REPORT FROM

Nordic Lung Congress 2024

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Chiesi

Warm greetings from Helsinki!

"Reisen bildet!" (travel broadens the mind), you would say in German, meaning that all impressions, encounters, views and conversations during travels will leave a mark and teach you something new and exciting. This could never be truer than for our journey to the Nordic Lung Congress 2024 in Helsinki!

Here are some of my personal learnings during these three days in June:

- There is hardly anything more beautiful than the Nordic summer with a blue sky and sun reflections on the ever-present water!
- Light summer nights are best enjoyed from the roof top of the convention centre with a beautiful view over the sea, the city, and the sunset.
- Finnish strawberries are VERY tasty, and cream cake with Finnish strawberries is divine.
- Strawberries, goat cheese, and pine nuts are a terrific combination on pizza!
- The combination of Karelian rice pie and strawberries on the other hand will cause you sceptic glances from your Finnish colleague (and he was right, that was not the best match I made during breakfast).
- Finnish karaoke bars are definitively "educating" to visit- an experience on the very edge of my comfort zone.

Of course, Chiesi´s Nordic Medical team learned a lot during the lectures and sessions we attended during the conference, and we are happy to share our learnings in our latest conference newsletter with you!

Enjoy the reading, and enjoy the summer!

Barbara Fuchs
Medical Manager, Chiesi Nordics

What has the ongoing development of biologics taught us about COPD so far?

PRESENTED BY LOWIE VANFLETEREN, SWEDEN

Summary: With the first biologics for treatment of severe COPD presumably close to approval, we stand at the edge of a new era. As with severe asthma, the development of these drugs for COPD taught us some important lessons on patho-mechanisms and different phenotypes of the disease. How would a person living with COPD look like that might have beneficial effects of treatment with biologics?

Reduce risk, as well as symptoms

During his lecture, Lowie Vanfleteren did not only elegantly summarise the data generated during the clinical development programs of biologics in COPD, but importantly, he also shared his current expert understanding on which emerging patient characteristics will be in focus to select the individuals with best chances for good treatment responses.

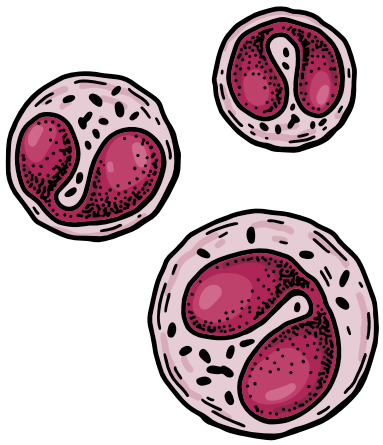
He reminded us of the two goals of COPD treatment: to reduce symptoms for the individual, and to reduce the risk for both exacerbations and progression of the disease. Basically, all persons living with COPD will sooner or later exacerbate.

Key considerations: prior exacerbations and eosinophils

Two recognised risks factors are prior exacerbations and elevated blood eosinophil counts. The treatment effect of inhaled corticosteroids relates to the extent of blood eosinophils present[1]. As shown by Bafadhel et al 2011, eosinophilic inflammation is present in ca 28% of COPD exacerbations[2]. Vanfleteren shows us the schematic overview of Type 2 inflammation in the lung that we all recognise from lectures on severe asthma. He points us to the fact that there are triggers of Type 2 inflammation that we sometimes tend to overlook, eg. cigarette smoking leading to the induction of cytokines and alarmins such as IL-33, TSLP, IL-4, IL-5 and IL-13. All these cytokines display valid targets for biologics in COPD, surely for the overlapping phenotypes of asthma and COPD.

Know the type of exacerbation

The clinical development programs for these antibodies found that efficacy is again related to the level of eosinophil counts. Thus, to define a threshold to predict beneficial effects is very important. Even though the fraction of exhaled nitric oxide (FeNO) is comparable low in COPD, biologics have shown to reduce the FeNO levels. It crystallises more and more that biologics can become powerful tools to reduce OCS-sensitive exacerbations, but less so exacerbations that would need treatment with antibiotics. Vanfleteren mentions a disease-label free, treatable traits approach for the use of biologics in severely diseased persons: it is important to identify the right medicine for the person you try to help.



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Health effects of vaping and role in smoking cessation

PRESENTED BY MAGNUS LUNDBÄCK, SWEDEN **AND** LINNEA HEDMAN, SWEDEN

Summary: Although considered less harmful than conventional cigarettes, vaping e-cigarettes are not without health impact. Long term health impact remains to be seen, but short-term effects include potential to cause cardiovascular effects and cellular injury. By and large, vaping is more likely to increase - not decrease the population with nicotine addiction in the world.

Are e-cigarettes a less harmful replacement for smoking cigarettes?

That is what all major tobacco industries, all with e-cigarette brands of their own, argue. However, the major target group for these products are not smokers, but nicotine-naïve youths and children. Marketed aggressively in social media channels such as TikTok and Snapchat, they reach a young audience, under the radar for most grown-ups. The fruity and candy-like flavors also happen to be just what kids like.

Rocketing market

The market is growing rapidly and the global market for these products has been estimated to 28 billion dollars. According to a national survey among teenagers in Sweden, the share of teenagers in the 11th school year that had vaped at least once in the past 30 days increased from roughly 5% in 2021 to a jaw-dropping 25% the following year. (Report from CAN, the Swedish Council for Information on Alcohol and Other Drugs).

Lung injury from use

The first wakeup call was in 2019, with the identification of EVALI (e-cigarette or vaping use-associated lung injury). More than 2500 cases were found, whereof 60 fatal cases, often (but not always) associated with use of THL (cannabis oil) with additive Vitamine E acetate.

A harmful cocktail

The aerosol from e-liquids has been found to contain fine and ultrafine particles, reaching all parts of the lungs. These particles contain carcinogenic substances (nitrose amines, polycyclic aromatic hydrocarbons (PAH)), and formaldehyde, triggering inflammation, reactive oxygen species which impose oxidative stress and metals, causing allergies. In the frustrating wait to learn long term consequences of e-cigarettes, vaping and heated tobacco product use, short-term human studies might indicate future risks. What is known is that vaping increases airway obstruction, increases the concentration of particles in lungs, elevates blood pressure, pulse and numbers of endothelial progenitor cells.

A missing measurement: vaping exposure

The exposure from the use of e-cigarettes cannot be easily quantified in analogy with the standard “pack years” for quantifying exposure of cigarette. For studies on correlation between exposure and risks, a standardized measure will be needed.

Short term effects

Cardiologist Magnus Lundbäck and team have been looking specifically at cardiovascular effects of short-term exposure and have found that vaping nicotine is associated with increased arterial stiffness[1] and increased levels of blood markers for vascular stress and vascular injury and increased thrombosis[2].

Can vaping cause COPD or lung cancer?

In animal studies, e-cigarette use causes emphysema and COPD but as these diseases develop over time, it might still be a while before vaping can be linked to COPD in humans. Answering a question from the audience on whether vaping can cause lung cancer, Magnus responded that it is highly likely given the proof of inflammatory response, presence of markers of cell injury and e-liquid content of carcinogenic substances.

Are e-cigarettes helpful in smoking cessation?

The decision to quit smoking is a personal decision, and the majority of quit attempts are unassisted, and the most successful ones are the spontaneous quit attempts, without cutting down[3]. In some countries, e.g. the UK, e-cigarettes are recommended as nicotine replacement products, even in pregnancy. However, according to behavioral scientist Linnea Hedman, most of the studies on use of vaping as smoking cessation tool include people that were already motivated to stop smoking. Hedman presented the outcome of a systematic review[4] on e-cigarette smoking and subsequent smoking cessation, finding no quality evidence for use of e-cigarettes as way to stop smoking.

So - how to stop?

She ends with a recommendation to use WHO's "A guide for tobacco users to quit"[5] and to make use of local phone smoking cessation help numbers. Focus, says Hedman, should be to aim for freedom from dependency.

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The human factor – from insights to needs of persons living with COPD

Summary: Which unmet needs and challenges do people living with COPD see for themselves, which impact did the diagnosis of COPD have on them, how do they feel about their treatment, and finally: what would they wish for if they had a magic wand? The HOPE study-team set off to perform semi-structured interviews with individuals from eight European countries including Denmark and Sweden to find out.

Symptoms leading to diagnosis

Scichilone et al ran a study[1] of semi-structured interviews with sixty-two persons living for at least six months with a diagnosis of COPD conducted by human factors experts to investigate their perspectives and requirements. The results show that difficulty breathing and coughing were the most frequent symptoms leading to diagnosis. The majority of participants (58%) felt negatively affected by the diagnosis as it reduces their ability to be active, and to participate in social life and hobbies. When living with the disease, reduced physical ability, challenges to mobility, and breathing problems were most bothersome. Some participants described a positive impact of the diagnosis, being able to reduce or even stop smoking after receiving more information, smoking cessation treatment, or quitting for a family member and the threat of death.

Treatment: influence, adherence and training

Most participants (67%) report that they were not involved in the selection of their present treatment. Feelings connected to their treatment were mostly positive or neutral. The participants also revealed their best strategies to remember to take their medications, either in conjunction with other medicines, routines or habits such as tooth brushing. However, some also reported that feeling unwell prompts them to take their medication.

Persons living with COPD report that information about their treatment was provided to them in training provided by health care. Thirty-one percent of participants revealed that they did not receive any training about their treatment.

Sources of information and support

Information was collected by family and friends, as was it collected online. Online sources of information felt not trust-worthy, and there was also an unwillingness to read more about their condition due to fear.

To improve their situation, persons living with COPD would like to have easier access to health care personnel, physiotherapy, smoking cessation support, workshops for families and friends to increase understanding for the disease, among other.

The ultimate wish

When asked “If I had a magic wand, I´d wish for…?”, most persons living with COPD were clear in their answer: TO FIND A CURE.

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Towards minimizing carbon footprint of MDI

Metered-dose inhalers (MDI) contain propellants to pressurize the inhaler so that the drug formulation is delivered as an aerosol. The use of propellants is safe for the users, but being greenhouse gases, they contribute to a higher carbon footprint. As not all patients can be switched to other inhaler types, MDIs with alternative propellants are under development. These propellants must have considerably lower global warming potential, without compromising pharmacokinetic properties.

Hence, three posters were presented to share the development of a replacement for the currently used propellant. These studies aimed at answering these questions:

- Is the novel formulation bioequivalent to the MDI on the market?
- Can relative lung bioavailability and total systemic exposure in healthy volunteers be demonstrated?
- Is the bronchoconstriction potential and safety profile in line with the current MDI?

Bioequivalence

Bioequivalence was fully demonstrated for beclomethasone (measured as active metabolite B17MP) and formoterol in healthy volonteers when comparing a triple fixed, high-dose BDP/FF/GB* with current and novel propellant, respectively. For glycopyrronium, the 90% CI were marginally above the bioequivalence upper limit, which was not considered clinically relevant.

Bioequivalence and bioavailability

Comparing a triple fixed dose BDP/FF/GB in medium dose with current and novel propellant, respectively, in healthy volunteers, bioequivalence was fully demonstrated for beclomethasone (measured as active metabolite B17MP), formoterol and glycopyrronium. For pulmonary availability, bioequivalence was demonstrated for formoterol. For beclomethasone and glycopyrronium, the 90% CIs were marginally outside the bioequivalence limits which was considered not clinically relevant.

Bronchoconstriction potential

In the third study, comparing sprays with no active principle, no propellant-induced bronchoconstriction event was observed, and the safety profile was equivalent between the two propellants in patients with mild asthma. Taste sensation was included as exploratory objective, but no taste difference between the two propellants was reported.

Conclusion

Safety and tolerability of both propellants were similar in all three studies. The outcome of these studies also supports the continued development to reduce carbon emissions from MDI by replacing propellant to ensure continued availability of spray as a therapeutic option.

** BDP=Beclomethasone DiPropionate; FF=Formoterol Fumarate; GB=Glycopyrronium Bromide*

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Medical director

8659-18.06.2024

Cardiovascular risk in Chronic Obstructive Lung Disease

PRESENTED BY OSKAR WALLSTRÖM, SWEDEN

Summary: On the last day of the NLC, Dr. Oskar Wallström, MD and PhD student from the University of Gothenburg, presented an insightful talk on the hot topic of cardiovascular risk in chronic obstructive lung disease (COPD). With the intimate interplay between CVD and COPD, integrated care approaches are needed to treat the patient, rather than its separate diseases.

COPD and Cardiovascular Disease - Overlapping Risk Factors

COPD is a prevalent chronic disease and the third leading cause of death globally, accounting for more than 3 million deaths annually (WHO, 2019). Prevalence of cardiovascular disease (CVD) is notably higher in COPD patients, reflecting a complex interplay between CVD and COPD due to shared risk factors, pathophysiology, and symptoms[1].

CVD as a Risk Factor for Hospitalization in COPD

CVD has been identified as a significant risk factor for future hospitalization in COPD patients, independent of the severity of their lung disease[2]. This highlights the need for comprehensive cardiovascular care in managing COPD patients.

Exacerbations may trigger Cardiovascular Events

There is mounting evidence that COPD patients are particularly vulnerable to cardiovascular events during periods of exacerbation. For instance, Donaldson et al. (2010) demonstrated that the risk of myocardial infarction is significantly increased during the initial 1 to 5 days following an exacerbation compared to periods without exacerbation[3]. Along with findings indicating an elevated risk extending up to one year after an exacerbation[4], the necessity of close monitoring of COPD patients may last for one year post-exacerbation.

Heart Failure: A Common Condition in COPD

Considering its high prevalence, COPD patients should be assessed for heart failure. Various diagnostic tools are available for clinical examination, with particular emphasis on pro-BNP and troponin levels, which have been associated with poor prognosis in these patients.

Triple Therapy and Cardiovascular Risk

It is well-established that triple therapy, combining corticosteroids, long-acting beta-agonists, and long-acting muscarinic antagonists, reduces exacerbations and hospitalizations, improves lung function, and enhances quality of life in COPD patients compared to dual therapy[5-8]. However, the effect of triple treatment on cardiovascular events and the risk of premature death remains to be elucidated. Several post-hoc analyses of phase-III trials, although not specifically powered to examine mortality, have suggested a decreased risk of all-cause mortality with triple treatment[9-11]. These findings should be interpreted with caution due to the exploratory nature of the studies.

Take Home Message

By understanding and addressing the cardiovascular risks associated with COPD, healthcare providers can improve overall patient outcomes and quality of life.

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The phenotypes of acute exacerbations of COPD

PRESENTED BY PROF MAARTEN VAN DEN BERGE, NETHERLANDS

Summary: There are different exacerbation subtypes within COPD. Recognition of the exacerbation subtype is important as it may have an impact on treatment decisions. Comorbidity and severity of disease must also be considered. It is not always easy to accurately diagnose an exacerbation or to objectively grade its severity.

What are exacerbations?

Exacerbation is considered as an acute worsening of the patient's usual pattern of respiratory symptoms beyond normal day-to-day variability. These include increased dyspnoea, worsening of cough, increased sputum volume and sputum purulence. Thinking about severity, a moderate exacerbation is usually treated with prednisolone and/or antibiotics and severe cases need hospitalization and may lead to death.

Triggers of exacerbation

Of the different subtypes of exacerbations, viral cause is the most important, but due to limited testing, there is limited data of its role. Triggers may also be bacteria, eosinophilic type 2-inflammation and other factors.

Exacerbations are not unannounced

The term acute exacerbation is misleading, says Prof. van der Berge, as it has been shown that the worsening of the symptoms starts already seven days before the actual event[1]. This timepoint could be an excellent opportunity to intervene particularly in the case when the subtype of the exacerbation is known. For example, patients with higher eosinophilic count have a higher risk for exacerbations[2,3]. In these cases, treating the patient with corticosteroid-containing inhalation therapy could help avoid escalation. Eosinophils are increased during exacerbations in a certain subset of patients, not in all[4].

Systemic corticosteroids and antibiotics in treating COPD exacerbations

Comparing outcomes for patients suffering from exacerbation, receiving either standard of care (prednisolone and antibiotics) or biomarker-based treatment, study results support the latter approach. Results from the original study[5] by the OXFORD-group, published in 2012, were confirmed in 2024[6]. In the biomarker arm, patients received antibiotics plus either prednisolone or placebo. Lung function, health status and symptoms were similar in both groups. However, symptom recovery was slower in the patients who received prednisolone if their eosinophilic count was low. The conclusion was that prednisolone should only be given to the right phenotypes of exacerbations to avoid harming the patients. If the patient already has taken prednisolone, this will impact biomarker count, and this should be checked.

Antibiotics or not?

An old (but landmark) study published in 1987 showed that exacerbating patients treated by antibiotics vs. placebo had a better outcome[7]. The same study identified three exacerbation subtypes:

1. Increased dyspnea, sputum volume and sputum purulence
2. Two of three above mentioned symptoms present
3. One of the above symptoms present AND Upper respiratory infection, fever, increased wheeze or cough or increased respiratory or heart rate

Antibiotics were beneficial only in the first subtype of exacerbations.

Exacerbation severity

Exacerbation severity is divided in three categories:

1. Mild: events that result in change of COPD medications for>2 days.
2. Moderate: Events requiring treatment with antibiotics and/or systemic corticosteroids
3. Severe: Events that result in hospitalization or ER visit[8].

Severity of COPD exacerbations: The Rome proposal

The severity of an exacerbation relies exclusively on a patient's perception of increased respiratory symptoms and physician's perception regarding the treatment options, both subjective. The symptoms can be mimicked by other clinical conditions. Lack of measurable pathophysiological variables is another challenge. Published in 2021, the Rome proposal suggests a new approach of diagnosing COPD exacerbations and their severity. The assessment should include ruling out other clinical causes of symptoms (e.g. heart failure, pneumonia or pulmonary embolism[9]).

Post-exacerbation vulnerability

Risk of coronary symptoms of heart failure increases during and shortly after an COPD exacerbation. The risk of acute coronary syndrome increases almost 10-fold, and the risk of heart failure increases 27-fold during the first seven days. It is not fully understood what the causes behind these increases are[10].

The bottom line

Understanding and recognizing the exacerbation subtype is important as it provides guidance for treatment decisions.

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Follow-up of asthma in primary care

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Summary: Uncontrolled disease is a common problem throughout all treatment steps in asthma[1]. Various factors, such as lifestyle, treatment adherence, inhalation techniques and other comorbidities may influence respiratory symtoms[2] and therefore systematic follow-ups may be needed to address these factors. A twelve year long study revealed there is great potential for improvement both when it comes to frequency and quality of follow-ups.

Why checkups matter

Regular checkups of asthma are associated with improvement in asthma control[3]. Continuity of care in asthma is associated with higher adherence to medication[4] and with better knowledge of asthma and self-care.[5]

The occurrence of planned asthma follow-up contacts and quality of these visits in primary health care in Finland was studied in a real-life retrospective setting. Results has been reported in at least three scientific papers.[6,7,8]

Documentation gaps

The most frequently recorded asthma detail were respiratory symptoms, which was documented in 79% of the consultations and in 86,8% of the consultations if both a nurse and GP attended.[7] Interestingly, comorbidities associated with asthma (including obesity, nasal conditions and obstructive sleep apnea), life-style factors (including exercise habits, diet and alcohol use), asthma symptoms and patient guidance were in general rarely documented at scheduled asthma contacts in primary health care.

Weight loss, a rare advice

The study population mean age was 59 years and had a BMI average over 28. Even though obesity is associated with uncontrolled asthma and with increased risk of exacerbations[2], information on BMI was only found in 1.5% of the cases. Exercise habits were more frequently documented, specifically in 16% of the cases and more likely to be documented if a nurse attended the consultation. Recommendation to lose weight or increase the activity levels were only given in 0.9% and 0.6% of consultations, respectively[7].

Lifestyle and inhalation techniques

Other life-style factors such as diet and alcohol consumption were documented in <1% of the cases.[7] When taking into account that approximately 1/3 of the patients did not have asthma control, it is surprising that inhalation technique was not mentioned in more often than 2.2% of the visits and revised in 2.2% of the visits. Nurses were however significantly better than doctors at addressing inhalation technique (mentioned in 8.7% of the visits and revised in 7.8%).[7]

Allergies

Allergic rhinitis contributes to poorer asthma control and risk of exacerbations. Treating coexisting allergic rhinitis can improve asthma control and reduce healthcare utilization.[8] Rhinitis was only recorded in less than 10% of the patients, even though 70% of the study population had rhinitis.[7]

Summary:

Results from this longitudinal study shows advantages when both GP's and nurses are involved in the care of asthma patients and results may help to identify potential health-care practice-related causes of uncontrolled and difficult-to-treat asthma, and which areas require more urgent training and attention.

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