low, normal, or high-blood eosinophils in either cohort. Eosinophil counts <50/μL were more strongly associated with infection (91 vs. 51.9%, p = 0.001), distinguished patients with longer median hospital stays (7 vs. 4 days, p < 0.001), and were associated with lower 12-month survival (82.4 vs. 90.7%, p = 0.028; pooled data of both cohorts) than eosinophil counts >150/μL.

Conclusions: Low and high blood eosinophil counts in hospitalized patients with AECOPD provide a practical clinical distinction that can potentially be used to inform management strategies. Prospective studies are needed to evaluate if this strategy can guide discriminate use of antibiotics and/or corticosteroids.

"Blood eosinopenia in acute exacerbations of chronic obstructive pulmonary disease (AECOPD): A new phenotype?"

COMMENT

Chronic obstructive pulmonary disease (COPD) is a disease where fixed airway obstruction is the common denominator, but varied symptomatology and response to existing therapies contribute to its heterogeneity and variable disease trajectory.

Approximately 15–40% of COPD exacerbations are eosinophil driven with no evidence of infection. The GOLD (Global initiative for chronic Obstructive Lung Disease) guidelines have incorporated the role of inhaled corticosteroids (ICS) in patients with >3% (>300 cells/mL) eosinophils and in frequent exacerbators.

The authors have used eosinophil count as a simple biomarker to help in decision making in the treatment of acute exacerbation of chronic obstructive pulmonary disease (AECOPD). A retrospective derivation cohort of 242 subjects with AECOPD was followed up with a prospective validation cohort of 99 subjects with AECOPD. Associations between eosinopenia (<50/mm^3), high eosinophil counts (>150/mm^3) and clinical outcomes were evaluated. Infective or noninfective causes of the AECOPD were based on results of viral polymerase chain reaction (PCR) and C-reactive

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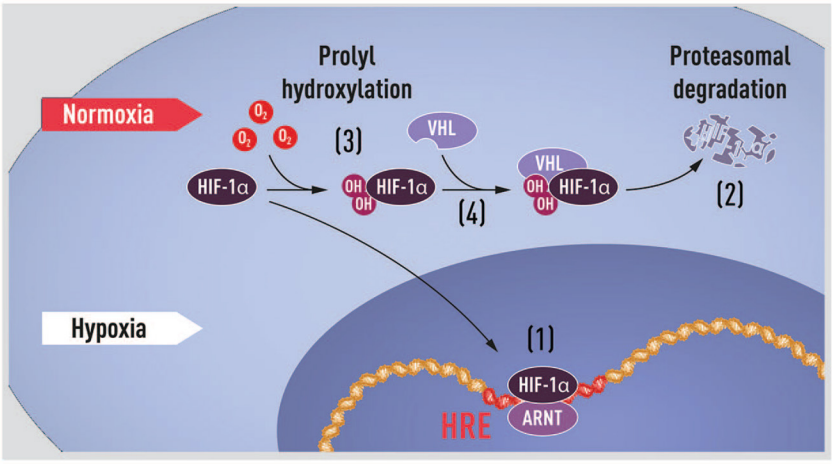
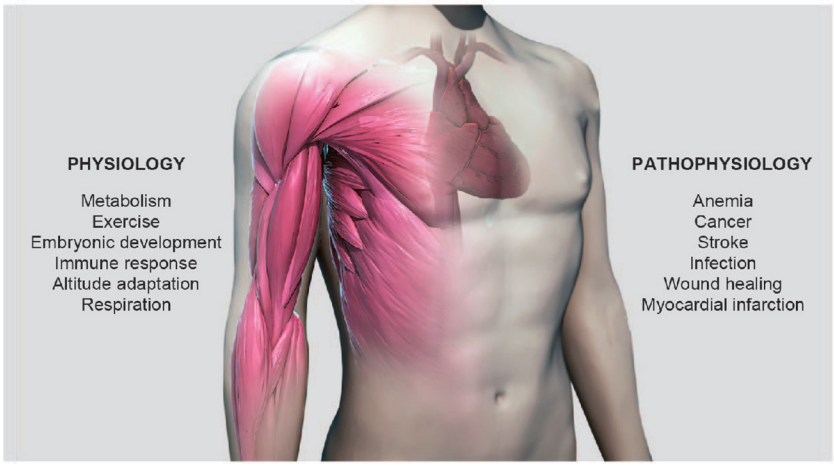
The Noble Prize for Physiology or Medicine 2019

The Noble Prize for Physiology or Medicine 2019 was awarded jointly to **William G. Kaelin, Jr,** *Massachusetts, USA*, **Sir Peter J. Ratcliffe**, *London, UK* and **Gregg L. Semenza**, *Maryland, USA*, "for their discoveries of how cells sense and adapt to oxygen availability."





Oxygen sensing is central to a large number of diseases. Intense ongoing research efforts are now focused on developing drugs that can interfere with different disease states by either activating, or blocking, the oxygen-sensing machinery.

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