CICM (India) Respiratory Updates

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Editorial Board

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CICM (India)

Respiratory Updates

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From Chairman's desk

Dear friends

Best wishes from Saans Foundation, New Delhi.

Saans foundation has come long way since its inception in 2000. Advocacy and structured manner of handling patients have really helped in creating confidence in our cohorts. Every patient is handled in a systematic way and a structured protocol is followed .Thanks to our team of professionals who have painstakingly dedicated their life for patient care. Our core competence in Respiratory and Sleep care is slowly reaching to deeper pockets of society.

Saans Foundation initiative with Fourts pharmaceuticals , Clinics in Chest Medicine, CICM India is innovative academic platform to connect like minded professionals and CICM is working very cohesively to help patients and professionals for better insights and structured patient care management.

Ever since it's inception at our inaugural conference at Le Meriden, New Delhi December 15, 2019, CICM, India is slowly reaching out to professionals.

CICM tag line a journey from " innovation to evolution" is aiming to connect all relevant to respiratory care practices through its tailor made tools and digital technology. Our community outreach initiatives like FIGHT COVID initiatives, Professional manual on respiratory diseases, Hands on work shop to Webinar meets have been hugely appreciated. Healer award to commemorate professionals who has been working with COVID patients is an commendable gesture of CICM.

Our newsletter is primarily aiming to create awareness in the society so that good practice parameters can be followed and doctor patient relationship becomes healthier.

The need of the hour is a good simple community awareness and academic newsletter covering important relevant to current scenario. Our vision is to create awareness so the community at large can learn to live better through regular physical activity, nutrition guidelines, correct treatment and right preventive approach guidelines and the latest trends in respiratory.

Warm personal regards
Dr. PP Bose
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What's new in pulmonary and critical care medicine

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ASTHMA

Risk factors for thunderstorm asthma (July 2022)

"Thunderstorm asthma" refers to asthma exacerbations that occur in the hours after a thunderstorm, especially storms occurring during pollen seasons. The mechanism appears to involve rupture of water-logged pollen grains, which releases allergenic debris that is swept up by strong cross currents and deposited in concentrated form at ground level. In a multicenter study of adults with a past diagnosis of thunderstorm asthma and/or seasonal allergic rhinitis, risk factors for thunderstorm asthma included higher pollen-specific immunoglobulin E levels, eosinophil counts, and fractional exhaled nitric oxide levels as well as asthma that was not optimally controlled [1]. Clinicians and patients should be aware that thunderstorms can precipitate asthma and patients with pollen allergies and asthma should avoid the outdoors during and after thunderstorms occurring during pollen seasons.

Tobacco and pool exposure synergy in the risk of adolescent asthma (June 2022)

Population studies have found an association between adolescent exposure to chlorinated swimming pools and the development of asthma, especially among those with an atopic predisposition. In a new cross-sectional study of over 2300 adolescents in the United States from the National Health and Nutrition Examination Survey (NHANES) cohort, researchers evaluated tobacco and chlorine/bromine derivatives in the blood and assessed their association with current or lifetime asthma. They discovered a heightened risk of asthma with exposure to both tobacco and water disinfection byproducts relative to either exposure alone [2]. Assessment of these exposures by history may be helpful in the evaluation and counseling of adolescents at risk for asthma.

Patient-activated reliever-triggered inhaled glucocorticoid strategy (PARTICS) (May 2022)

A patient-activated reliever-triggered inhaled glucocorticoid strategy (PARTICS) involves the use of inhaled glucocorticoids in addition to beta-2 agonists whenever rescue medication is used. Two recent trials in patients with poorly controlled moderate-severe asthma found that PARTICS reduced the annualized rate of severe exacerbations by approximately 0.15 compared with usual care [3,4]. Practically, this strategy currently requires patients to carry multiple rescue inhalers, which may be unattractive to many patients. Nevertheless, PARTICS adds to growing evidence for increased effectiveness of inhaled glucocorticoids in addition to rescue therapy in preventing asthma exacerbations and may be a useful alternative reliever regimen.

COPD

Fazirsiran for liver disease due to severe alpha-1 antitrypsin deficiency (July 2022)

Adults with severe alpha-1 antitrypsin (AAT) deficiency are at risk for liver injury, but the only available treatments are supportive cirrhosis care and liver transplantation. Fazirsiran, an investigational inhibitory RNA (RNAi) agent designed to prevent toxic accumulation of AAT protein in the liver, was evaluated in 16 patients with PI*ZZ AAT deficiency [5]. Subcutaneous administration of fazirsiran led to decreased liver AAT levels, reduced portal inflammation, and, in nearly half the patients, regression of fibrosis at 24- or 48-week follow-up. Fazirsiran was well-tolerated without evidence of pulmonary function decline or chronic obstructive pulmonary disease exacerbations. Additional data are needed to establish the utility of this agent in clinical practice.

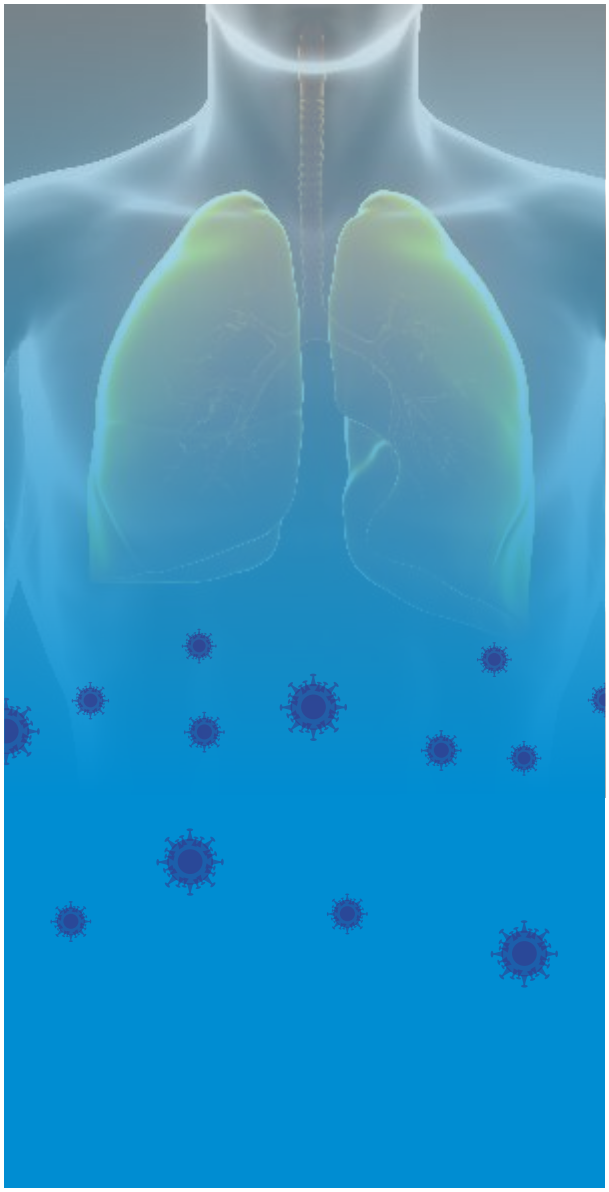
CRITICAL CARE

De-escalation of fluid therapy in sepsis (June 2022)

In patients with sepsis, there is little guidance regarding when and how intravenous fluids (IVF) should be de-escalated following initial resuscitation. In a recent trial of over 1500 adults with sepsis who had received at least 1 liter of fluid and were within 12 hours of the onset of shock, individuals assigned to restrictive IVF strategy (ie, infusion stopped; small boluses given when needed for organ perfusion, low urine output, or insensible losses) compared with a standard IVF strategy had similar 90-day mortality and adverse effects [6]. These data support the safety of a restrictive approach to fluid de-escalation. However, the volume of fluid in both groups was lower than that previously reported in early resuscitation sepsis studies suggesting that practice has evolved toward a de-escalation approach that is restrictive. More studies are needed to further guide postresuscitation fluid therapy in patients with sepsis.

Vitamin C alone not effective in sepsis (June 2022)

Early observational evidence suggested a possible mortality benefit from intravenous (IV) vitamin C in combination with thiamine and hydrocortisone in patients with sepsis. However, several randomized trials have since reported a lack of benefit from this combination. A recent trial of 872 patients with septic shock (and on a vasopressor) has reported that IV vitamin C alone also had no effect on 28-day mortality (35 versus 32 percent) or persistent organ dysfunction (9 versus 7 percent) [7]. One patient had severe hypoglycemia and another had anaphylaxis in response to vitamin C. We continue to recommend against the routine use of vitamin C alone or in combination with thiamine or hydrocortisone.



Awake pronation may not be beneficial in COVID-19-related acute hypoxemic respiratory failure (June 2022)

Based upon limited data suggesting a potential benefit, awake pronation has been used as a strategy to avoid intubation in patients with acute hypoxemic respiratory failure due to COVID-19. However, two recent trials in this population did not find a difference in intubation rates, length of stay, or mortality with awake pronation versus standard of care [9,10]. As an example, in one of the trials, the intubation rate with pronation was 34 versus 41 percent (hazard ratio 0.81, 95% CI 0.59-1.12) [9]. While pronation was associated with higher levels of oxygen support on day 5, the clinical significance of this is uncertain given the lack of difference at subsequent timepoints [9,10]. Because there were methodologic issues with these studies and the imprecise effect estimates suggest that a benefit cannot be ruled out, we continue to suggest awake pronation in this population until further data become available.

Routine preintubation fluid bolus does not prevent cardiovascular collapse in critically ill adults (June 2022)

Hypotension occurs in up to 50 percent of critically ill patients during and after intubation, and can cause cardiac arrest. If time permits, preintubation hemodynamic optimization is recommended, including correction of hypovolemia. However, in a randomized multicenter trial in >1000 critically ill adults, routine administration of a 500 mL intravenous (IV) fluid bolus prior to intubation did not reduce the incidence of cardiovascular collapse compared with no fluid bolus [8], consistent with a previous smaller trial. Methods to reduce peri-intubation hypotension should be individualized and may include use of etomidate or ketamine for induction, use of vasopressors, and IV fluid if necessary.

Early versus late tracheostomy in patients with stroke (May 2022)

Data suggest that in most patients who are mechanically ventilated, there is no major advantage to performing early tracheostomy (ET, eg ≤5 days). However, data are limited in specific populations. In a recent randomized trial of 382 patients with stroke who required mechanical ventilation, patients who underwent ET did not experience improved functional outcome when compared with those who received usual care with ventilator weaning and a tracheostomy, if required, after 10 days (44 versus 47 percent) [11]. While 95 percent of patients in the ET group received the intervention, only two-thirds in the usual care group needed a tracheostomy, supporting observations in other trials that ET may lead to unnecessary surgery. These data support our practice of an individualized approach to the timing of tracheostomy with most patients undergoing the procedure between 7 and 21 days.

Socioeconomic disadvantage contributes to symptoms after ICU admission (April 2022)

Whether socioeconomic factors contribute to the development of chronic physical or psychological symptoms associated with post-intensive care unit syndrome (PICS) was recently described. In one report of over 500 intensive care unit hospitalizations in older adults (>65 years), socioeconomic disadvantage (as defined by dual eligibility for Medicare-Medicaid) was associated with a 28 percent increase in physical disability and a 10-fold increase in the risk of transitioning to dementia, compared with older adults who were less disadvantaged [12]. Specific socioeconomic issues that contribute to this disparity are unclear and need further study.

High-flow oxygen in patients with COVID-19 (April 2022)

For patients with COVID-19 and acute hypoxemic respiratory failure, use of advanced noninvasive modalities (such as oxygen through high-flow nasal cannula [HFNC] or noninvasive ventilation) is a commonly used strategy to reduce the need for intubation. In a randomized trial of 220 such patients, intubations rates were lower with oxygen delivery through HFNC compared with standard low flow delivery [13]. HFNC also reduced time to clinical recovery, but the mortality difference was not statistically significant. Despite excluding several medical comorbidities, this trial supports our suggestion to use HFNC as an option for noninvasive oxygenation in individuals with COVID-19 who have advanced oxygen needs.

Corticosteroid regimens for COVID-19-related organizing pneumonia (April 2022)

Data to support the use of corticosteroids in patients who develop organizing pneumonia as a complication of COVID-19 are limited. In a recent open-label randomized trial, improvements in respiratory symptoms, lung imaging, and pulmonary function were reported, with no difference in outcomes between high- and low-dose prednisolone regimens (40 mg/day for one week, 30 mg/day for one week, 20 mg/day for two weeks, 10 mg/day for two weeks versus 10 mg/day for six weeks) [14]. These data support the efficacy of low-dose corticosteroid regimens in patients with COVID-19-related organizing pneumonia, although placebo-controlled randomized trials are needed to better inform this treatment decision.

Predictive model for acute kidney injury following cardiac surgery (March 2022)

A model has been proposed to predict the development of acute kidney injury (AKI) following cardiac surgery. The derivation model used basic metabolic panel laboratory values from over 58,000 adult patients who underwent cardiac surgery [15]. The model had excellent predictive discrimination for moderate to severe AKI within 72 hours after surgery (area under the curve [AUC] 0.876) and similarly performed well in the validation cohort (AUC 0.860). Further data are needed to determine whether such a model improves clinical outcomes before it can be routinely used in the clinical setting.

No benefit for prophylactic antiseizure medication in adults after resuscitation from cardiac arrest (March 2022)

Whether prophylactic antiseizure medication benefits adult survivors of cardiac arrest who are at risk of seizures is unclear and clinical practice varies. In a recent open-label trial of 172 adults who had rhythmic and periodic electroencephalographic (RP-EEG) patterns that indicate significant brain injury following resuscitation from cardiac arrest, poor neurologic outcome (severe disability, coma, or death) at three months was not significantly different for those assigned to prophylactic antiseizure medication and standard care compared with standard care alone (90 versus 92 percent, respectively); approximately 80 percent of patients died by three months in both groups [16]. These findings suggest that antiseizure medications do not reduce adverse neurologic outcomes or death in patients resuscitated from cardiac arrest who have RP-EEG and support our current practice of not using prophylactic antiseizure medication.

Fluid resuscitation with saline or buffered crystalloid in adults (March 2022, Modified March 2022)

The choice between normal saline (NS) and a buffered salt solution (BSS) for initial fluid resuscitation in adults is debated. Recent large trials have failed to show superiority of one over the other [17-19]. In a new meta-analysis of six randomized trials with low risk of bias in nearly 35,000 adults requiring fluid resuscitation, BSS led to small and statistically nonsignificant reductions in both 90-day mortality (risk ratio [RR] 0.96, 95% CI 0.91-1.01) and acute kidney injury (RR 0.96, 95% CI 0.89-1.02) compared with NS [20]. Many of the trials had limitations including poor recruitment, low volumes of administered fluid, and unavailable data. In addition, the two types of fluids have differing advantages and disadvantages depending on blood chemistries and volume status. We suggest that the choice between fluids be individualized and re-evaluated following initial resuscitation.

Noninvasive respiratory support for patients with COVID-19 and acute hypoxemic respiratory failure (February 2022)

In patients with COVID-19 and acute hypoxemic respiratory failure despite conventional oxygen therapy, the best approach to escalation of noninvasive respiratory support is unknown. In a randomized, multicenter trial of over 1200 patients with acute hypoxemic respiratory failure due to COVID-19, continuous positive airway pressure (CPAP), but not high flow oxygen via nasal cannula (HFNC), reduced intubation rates compared with conventional oxygen (33 versus 41 percent) [21]. Thirty-day mortality was not significantly different for either modality compared with conventional oxygen. However, important limitations of this study include the open-label design, early cessation of the trial, and high crossover between groups. For patients with COVID-19 who have increasing oxygen needs and do not have conditions best treated with noninvasive ventilation (NIV; hypercapnic respiratory failure due to an exacerbation of chronic obstructive pulmonary disease or acute cardiogenic pulmonary edema), we trial NIV (CPAP or bilevel positive airway pressure), HFNC, or cycle between both until patients demonstrate improvement or deterioration. The tolerability of the device and patient comfort often determine the best modality.

Prolonged duration of symptoms in COVID-19 ICU survivors (February 2022)

The duration of symptoms following COVID-19 is unclear. A recent study reported that three-quarters of intensive care unit COVID-19 survivors had physical symptoms at one year. These included physical weakness (39 percent), joint symptoms (26 percent), and myalgia (21 percent) [22]. Mental symptoms were reported by 26 percent and cognitive symptoms by 16 percent of survivors. These symptoms are consistent with post-intensive care syndrome (PICS) and need to be addressed during recovery from COVID-19.

Three-step program of caregiver support for the dying patient (February 2022)

The optimal approach to support caregivers of dying patients in the intensive care unit (ICU) is unknown. One study described a successful approach with a three-step, physician-driven, nurse-aided support strategy for 875 relatives of patients dying in the ICU [23]. The first step was an end-of-life conversation, the second was a physical presence of health care personnel in the room during the dying process, and the third was a meeting to express condolences after death. Compared with standard care, at six months, the three-step program reduced the number of relatives with prolonged grief (PG) symptoms (21 versus 15 percent) and the median prolonged grief-13 questionnaire score (19 versus 21). This study supports the practice of a structured system designed to improve communication and empathy to caregivers of the dying in the ICU but may not be generalizable.

INTERSTITIAL LUNG DISEASE

Phosphodiesterase 4B inhibitor therapy in idiopathic pulmonary fibrosis (July 2022)

Although antifibrotic therapy with pirfenidone or nintedanib can slow progression of idiopathic pulmonary fibrosis (IPF), phosphodiesterase 4B (PDE4B) inhibitors are a novel class of agent with both antifibrotic and immunomodulatory effects. In a randomized trial in 97 patients with IPF, the oral PDE4 inhibitor BI 1015550 prevented decline in forced vital capacity over 12 weeks compared with placebo [24]. The effect was smaller but still significant in patients on background antifibrotics. Thirteen patients (13 percent) discontinued the agent for toxicity, with the most common adverse effect being diarrhea. Additional evaluation of this inhibitor in phase III clinical trials is anticipated.

Empiric treatment of gastroesophageal reflux in idiopathic pulmonary fibrosis (July 2022)

Gastroesophageal reflux (GER) has been hypothesized to play a role in idiopathic pulmonary fibrosis (IPF) progression as a source of ongoing injury and inflammation in the lower lobes of the lung. An international practice guideline committee reviewed the limited available data on antireflux therapies for GER in patients with IPF and concluded that these therapies should not be used empirically to improve pulmonary outcomes [25]. UpToDate agrees with this approach, although more research is needed in this area.

PULMONARY VASCULAR DISEASE

Mortality from pulmonary hypertension in thalassemia (April 2022)

Individuals with thalassemia are at risk for pulmonary hypertension due to a combination of risk factors, especially hemolysis and iron overload. A new study monitored 24 individuals with thalassemia who had right heart catheterization-documented pulmonary arterial hypertension (PAH) [26]. The median age was 46.5 years. During a median of four years of follow-up, 13 patients died, and 10 of the deaths were attributed to PAH. Survival strongly correlated with PAH therapy. Patients with thalassemia and PAH need routine monitoring and multidisciplinary treatment by clinicians with expertise in treating PAH [27].

Adjusted D-dimer targets for deep vein thrombosis (March 2022)

The optimal strategy to diagnose deep vein thrombosis (DVT) is unknown. One recent study described an approach that excluded DVT when the D-dimer was <1000 ng/mL (in patients with a low Wells pretest probability) or <500 ng/mL (in patients with a moderate clinical pretest probability) (calculator 1) [28]. Using this strategy, only 0.6 percent of those in whom DVT was excluded developed DVT during the three-month follow-up. In addition, it was estimated that this approach reduced the need for ultrasonography by almost 50 percent. However, this strategy was not directly compared with the traditional approach that uses a single cutoff D-dimer value of <500 ng/mL, and further study is needed before it can be routinely used for the diagnosis of patients with suspected DVT.

OTHER PULMONARY MEDICINE

Vaccination status and prevalence of "long COVID" symptoms (July 2022)

In a new prospective observational cohort study of 2560 patients with mild COVID-19, COVID-19 vaccination was associated with a decreased prevalence of postacute sequelae of SARS-CoV-2 infection (PASC) in a dose-dependent fashion (three doses 16 percent, two doses 17.4 percent, and one dose 30 percent) compared with unvaccinated individuals (42.8 percent) [29]. This finding appeared to be independent from the COVID-19 variant. This study provides additional evidence that COVID-19 vaccination, in addition to reducing the risk of COVID-19 infection, may also decrease PASC in vaccinated patients with mild infection.

Persistent symptoms following COVID-19 (June 2022)

A longer recovery course is expected in patients with COVID-19 who require hospitalization; however, patients who never require hospitalization also often report prolonged and persistent symptoms. In a recent study that compared the presence of persistent symptoms in patients with mild COVID-19 with symptoms in controls who had no history or serologic evidence of previous COVID-19, a higher proportion of patients with COVID-19 had two persistent symptoms at five months (55 versus 13 percent) [31]. Most symptoms (ie, fatigue, dyspnea, parosmia, and concentration impairment) were similar to previous reports. Patients recovering from COVID-19 also had a shorter six-minute walk distance (560 versus 590 meters) and a lower quality of life. No significant differences were found in routine laboratory and rheumatologic tests, inflammatory or immunologic markers, pulmonary function tests, echocardiography, neurocognitive testing, or serologic tests for SARS-CoV-2. Further data are needed to improve our understanding of the cause of persistent symptoms in patients recovering from mild COVID-19.

Risk of long COVID in Delta versus Omicron variants (June 2022)

Persistent symptoms following acute COVID-19 infection (eg, long COVID) are common. Recent evidence suggests that the prevalence of persistent symptoms may vary depending on the COVID-19 variant. In an observational study including over 97,000 vaccinated individuals in the United Kingdom, subsequent infection with the Omicron variant was associated with a lower risk of developing persistent symptoms compared with Delta (4.5 versus 10.8 percent) [30]. Findings were consistent regardless of the interval between vaccination and infection. However, methodologic issues (eg, self-reporting through an electronic "app" and shorter duration of follow-up for Omicron versus Delta patients) limit the interpretation of these findings, and further research is needed.

Emerging Role of N-acetylcysteine in the management of chronic obstructive pulmonary disease

Systematic review and meta-analysis of the efficacy of N-acetylcysteine in the treatment of acute exacerbation of chronic obstructive pulmonary disease

N acetylcysteine administration could sharply reduce symptoms of cough, sputum and dyspnea in patients with AECOPD, with an improvement rate of 1.09 times compared with the control group.

NAC improves the lung function in FEV1 and FEV1/FVC and symptoms of patients by reducing the oxidative stress-induced lung damage, inhibiting the thickening of the tracheal epithelium, and reducing the lung damage caused by the immune inflammatory response.

In addition, NAC dilutes sputum to make it easier to expel quickly, hinder the growth of bacteria, and protects lung function.

N-Acetylcysteine Improves Inflammatory Response in COPD Patients by Regulating Th17/Treg Balance through Hypoxia I nducible Factor-1a Pathway

Th17 cells and Treg cells, as subgroups of $CD4^+$ T cells played an important role in balancing COPD patients immune status.

During acute exacerbation patients with COPD, the ratio of Treg and Th17 cells in the peripheral blood has changed significantly, which led to the appearance of an inflammatory response. Imbalance between these two subgroups might be one of the causes of COPD.

NAC rebalances the Th17/Treg ratio. NAC could protect patients with COPD by suppressing Th17 immune responses and modulating the Th17/Treg balance in favor of Treg cells.

In COPD patients NAC has good therapeutic effect and improves immune status of COPD patients which might be through regulating the HIF1-a expression.

In Patients with COPD, N-Acetylcysteine Inhibits Synthesis of IL-18 in Macrophage by Suppressing NLRP3 Expression to Reduce the Production of IFN-g from NK Cells

Over expression of IL-18 in the airways in patients with COPD has been shown and can lead to emphysema, the development of fibrosis in the bronchi and blood vessels of the lungs, and the formation of pulmonary hypertension.

IL-18 can also participate in inflammation and hyperreactivity of the respiratory tract in asthma and promote the recruitment of eosinophils to the airways.

NAC could influence the inflammasomes in macrophages to downregulate the synthesis of IL-18, thus improving the immune and inflammation status in COPD Patients.

Evaluation of Safety and Efficacy of AllerBio in the Patients with Perennial Allergic Rhinitis

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To evaluate the efficacy and safety of AAP-2 (Synergistic combination of Lactobacillus Paracasei GMNL-133 & L.fermentum GM-090) in the treatment and prevention of perennial allergic rhinitis.

ABSTRACT

Background: Probiotics have proven beneficial in a number of immune-mediated and allergic diseases. Several human studies have evaluated the efficacy and safety of probiotics in allergic rhinitis; however, evidence for their use has yet to be firmly established.

Background: Probiotics have proven beneficial in a number of immune-mediated and allergic diseases. Several human studies have evaluated the efficacy and safety of probiotics in allergic rhinitis; however, evidence for their use has yet to be firmly established.

Objectives: To evaluate the safety and efficacy of AllerBio, an Anti-Allergic Probiotic, AAP-2 (Synergistic combination of Lactobacillus Paracasei GMNL-133 & L.fermentum GM-090) in the treatment and prevention of perennial allergic rhinitis.
Methods: An Open label single arm study was done by analysing 34 participants, who met the inclusion/exclusion criteria. This is a Post Marketing Surveillance Proof of concept study of duration around 3 month (1- Month Intervention Period & following 2 Month Observational Period).

Results: The findings from this study show that the AllerBio had a beneficial impact on overall Quality of life of the participants with Allergic Rhinitis. It also showed a fall in the IgE after the end of therapy.

Conclusion: This AllerBio is Cost Effective and does not precipitate the adverse effect as much as other Standard therapies of Allergic Rhinitis and this is a promising therapeutic option for the future by effectively reducing the free IgE antibodies in the serum.

Key Words – Perennial Allergic Rhinitis, Lactobacillus, Probiotic, RQLQ

INTRODUCTION AND BACKGROUND:

Allergic rhinitis (AR) is an allergic inflammation of the nasal airways with a rapidly increased prevalence in the past decades1. Common symptoms of AR are nasal itching, sneezing, rhinorrhoea, and nasal congestion. In addition, some patients experience symptoms of allergic rhino conjunctivitis, such as watery or itchy or red eyes. Severe AR can affect the quality of life, sleep, and work performance2.

The physiology behind allergic rhinitis states that when a susceptible individual gets exposed to an allergen generally a protein which is having a capacity to precipitate an allergic reaction, the body's immune system tends to produce a specific antibody as a defence mechanism to fight against the foreign body entry. This IgE antibody engulfs the surface of the mast cells which are present in the nasal mucosa3,4,5. Drugs like antihistamines, nasal decongestants are prescribed to arrest the symptoms of allergic rhinitis and immunotherapy6,7. If the condition is not being cured with all these treatment strategies, there is a surgical procedure called Turbinoplasty which may be potent against persistent allergic rhinitis8.

The rapid increase in immune-mediated disorders such as allergic disease is strongly linked to reduced early microbial exposure. The gut microbiota represents the greatest microbial exposure by far and is central to the development of immune regulation. The specific composition of the gut microbiota may affect the risk of developing allergic disease. This finding provided the foundation for intervention studies designed to modify gut microbial composition for the treatment of allergic disease. The effects of beneficial bacteria (probiotics) or resistant starches or fiber (prebiotics) that selectively stimulate a limited number of beneficial bacteria have been evaluated in allergy treatment studies9.

Since conventional allergy medication for asthma or allergic rhinitis (AR) can cause side effects which limit the patients' quality of life. In particular, probiotic bacteria, such as Lactobacillus species, have shown anti-allergic effects in various mouse and human studies. For instance, administration of some Lactobacillus species resulted in nasal and ocular symptom relief and improvement of quality of life in children and adults suffering from rhinitis10.

One of the most important aspects of the beneficial effect to the host organism is that the probiotics can interact with the host immune system and may modify the natural course of the allergic disease, while how probiotics may influence the immune system remains unclear. Studies indicated that probiotics are a profitable therapeutic treatment of allergic rhinitis. This study highlights the most recent findings regarding the important role of probiotics in the treatment of allergic rhinitis.

The aim of this study was, therefore, to evaluate the efficacy and safety of Allerbio, an Anti-Allergic Probiotic, AAP-2 (Synergistic combination of Lactobacillus Paracasei GMNL-133 & L.fermentum GM-090) in the treatment and prevention of perennial allergic rhinitis.

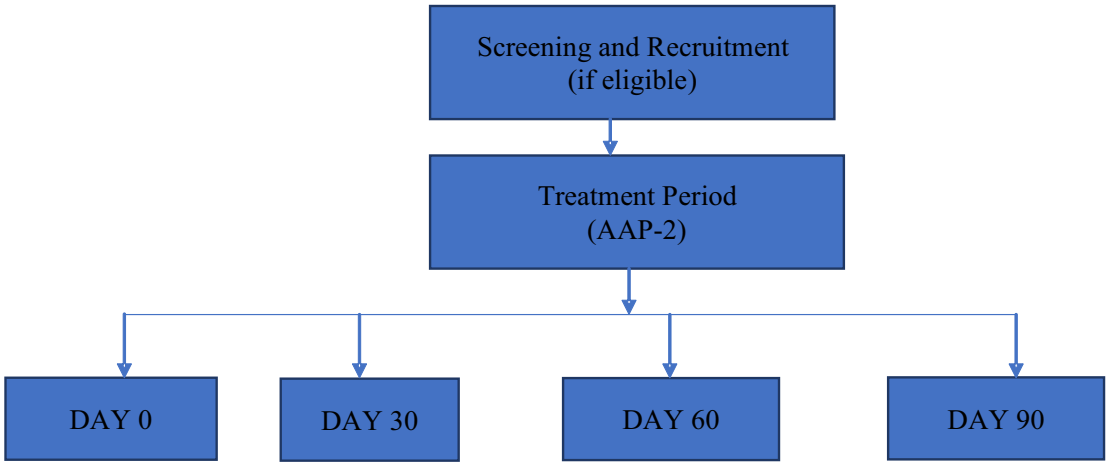
METHODOLOGY:

This study was an open-label, single-center, post-marketing surveillance study with three months study duration period in which one month was an interventional period and two months was an observational period. Participants aged 1-60 years with perennial allergic rhinitis characterized by intermittent or continuous nasal symptoms for more than one year were included. Written informed consent was obtained from the participants. Participants who had concurrent steroid treatment (oral or parenteral) and immune therapy or who were previously diagnosed with neuropsychiatric or congenital immunodeficiency or probiotic allergy were excluded.

A total number of 34 participants were enrolled and analysed. The participants was prescribed with a sachet of AllerBio per day. Follow-up visits were scheduled at day 30, day 60, and day 90.

The primary endpoints of the study were reduction in specific IgE levels, changes in symptom scores on the Rhinoconjuctivitis Quality of Life questionnaire (RQLQ), and severity & frequency of allergic rhinitis. The secondary endpoints of the study were number of relapses of allergic symptoms, severity of allergic symptoms during relapses.

As the study involved paediatric population, Paediatric Rhinoconjuctivitis Quality of Life questionnaire (PRQLQ) is used for children and RQLQ is used for adult participants. The PRQLQ has 5 domains (nasal symptoms, ocular symptoms, practical problems, activity limitation and other symptoms) and RQLQ has 6 domains (nasal symptoms, ocular symptoms, practical problems, non-hay fever symptoms, sleep symptoms and emotional symptoms).



STATISTICAL ANALYSIS:

Both the numerical and categorical variables were statistically analyzed. Descriptive statistics was done to obtain the central tendencies of the continuous data like, Age, RQLQ Score and IgE value. To understand the difference in variable details of each participant, measure of dispersion has been done by using Standard deviation. ANOVA test was performed to understand the change in score at every visit with the baseline scores. The secondary end points like; Need of rescue medicine, Time of 1st exacerbation of the allergic symptoms during follow-up period, Number of relapses of allergic symptoms and Severity of allergic symptoms during relapses; were categorized and represented by its occurrence and percentages. The data was analyzed using SPSS v.22.0 and Microsoft Excel 2016.

RESULTS:

Table-1: Summary of Demographic Characteristics

Characteristics/Statistics	Overall (N=34)
Age (years)	
N	34
Mean	13.69
SD	10.43
Median	12.00
Min; Max	(2, 46)
Gender, n(%)	
Female	9 (26.5%)
Male	25 (73.5%)

A total of 34 patients were enrolled. Male patients were higher (25 [73.5%]) than female patients 9 (26.5%). The mean (SD) age was 13.69 (±10.43) years.

Table-2: Summary of Reduction in IgE

Visit	Statistics	Overall
Visit 1 (Day 1)	N	34
	Mean	774.12
	SD	19.94
	Median	769.00
	Min; Max	(747, 820)
Visit 2 (Day 30)	N	34
	Mean	280.09
	SD	31.15
	Median	280.00
	Min; Max	(210, 360)
Change from baseline to		
Visit 2	N	34
	Mean	-494.03
	SD	13.79
	Median	-467.50
	Min; Max	(120, -506)
	P value	<0.001

Note: P-values are based on one way repeated measure ANOVA with change in SS score \ The mean (SD) IgE has decreased from 774.12 (19.94) at baseline to 280.09 (31.15) at Visit-2. Thus, the mean (SD) change in IgE value from baseline was 494.03 (13.79). A statistically significant decrease in mean IgE from baseline (p 0.0001) was observed at Day-30 .

Table-3: Summary and Change from Baseline for RQLQ Total Score

Visit	Statistics	Overall
Visit 1	N	34
	Mean	61.74
	SD	23.23
	Median	62.00
	Min; Max	(21, 125)
Visit 2	N	34
	Mean	34.53
	SD	12.26
	Median	32.50
Change from baseline to		
Visit 2	N	34
	Mean	-27.21
	SD	13.79
	Median	-24.50
	Min; Max	(-62, -9)
	P value	<0.001
Visit 3	N	34
	Mean	21.65
	SD	8.38
	Median	22.00
	Min; Max	(4, 41)
Change from baseline to		
Visit 3	N	34
	Mean	-40.09
	SD	19.92
	Median	-41.00
	Min; Max	(-90, -11)
	P value	<0.0001

Note: P-values are based on one way repeated measure ANOVA with change in SS score

The mean (SD) RQLQ total score has decreased from 61.74 (23.23) at baseline to 34.53 (12.26) at Visit-2 and to 21.65 (8.38) at Visit-3. Thus, the mean (SD) change in RQLQ score from baseline was 27.21 (12.79) and 40.09 (19.92) at Visit-2 and Visit-3, respectively. A statistically significant decrease in mean RQLQ from baseline (p 0.0001) was observed at both post-baseline visits (Figure 1).

Figure-1 Line Plot for Mean + SD RQLQ Total Score by Visit

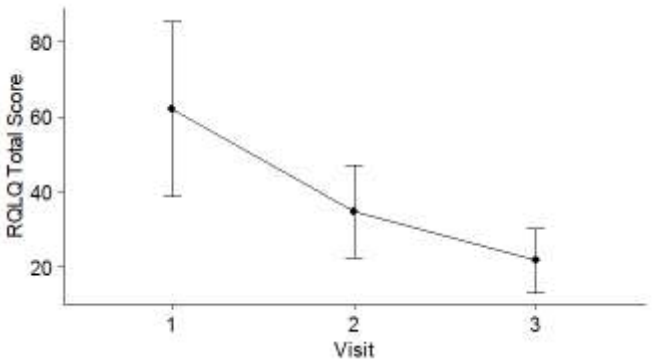


Table-4: Summary and Change from Baseline for Total Score of Symptom Severity

Visit	Statistics	Overall
Visit 1	N	21
	Mean	45.38
	SD	2.80
	Median	46.00
	Min; Max	(40, 51)
Visit 2	N	21
	Mean	36.95
	SD	2.56
	Median	37.00
	Min; Max	(31, 42)
Change from baseline to		
Visit 2	N	21
	Mean	-8.43
	SD	2.75
	Median	-8.00
	Min; Max	(-14, -4)
	P value	<0.0001
Visit 3 actual values	N	21
	Mean	24.48
	SD	3.20
	Median	24.00
	Min; Max	(19, 35)
Change from baseline to		
Visit 3	N	21
	Mean	-20.90
	SD	3.49
	Median	-20.00
	Min; Max	(-28, -12)
	P value	<0.0001

Note: P-values are based on one way repeated measure ANOVA with change in SS score

The mean (SD) total score of Symptom Severity has decreased from 45.38 (2.80) at baseline to 36.95 (2.56) at Visit-2 and to 24.48 (3.20) at Visit-3. Thus, the mean (SD) change in SS score from baseline was 8.43 (2.75) and 20.90 (3.49) at Visit-2 and Visit-3, respectively. A statistically significant decrease in mean SS from baseline (p 0.0001) was observed at both post-baseline visits (Figure 2)

Figure-2 Line Plot for Mean + SD Total Score SS by Visit

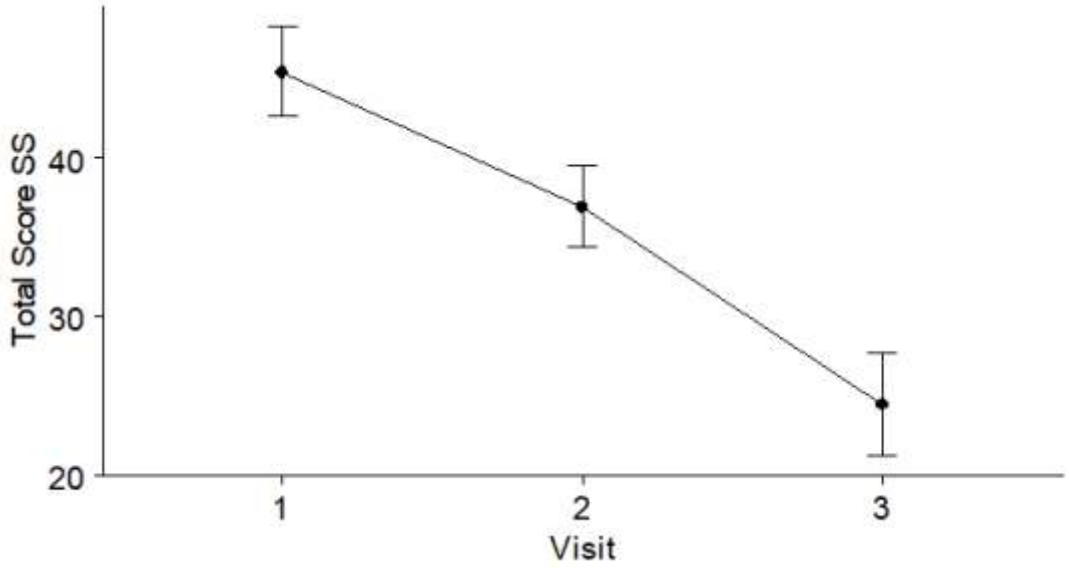


Table-4: Summary and Change from Baseline for Total Score of Symptom Frequency

Visit	Statistics	Overall
Visit 1	N	21
	Mean	9.71
	SD	5.45
	Median	9.00
	Min; Max	(4, 28)
Visit 2	N	21
	Mean	7.52
	SD	2.71
	Median	7.00
	Min; Max	(3, 14)
Change from baseline to		
Visit 2	N	21
	Mean	-2.19
	SD	4.11
	Median	-2.00
	Min; Max	(-17, 3)
	P value	0.0239
Visit 3	N	21
	Mean	5.86
	SD	2.67
	Median	5.00
	Min; Max	(1, 10)
Change from baseline to		
Visit 3	N	21
	Mean	-3.86
	SD	4.78
	Median	-3.00
	Min; Max	(-19, 4)
	P value	0.0014

Note: P-values are based on one way repeated measure ANOVA with change in SS score

The mean (SD) total score of Symptom Frequency has decreased from 9.71 (5.45) at baseline to 7.52 (2.71) at Visit-2 and to 5.86 (2.67) at Visit-3. Thus, the mean (SD) change in SF score from baseline was 2.19 (4.11) and 3.86 (4.78) at Visit-2 and Visit-3, respectively. A statistically significant decrease in mean SF from baseline with p value of 0.0239 & 0.0014 at visits-2 and Visit -3 respectively (Figure 3).

Figure-3 Line Plot for Mean + SD Total Score SF by Visit

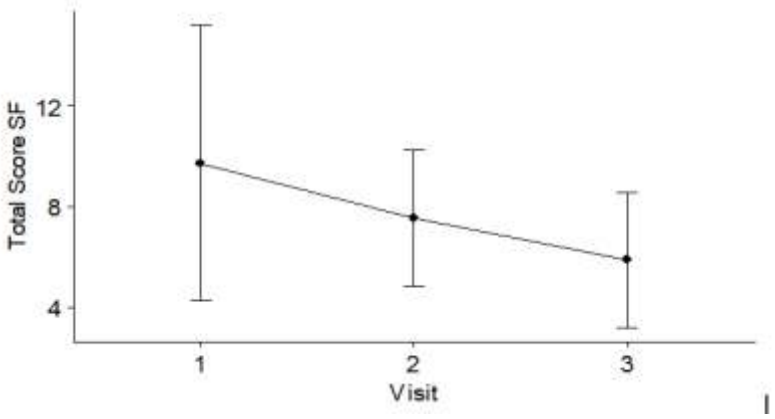


Table-5: Summary of relapses of allergic symptoms and Severity of during relapses

Parameter	Visit/Study Day	n	Percent (%)
Number of relapses of allergic symptoms	Day-60	3	8.8
Number of relapses of allergic symptoms	Day-90	1	2.9
Number of relapses of allergic symptoms	Nil	29	88.2

A total of 29 (88.2%) patients had no relapses of allergic symptoms and 3(8.8%) patients had relapses during the period of Day-30 to Day-60.

Table-6: Summary of Investigator's Assessment Scale Results

Assessment Scale	n	Percent (%)
Excellent-Desired improvement	12	35.3
Fair-Moderate improvement	3	8.8
Good-Marked improvement	19	55.9

A total of 19 (55.9%) patients had shown Good-Marked Improvement followed by 12 (35.3%) Excellent- Desired Improvement as per Investigator's Assessment scoring.

Table-7: Summary of Adverse Event

Parameter	Visit/Study Day	n	Percent (%)
Observed side-effects	Nil	34	100

No AEs or other side effects were reported during the study.

DISCUSSION:

In this study, one of the primary endpoint is the reduction of IgE antibody by using the investigational product, AllerBio an anti-allergic probiotic. The substantial reduction in the IgE level, i.e.63% at end of Day-30 as compared to baseline could be attributed to usage of Allerbio in the study population.

Oliver Pfaar et. al, 2021 performed a systematic literature review including randomized controlled trials, meta-analyses, and reviews on the treatment of Allergic Rhinitis with omalizumab, a monoclonal antibody and concluded that the use of omalizumab in the treatment Allergic Rhinitis results in the reduction of IgE antibody of about 84% [24]. Same like the monoclonal antibody , this anti-allergic probiotic has proven its effectiveness in the reduction of IgE antibody and improves the quality of life in the patient associated with allergic rhinitis.

In this study , one of the most important evaluation parameter is the changes in symptom scores on the RQLQ questionnaire by using the investigational product, AllerBio an anti-allergic probiotic and concluded that by the usage of AllerBio, the mean score value at visit 3 (Mean ± Std. deviation: 21.65 ± 8.38) with a mean difference of 40.09 ± 19.92 [Table 3]. The QOL of the participant at visit 3 after administering Allerbio for 60 days was much better compared to the visit 1 and 2; and was statistically significant. In similar to this study, W. Hamizan Aneeza et. al, 2013 did a randomised controlled trail to evaluate the Efficacy of mometasone furoate and fluticasone furoate on persistent allergic rhinoconjunctivitis and concluded that both mometasone furoate and fluticasone furoate are effective as single-modality treatment of allergic rhino conjunctivitis and there was significant reduction in the symptom scores after 2 months with the ($p < 0.05$) [25].Though there is a improvement symptoms score in two studies , the intranasal steroids are known precipitate many adverse effects in the patient. So the AllerBio , probiotic can be recommended has it proven to reduce the symptom scores with the (p value= < 0.0001) at visit 3 and does not precipitate the as much as serious adverse effects comparing to the intranasal steroid.

In this study, the primary end point is Reduction in the Severity & frequency of the symptoms of allergic rhinitis using Allerbio and concluded that the Symptom Severity Score of the participant at visit 3 after administering Allerbio for 60 days was much better compared to the visit 1 and 2; and was statistically significant. In addition, the Symptom Frequency Score of the participant at visit 3 after administering Allerbio for 60 days was much better compared to the visit 1 and 2; and was statistically significant with the (p Value = 0.0014). In similar to this study, Ganesh S. Pentewar et. al, 2019 did an open-label, 4-arm, parallel group, single center study to assess the quality of life measured by rhinoconjuctivits quality of life questionnaire in patients of allergic rhinitis treated with commonly used oral antihistamines and concluded that the severity and frequency of the symptoms have reduced drastically with the p value 0.000111. So it is evident that the investigational product, AllerBio is as effective as Oral Antihistamine in the treatment of Allergic Rhinitis.

CONCLUSION:

Although allergic Rhinitis is not a life threatening disease, it is associated with poor quality of life. This study has proved that the investigational Product , AllerBio has significant impact on the improvement of the quality of life for the patients with perennial Allergic Rhinitis. In addition, comparing to the standard therapy of Allergic Rhinitis like Intranasal Steroids , Monoclonal antibodies, Oral Antihistamine etc , this AllerBio is Cost Effective and does not precipitate the adverse effect as much as other Standard therapies of Allergic Rhinitis and this is a promising therapeutic option for the future by effectively reducing the free IgE antibodies in the serum. A pivotal study with large sample size would be needed to ascertain this results.

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Levocetirizine and montelukast in the COVID-19 treatment paradigm

International Immunopharmacology 103 (2022) 108412

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ABSTRACT

Levocetirizine, a third-generation antihistamine, and montelukast, a leukotriene receptor antagonist, exhibit remarkable synergistic anti-inflammatory activity across a spectrum of signaling proteins, cell adhesion molecules, and leukocytes. By targeting cellular protein activity, they are uniquely positioned to treat the symptoms of COVID-19. Clinical data to date with an associated six-month follow-up, suggests the combination therapy may prevent the progression of the disease from mild to moderate to severe, as well as prevent/treat many of the aspects of 'Long COVID,' thereby cost effectively reducing both morbidity and mortality.

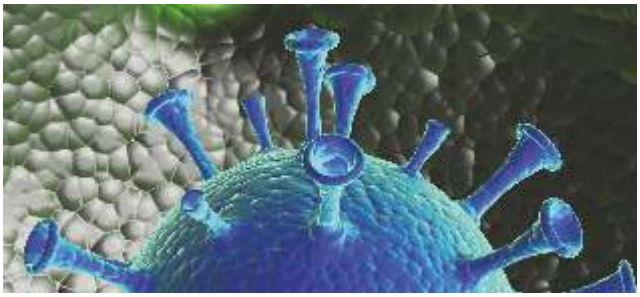
LEVOCETIRIZINE MECHANISM OF ACTION

Levocetirizine, a third-generation antihistamine, classically downregulates the H1 receptor on the surface of mast cells and basophils to block the IgE-mediated release of histamine. Histamine has been well characterized by its effects on the body, including in part, its function as a neurotransmitter, dilation of blood vessels which in turn increases permeability and lowers blood pressure, contraction of smooth muscle in the lung, uterus, and stomach, and as a source of sneezing, itching, and congestion. Levocetirizine is considered by harmacologists an 'insurmountable' H1 receptor antagonist [23]. It has been objectively established as the most potent of the five modern generation antihistamines (levocetirizine, cetirizine, fexofenadine, loratadine, and desloratadine) through histamine wheal and flare data [10,24–27]. Levocetirizine, given its low volume of distribution and high receptor occupancy, is also among a select group of H1 receptor antagonists which can inhibit NF-kB and activator protein-1 (AP-1) activity through H1 receptor-dependent and independent mechanisms [9,21,22]. Induction of such activity follows in a dose-dependent manner to decrease, inter alia, tumor necrosis factor- induced production of the chemokine RANTES (Regulated upon activation, normal T cell expressed and presumably secreted). RANTES expression, mediated exclusively through NF-kB, attracts eosinophils, monocytes, mast cells and lymphocytes,activates basophils, and induces histamine release from these cells.

MONTELUKAST MECHANISM OF ACTION

Montelukast functions at the CysLT1 receptor to inhibit the physiologic action of leukotriene D4 (LTD4). Leukotrienes are protein mediators of inflammation similar to histamine; however, 100-1000x more potent on a molar basis than histamine in the lung. LTD4 is the most potent cysteinyl leukotriene in contracting smooth muscle, thereby producing bronchoconstriction. Contemporary cell and animal science support the use of montelukast in patients with acute respiratory distress syndrome [28,29].

At the molecular level, distinct from CysLTR1 antagonism, montelukast has also been reported to inhibit the activation of NF-kB in a variety of cell types including monocytes/macrophages, T cells, epithelial cells, and endothelial cells, thereby interfering with the generation of multiple proinflammatory proteins [17]. Separately Robinson, et al. found that montelukast independently inhibited resting and GM-CSF-stimulated eosinophil adhesion to VCAM-1 under flow conditions [14].



MONTELUKAST POTENTIAL DUAL EFFECT - ENZYME INHIBITION AND COVID-19 VIRUS ENTRY

An expanding body of molecular science favorably supports montelukast as a potential therapeutic in the treatment of COVID-19. Multiple in silico and in vitro studies have depicted the dual potential of montelukast to inhibit the SAR-CoV-2 main proteinase 3CLpro as well as viral entry into the host cell (Spike/ACE2). The anti-inflammatory drugs: montelukast, ebastine, a second-generation antihistamine, and steroid, Solu-Medrol (methylprednisolone) exhibit remarkable affinities to 3CLpro. 3CLpro plays an essential role in processing polyproteins, the resultant products of which are subsequently utilized in the production of new virions. Additionally, there is a known clinical crossover between ebastine and levocetirizine, the latter considered more potent.

DISCUSSION

To investigate patient outcomes, 53 consecutive COVID-19 test (+) cases (ages 3–90) from a well-established, single-center practice in Boston, Massachusetts, between March – November 2020, were treated with levocetirizine and montelukast in addition to then existing protocols [2]. In review, thirty-four patients (64%) were considered mild, 17 (32%) moderate, and 2 (4%) severe. The 2 severe hospital cases also received remdesivir. One patient with nasal polyps received steroids and no one received monoclonal antibodies. No patient progressed to intubation or death. Many allergy and asthma patients had co-existing morbidities including obesity, diabetes and hypertension, which increased their risk for major complications associated with COVID-19, yet notably recovered well from the virus. Early treatment, particularly in younger patients, enhanced the clinical response, with resolution of headache and fever within the first 48 hours following initiation of therapy. Analyzed collectively, the data support improved patient outcomes for those treated with the combination of levocetirizine and montelukast over patients who were either left untreated or treated with the then existing protocols. Most patients treated with co-administration of levocetirizine and montelukast experienced symptom resolution. symptomatic patients [2]. These data suggest the combination therapy, underscored by their uniquely synergistic mechanisms of action, contributes to symptom relief for patients testing positive for COVID-19. The data also suggest the two drugs can be safely co-administered in COVID-19 patients over a wide age range (3–90), even those with significant comorbidities. Early in the pilot study levocetirizine was used interchangeably with cetirizine; however, the paradigm was subsequently refined to include only levocetirizine with montelukast. Cetirizine exists as a racemic mixture of levocetirizine [(R)-enantiomer] and dextrocetirizine [(S)-enantiomer]. The S-enantiomer is tenfold less active than levocetirizine and competes with the H1 receptor to defeat the otherwise clinically remarkable and titratable properties associated with the R-enantiomer. Levocetirizine has twice the affinity of cetirizine for the H1 receptor. . Conclusion Presently, one cornerstone in the COVID-19 treatment paradigm lies in the effective attenuation of inflammation elicited by the virus. Levocetirizine and montelukast, unlike many single target therapeutics, safely attenuate not only histamine and leukotriene D4, respectively, but also synergistically mitigate inflammation across a spectrum of signaling proteins, cell adhesion molecules, and leucocytes: NF-kB, ICAM-1, VCAM-1, IL-4, IL-6, IL-8, RANTES, GM-CSF, TLR-3, AP-1, and eosinophil and neutrophil quantity and migration. Moreover, both molecules in the United States are considered Pregnancy Category B and underscored by millions of days of patient use (montelukast, 1998 FDA approval; levocetirizine, 2007 FDA approval). As new COVID variants evolve in a global environment, one of many attributes of the repurposed combination lies in the ability to target cellular protein activity in contrast to viral proteins, an effect not likely to be negated by mutations in the virus genome. Levocetirizine and montelukast appear to offer a significant addition to the treatment of COVID-19, effectively mitigating symptoms without creating concurrent host toxicity. Cumulative data to date suggests the uniquely synergistic combination may reduce the progression and duration as well as prevent/treat many of the aspects of 'Long COVID,' thereby cost-effectively reducing both the morbidity and mortality associated with the disease.

Poor sleep linked to increased risk of COPD flare-ups

Date: June 6, 2022

Source: NIH/National Heart, Lung and Blood Institute

SUMMARY:

Poor sleep is associated with a significantly increased risk of life-threatening flare-ups in people with chronic obstructive pulmonary disease, or COPD, according to a new study. The risk for these flare-ups -- sudden bouts of worsening breathing -- was 25% to 95% higher in people who experienced poor sleep than in people who had good quality sleep. The findings suggest that poor sleep may be a better predictor of flare-ups than even a person's history of smoking

COPD, a progressive, incurable lung condition that makes breathing difficult, affects more than 16 million adults in the United States and is a leading cause of death. COPD flare-ups, also known as exacerbations, can last for days and even weeks and are triggered by a variety of factors ranging from pollutants to cold and flu viruses. Poor sleep can weaken the immune system of a healthy person and make them more susceptible to colds and the flu; and this vulnerability can increase in people with COPD.

Although scientists have long known that people with COPD often experience sleep disturbances, the role of poor sleep as a trigger of COPD exacerbations has been understudied, with major research on this topic providing conflicting evidence. The current study fills an important knowledge gap, investigators say.

"Among those who already have COPD, knowing how they sleep at night will tell me much more about their risk of a flare-up than knowing whether they smoked for 40 versus 60 years," said lead study author Aaron Baugh, M.D., a clinical fellow at the University of California San Francisco Medical School and a practicing pulmonologist. "That is very surprising and is not necessarily what I expected going into this study. Smoking is such a central process to COPD that I would have predicted it would be the more important predictor in the case of exacerbations."

For the study, the researchers followed 1,647 people with confirmed COPD who were enrolled in the Subpopulations and Intermediate Outcome Measures in COPD Study (SPIROMICS), a multi-center U.S. longitudinal study funded by the NHLBI and the COPD Foundation and designed to evaluate COPD subpopulations, outcomes, and biomarkers. All the participants in this specific study were current or former tobacco smokers with a confirmed diagnosis of COPD, and they underwent at least one initial sleep evaluation upon enrollment.

The researchers recorded COPD flare-ups over a three-year follow-up period and compared these measurements against the sleep quality of the participants. The researchers used a common tool for analyzing self-reported sleep quality -- a combination of seven sleep measures, including sleep duration, timing of sleep, and frequency of disturbances. The scores ranged from worse sleep quality to best sleep. The researchers reported their results after looking at how a person's risk for flare-ups changed after one year.

They found that in general, poor sleep quality was strongly associated with a higher total of COPD flare-ups. Compared to those participants with the best possible sleep, those who were at the threshold or at the base level of poor sleep had a 25% increased chance of having a COPD flare-up within the next year. Those with the worst sleep had a nearly 95% increased risk of having a COPD exacerbation within the next year.

CICM (India)
Respiratory Updates

Persistent Symptoms After Acute COVID-19 Infection in Omicron Era'

Source: J Korean Med Sci. 2022 Jul 11;37(27):e213

Young Hee Jung ,1* Eun-Hye Ha ,2* Kang Won Choe ,3 Seungbok Lee ,4
Dong Ho Jo ,3 and Wang Jun Lee 5

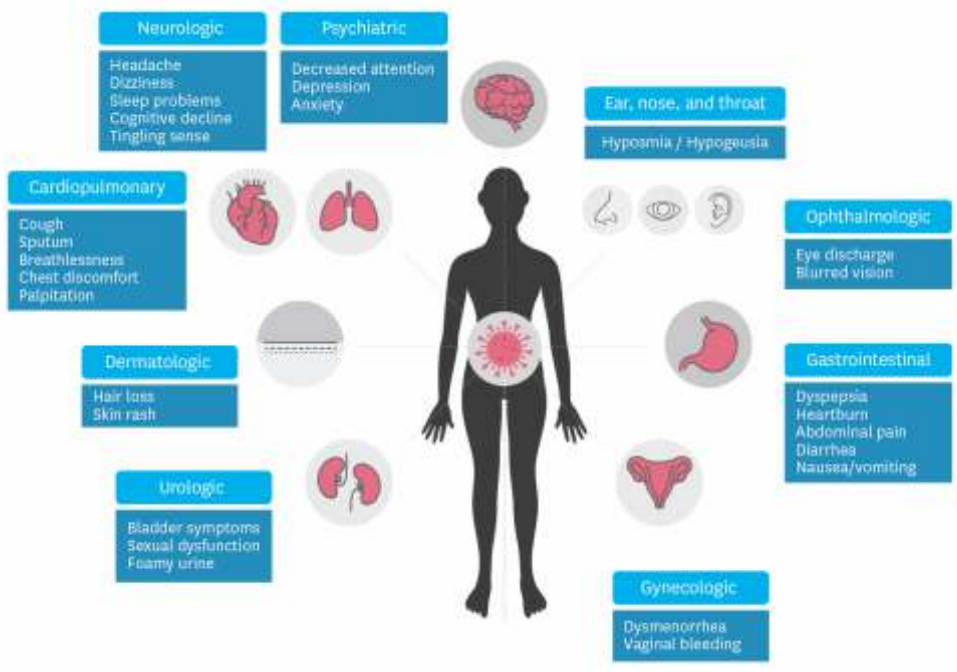
ABSTRACT

Background: We aim to compare the clinical characteristics and subjectively reported symptoms of the acute coronavirus disease (COVID) phase and those of the post-acute COVID phase to examine varying factors that affect the number of persistent symptoms and their categories.

Methods: We categorized 1,122 patients who visited the post coronavirus disease 2019 (COVID-19) clinic into two groups: "acute group" (< 4 weeks following diagnosis of COVID-19) and "post-acute group" (> 4 weeks following diagnosis of COVID-19). We statistically compared clinical characteristics between the two groups and determined which factors are associated with the number of persistent symptoms and their categories.

Results: The persistent symptoms of post COVID-19 conditions were classified into three categories as follows: Category A (the prevalence of symptoms is higher in the acute-visit group than in the post-acute-visit group), Category B (the prevalence of symptoms is not different between the two groups) and Category C (the prevalence of symptoms is higher in the post-acute-visit group than in the acute-visit group). Category A mainly included respiratory symptoms. Category B had generalized weakness, weight loss, cardiologic symptoms, hypogeusia, hyposmia, anxiety, and various gastrointestinal symptoms. Category C included fatigue, decreased attention, depression, blurred vision, hair loss, and sexual dysfunction. Anxiety, depression, fatigue and age were also associated with the number of symptoms and their categories, and anxiety is the most correlated factor ($P < 0.001$) among them.

Conclusion: The persistent symptoms of post COVID-19 condition involve multi-organ and continue for four weeks or greater. Therefore, long-term observation and multidisciplinary interventions are essential for patients with post COVID-19 conditions.



Home based pulmonary tele-rehabilitation under telemedicine system for COPD: a cohort study

Source: Zhang et al. BMC Pulmonary Medicine (2022) 22:284

Ling Zhang1†, Ayiguli Maitinuer2,3†, Zhichuang Lian2,3, Yafang Li2,3, Wei Ding2,3, Wenyi Wang2,3, Chao Wu2,3* and Xiaohong Yang1,2,3*

Abstract : Pulmonary tele-rehabilitation can improve adherence to pulmonary rehabilitation. However, there are few reports on home based pulmonary tele-rehabilitation. We assessed the effectiveness of home based pulmonary tele-rehabilitation under telemedicine system in patients with chronic obstructive pulmonary disease (COPD). Methods: This cohort study enrolled 174 patients with COPD who received home based pulmonary tele-rehabilitation under telemedicine system. The follow-up time was 12 weeks. Patients were grouped according to pulmonary rehabilitation weeks, number of rehabilitation times and total duration time, and when these three data were inconsistent, the two lowest values were grouped: control group (total rehabilitation weeks < 1 week, total number of rehabilitation times < 5, total duration time < 150 min, n = 46), pulmonary rehabilitation group 1 (PR-1) (1 week ≤ rehabilitation weeks < 4 weeks, 5 ≤ total number of rehabilitation times < 20, 150 min ≤ total duration time < 1200 min, n = 31), pulmonary rehabilitation group 2 (PR-2) (4 weeks ≤ rehabilitation weeks < 8 weeks, 20 ≤ total number of rehabilitation times < 40, 600 min ≤ total duration time < 2400 min, n = 23), pulmonary rehabilitation group 3 (PR-3) (8 weeks ≤ rehabilitation weeks < 12 weeks, 40 ≤ total number of rehabilitation times < 60, 1200 min ≤ total duration time < 3600 min, n = 40) and pulmonary rehabilitation group 4 (PR-4) (rehabilitation weeks = 12 weeks, total number of rehabilitation times = 60, total duration time = 3600 min, n = 34). The clinical data before and after rehabilitation were collected and evaluated, including dyspnea symptoms, 6-min walk distance (6MWD), diaphragmatic mobility, anxiety and depression.

Results : There was no significance difference between control group and PR-1 group. PR-2 group after rehabilitation had significantly decreased CAT and HAMA scores than control ($P < 0.05$). Compared with control, PR-3 group and PR-4 group after rehabilitation had significantly higher 6MWD and diaphragmatic motility during deep breathing, but significantly lower CAT score, mMRC score, HAMA score, and HAMD score ($P < 0.05$). Compared with before pulmonary rehabilitation, in PR-3 and PR-4 groups, the 6MWD and the diaphragmatic motility during deep breathing were significantly higher, while CAT score, mMRC score, HAMA score, and HAMD score (for PR-4 only) were significantly lower after pulmonary rehabilitation ($P < 0.05$). There was no significant difference between PR-3 group and PR-4 group ($P > 0.05$). In the 12-week pulmonary rehabilitation program, patients who completed at least 8 weeks, namely those in the PR-3 and PR-4 groups, accounted for 42.5% of the total number. Education, income and response rate to telemedicine system reminders were the main risk factors associated with home based pulmonary tele-rehabilitation.

Conclusions: Home based pulmonary tele-rehabilitation under telemedicine system for more than 8 weeks can significantly improve the dyspnea symptoms, 6MWD, diaphragmatic mobility during deep breathing, and negative emotions of patients with moderate to severe stable COPD.

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Respiratory Updates

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Atypical Post-COVID Sequel: Bronchiectasis

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CASE : A 49-year-old male patient was admitted with a com-plaint of exertional dyspnea. A physical examination re-vealed no pathological findings except for crepitation sounds in the auscultation of the thoracic baselines. Par-tial oxygen saturation in room air was 94%. The patient, who had been diagnosed previously with diabetes melli-tus and hypertension, had no smoking history, and had been hospitalized for approximately 1.5 months due to severe COVID-19 pneumonia (SARS-CoV2 PCR test ob-tained with nasopharyngeal sampling was positive) and respiratory failure 11 months earlier. A chest X-ray re-vealed diffuse ground-glass infiltration (Figure 1a). Dif-fuse ground-glass consolidations, including an air bron-chogram, were observed on chest CT taken in the post-COVID first month (Figure 1b, c and d). The patient's file revealed that the patient had been treated with Favipiravir, low molecular weight heparin, piperacillin-tazobactam and 1gr/day methylprednisolone (withdrawn and reduced) therapy for three days along with high-flow nasal oxygen therapy, and an oxygen concentrator was prescribed for home use at the time. No secondary bacterial infection agents grew in the sputum culture. The patient had no history of being treated for pneumonia or tuberculosis other than COVID-19, including in childhood; and there was no chronic cough or sputum complaint. A chest CT obtained at the post-COVID 11th month revealed bilat-eral bronchiectasis, peripheral air cyst in the left lung and peripheral atelectasis bands. Significant regression in fibrotic appearance (Figure 2) was noted when compared to the chest CT performed in the post-COVID third month. The patient was informed about the necessity of flu, pneumococcal and COVID-19 vaccines and was fol-lowed up.

DISCUSSION : Bronchiectasis can occur rapidly and cause sequel in cases of COVID-19 infection, and comorbidities and secondary infections may be predisposing factors for bronchiectasis (5). The presented case had diabetes mellitus and hypertension, and so blood sugar regulation may have been impaired during the period of steroid therapy. Despite the predisposition to secondary infec-tions after high-dose steroids, no growth was detected in the patient's sputum culture.High-resolution CT findings 3 months after discharge in China have revealed interstitial thickening (27.27%), pure ground glass opacity (7.27%) and crazy paving (5.45%) findings (9), and traction bronchiectasis secondary to post-COVID fibrosis is also common. Traction bronchiec-tasis is a subtype of bronchiectasis in which the bronchi become dilated secondary to mechanical traction due to fibrosis of the adjacent lung parenchyma, and lung injury resulting from invasive mechanical ventilation may also contribute to the process. It is not known how much of the bronchiectasis persists following the resolution of intersti-tial pneumonia. Enlarged or convoluted bronchi lose their ability to clear mucus effectively and may predispose the patient to recurrent infections (10). Although fibrotic changes were observed in our patient's post-COVID 3rd-month chest CT, most had regressed by the 11th month, although the bronchiectasis image persisted.

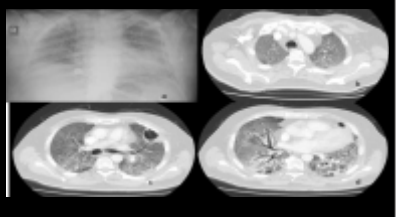

Figure 1: Chest X-ray at the time of hospitalization revealing bilateral ground-glass infiltration (a), in the 1st month post-COVID, revealing a peripheral air cyst in the left upper lobe, diffuse ground-glass and con-solidated areas, and bronchiectasis in the axial sections of a chest CT (b,c,d)

Bronchiectasis associated with COVID-19 is an atypical finding. In a retrospective study, bronchiectasis changes were described in one of 121 COVID-19 patients (11). Secondary bacterial infections, prolongation of weaning from mechanical ventilation, and length of hospital stay may lead to the formation of bronchiectasis (12). Our patient did not need invasive mechanical ventilation dur-ing his prolonged hospital stay of 1.5 months.Increased interleukin-6 has been associated with the incidence of severe bronchiectasis in tuberculosis patients (13). Interleukin-6 is an acute phase reactant that forms in the early phase of inflammation, and high Interleukin-6 levels have also been associated with poor prognosis in COVID-19 (14). Based on this relationship, we suggest that bronchiectasis may be seen more frequently in COVID-19 cases with severe pneumonia and respiratory failure.

CONCLUSION : Apart from post-COVID fibrosis and pulmonary thrombo-embolism, the present study draws attention also to iso-lated bronchiectasis. One of the first questions posed regarding the etiology of bronchiectasis in the years to come may be the patient's COVID-19 history.

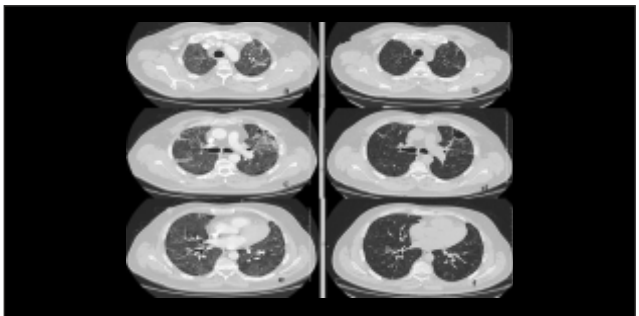

Figure 2: Chest CT axial sections showing persistent bronchiectatic changes despite persistent regression in fibrotic findings at the third month post-COVID (a,c,e) and 11th month post-COVID (b,d,f)

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