Welcome to the final issue of Respiratory Research Review for 2016 where we take a look slightly beyond the lung, first by reviewing the implications of our inactivity through sedentary behaviour at work or in front of a television and then looking at the management of COPD beyond the lung (Lancet).

The Lancet is leading the charge in bringing the global epidemic of inactivity to our attention and also in coming up with some solutions. Actually, as Ulf Ekelund and colleagues point out (Lancet), it was also the Lancet that published the seminal paper in 1953 showing that London bus drivers had a higher risk of death from coronary heart disease than bus conductors. The economic burden of physical inactivity is massive; the direct health cost alone is $5.0 billion for coronary heart disease, $6.0 billion for stroke, $37.5 billion for type 2 diabetes, $2.7 billion for breast cancer and $2.5 billion for colon cancer worldwide. In addition are the loss of earnings and the burden on the family in countries with less well-funded health systems (Lancet). Rodrigo Reis and colleagues publish a positive summary on how to ‘Scale up physical activity intervention worldwide: stepping up to larger and smarter approaches to get people moving’ (Lancet). The key message here is that we need to embrace the challenge, take up actions beyond translational research and engage on a higher level with local government, the Ministry of Education, transport planners and national government.

Our first article based on data of a million men and women brings it back to a personal level. Given that most of us need to entertain a sedentary lifestyle to earn a living, how active do we need to be to attenuate or eliminate the detrimental effects of sitting? The good news is virtually all of it can be attenuated with 60–75 minutes of moderately intense physical activity; the bad news is that this does not work if we watch more than 4 hours of TV a day. Physical activity may also uncover respiratory limitations in patients with airflow obstruction but near normal FEV₁ (Thorax). While an infective exacerbation of COPD reduces physical activity levels ( Eur Respir J), increased physical activity as encouraged through a pulmonary rehabilitation programme reduces hospital admissions (Cheast).

The Australian and New Zealand Society of Respiratory Science’s position statement on ‘Reference values for spirometry and their use in the test interpretation’ needs special mention. The authors review the advantages of the GLI (Global Lung Function Initiative) and recommend adopting this largest ever dataset as our key reference; it has particular strength in young adulthood and in older age. The careful reader will find that this GLI dataset and interpretation algorithm has been used in several articles chosen; it is mind-boggling that more than 70 reference value sets exist; many are small and most are rather old. We are reviewing two articles on drug treatments for COPD, both well designed and both positive, and a brilliant editorial by Edward Kerwin on the COPD ‘alphabet soup’ and how to restructure it in a simple way to guide us in our clinical practice: A for As needed SABA, B for Bronchodilator LAMA or LABA, C for Combination dual bronchodilator LABA/LAMA, D also for combination - Dual bronchodilator LAMA/LABA and E for Exacerbations of COPD – in particular clinical practice: A for As needed SABA, B for Bronchodilator LAMA or LABA, C for Combination dual bronchodilator LABA/LAMA, D also for combination - Dual bronchodilator LAMA/LABA and E for Exacerbations of COPD – in particular clinical practice: A for As needed SABA, B for Bronchodilator LAMA or LABA, C for Combination dual bronchodilator LABA/LAMA, D also for combination - Dual bronchodilator LAMA/LABA and E for Exacerbations of COPD – in particular clinical practice: A for As needed SABA, B for Bronchodilator LAMA or LABA, C for Combination dual bronchodilator LABA/LAMA, D also for combination - Dual bronchodilator LAMA/LABA and E for Exacerbations of COPD – in particular clinical practice: A for As needed SABA, B for Bronchodilator LAMA or LABA, C for Combination dual bronchodilator LABA/LAMA, D also for combination - Dual bronchodilator LAMA/LABA and E for Exacerbations of COPD – in particular clinical practice: A for As needed SABA, B for Bronchodilator LAMA or LABA, C for Combination dual bronchodilator LABA/LAMA, D also for combination - Dual bronchodilator LAMA/LABA and E for Exacerbations of COPD – in particular clinical practice: A for As needed SABA, B for Bronchodilator LAMA or LABA, C for Combination dual bronchodilator LABA/LAMA, D also for combination - Dual bronchodilator LAMA/LABA and E for Exacerbations of COPD – in particular clinical practice: A for As needed SABA, B for Bronchodilator LAMA or LABA, C for Combination dual bronchodilator LABA/LAMA, D also for combination - Dual bronchodilator LAMA/LABA and E for Exacerbations of COPD – in particular clinical practice: A for As needed SABA, B for Bronchodilator LAMA or LABA, C for Combination dual bronchodilator LABA/LAMA, D also for combination - Dual bronchodilator LAMA/LABA and E for Exacerbations of COPD – in particular clinical practice: A for As needed SABA, B for Bronchodilator LAMA or LABA, C for Combination dual bronchodilator LABA/LAMA, D also for combination - Dual bronchodilator LAMA/LABA and E for Exacerbations of COPD – in particular clinical practice: A for As needed SABA, B for Bronchodilator LAMA or LABA, C for Combination dual bronchodilator LABA/LAMA, D also for combination - Dual bronchodilator LAMA/LABA and E for Exacerbations of COPD – in particular clinical practice: A for As needed SABA, B for Bronchodilator LAMA or LABA, C for Combination dual bronchodilator LABA/LAMA, D also for combination - Dual bronchodilator LAMA/LABA and E for Exacerbations of COPD – in particular clinical practice: A for As needed SABA, B for Bronchodilator LAMA or LABA, C for Combination dual bronchodilator LABA/LAMA, D also for combination - Dual bronchodilator LAMA/LABA and E for Exacerbations of COPD – in particular clinical practice: A for As needed SABA, B for Bronchodilator LAMA or LABA, C for Combination dual bronchodilator LABA/LAMA, D also for combination - Dual bronchodilator LAMA/LABA and E for Exacerbations of COPD – in particular clinical practice: A for As needed SABA, B for Bronchodilator LAMA or LABA, C for Combination dual bronchodilator LABA/LAMA, D also for combination - Dual bronchodilator LAMA/LABA and E for Exacerbations of COPD – in particular clinical practice: A for As needed SABA, B for Bronchodilator LAMA or LABA, C for Combination dual bronchodilator LABA/LAMA, D also for combination - Dual bronchodilator LAMA/LABA and E for Exacerbations of COPD – in particular clinical practice: A for As needed SABA, B for Bronchodilator LAMA or LABA, C for Combination dual bronchodilator LABA/LAMA, D also for combination - Dual bronchodilator LAMA/LABA and E for Exacerbations of COPD – in particular clinical practice: A for As needed SABA, B for Bronchodilator LAMA or LABA, C for Combination dual bronchodilator LABA/LAMA, D also for combination - Dual bronchodilator LAMA/LABA and E for Exacerbations of COPD – in particular clinical practice: A for As needed SABA, B for Bronchodilator LAMA or LABA, C for Combination dual bronchodilator LABA/LAMA, D also for combination - Dual bronchodilator LAMA/LABA and E for Exacerbations of COPD – in particular clinical practice: A for As needed SABA, B for Bronchodilator LAMA or LABA, C for Combination dual bronchodilator LABA/LAMA, D also for combination - Dual bronchodilator LAMA/LABA and E for Exacerbations of COPD – in particular clinical practice: A for As needed SABA, B for Bronchodilator LAMA or LABA, C for Combination dual bronchodilator LABA/LAMA, D also for combination - Dual bronchodilator LAMA/LABA and E for Exacerbations of COPD – in particular clinical practice: A for As needed SABA, B for Bronchodilator LAMA or LABA, C for Combination dual bronchodilator LABA/LAMA, D also for combination - Dual bronchodilator LAMA/LABA and E for Exacerbations of COPD – in particular clinical practice: A for As needed SABA, B for Bronchodilator LAMA or LABA, C for Combination dual bronchodilator LABA/LAMA, D also for combination - Dual bronchodilator LAMA/LABA and E for Exacerbations of COPD – in particular clinical practice: A for As needed SABA, B for Bronchodilator LAMA or LABA, C for Combination dual bronchodilator LABA/LAMA, D also for combination - Dual bronchodilator LAMA/LABA and E for Exacerbations of COPD – in particular clinical practice: A for As needed SABA, B for Bronchodilator LAMA or LABA, C for Combination dual bronchodilator LABA/LAMA, D also for combination - Dual bronchodilator LAMA/LABA and E for Exacerbations of COPD – in particular clinical practice: A for As needed SABA, B for Bronchodilator LAMA or LABA, C for Combination dual bronchodilator LABA/LAMA, D also for combination - Dual bronchodilator LAMA/LABA and E for Exacerbations of COPD – in particular clinical practice: A for As needed SABA, B for Bronchodilator LAMA or LABA, C for Combination dual bronchodilator LABA/LAMA, D also for combination - Dual bronchodilator LAMA/LABA and E for Exacerbations of COPD – in particular clinical practice: A for As needed SABA, B for Bronchodilator LAMA or LABA, C for Combination dual bronchodilator LABA/LAMA, D also for combination - Dual bronchodilator LAMA/LABA and E for Exacerbations of COPD – in particular.
Does physical activity attenuate, or even eliminate, the detrimental association of sitting time with mortality?

Authors: Ekelund U et al., for the Lancet Physical Activity Series 2 Executive Committee and the Lancet Sedentary Behaviour Working Group

Summary: This was a harmonised meta-analysis of data from 1,005,791 participants from 16 studies providing outcome data associated with daily sitting or television viewing time and physical activity; 13 studies provided data on sitting time and all-cause mortality. During follow-up of 2–18.1 years, 81.4% of participants died. Compared with participants sitting for <4 hours per day and in the most active quartile (≥35.5 MET [metabolic equivalent of task]-hours per week), greater mortality was seen in those in the second lowest (<16 MET-hours per week) and lowest (≤2.5 MET-hours per week) activity quartiles who sat ≥4 hours per day (respective HRs 1.12 [95% CI 1.08, 1.16] and 1.27 [1.22, 1.31]), with the greatest mortality risk seen in those from the lowest activity quartile who sat ≥8 hours per day (HR 1.59 [1.52, 1.66]). Mortality was not affected by daily sitting time in participants in the highest activity quartile. Data from six studies reporting data on television viewing time (n=465,450) reported 43,740 deaths, with the risk significantly increased by watching television for ≥3 hours per day for all activity quartiles except the highest, where it was significantly increased by watching television for ≥5 hours per day (HR 1.16 [1.05, 1.28]).

Comment: This international study combined data on more than 1 million men and women on both daily sitting and TV viewing time and explored the effect on all-cause mortality, cardiovascular mortality and breast and colorectal cancer mortality. They analysed the effect of different levels of physical activity to answer the question: if one is active enough, does this attenuate or eliminate the detrimental effects associated with daily sitting? Bottom line: daily, moderately intensive physical activity of 60–75 minutes seems to eliminate the increased risk of death associated with high sitting times. However, even this high activity level doesn’t eliminate the risk with increased TV viewing time.

Reference: Lancet 2016;388(10,051):1302–10

Asymptomatic subjects with airway obstruction have significant impairment at exercise

Authors: Soumagne T et al.

Summary: This research compared dyspnoea, exercise tolerance and ventilatory constraints on tidal volume expansion in 20 consecutive asymptomatic patients with persistent mild airway obstruction (postbronchodilator FEV1/FVC z-score –2.14; FEV1, z-score –1.02) who underwent incremental cycle cardiopulmonary exercise testing versus 20 matched symptomatic patients with COPD (FEV1/FVC z-score –2.36; FEV1, z-score –1.02) and 20 healthy matched controls with normal spirometry. Compared with controls, the asymptomatic patients with airway obstruction had higher dyspnoea ratings during incremental exercise and lower peak oxygen consumption and peak power output, and significantly more frequently had dynamic hyperinflation. Compared with patients with COPD, the asymptomatic patients with airway obstruction significantly more frequently had dynamic hyperinflation, but the other parameters were similar.

Comment: This French study is beautifully designed taking advantage of the higher clinical relevance of the GLI. They selected asymptomatic participants who had an FEV1/FVC ratio below the lower limits of normal and a reduced FEV1, and compared them with patients with COPD and matched controls. In this carefully selected group, the participants had a lower V̇O2max during testing, described more dyspnoea at any given work rate and had a suggestion of hyperinflation. Bottom line: we can identify airways disease early; however, at this stage we have no evidence that any pharmacological interventions would alter outcomes.


Reference values for spirometry and their use in test interpretation: a Position Statement from the Australian and New Zealand Society of Respiratory Science

Authors: Brazzale D et al.

Summary: This statement from the ANZSRS (Australian and New Zealand Society of Respiratory Science) provides background information and recommendations for interpreting spirometry results in clinical practice. The statement highlighted the importance of: i) benchmarking each patient’s results to population reference data; ii) providing a platform for a statistically and conceptually based approach for interpreting the results; and iii) using the most up-to-date and relevant reference equations for test interpretation. As such, adoption of the GLI 2012 spirometry reference values for test interpretation was recommended, as was interpreting results based on the lower limits of normal from reference values and the use of z-scores where available.

Comment: The last article is an example of how the accuracy and interpretation of lung function tests have improved over the last 20 years. Our current ATS/ERS guidelines on lung function interpretation are more than 10 years old, the severity assessment varies significantly between major international societies and they are vague in recommending reference data. Actually, more than 70 spirometric reference sets have been published since the 1960s. The GLI was led by respiratory scientists and collected data on more than 160,000 individuals aged 3–95 years. Bottom line: this position statement explores the evidence, gives the rationale and makes a strong case for adoption of the GLI data.

Reference: Respirology 2016;21(7):1201–9
Physical activity and exercise capacity in patients with moderate COPD exacerbations

Authors: Alahmari AD et al.

Summary: This study investigated changes in physical activity and exercise capacity that occur during moderate COPD exacerbations. Fifty outpatients with COPD had 6MWT distance and quadriceps maximum voluntary contraction values measured when they were stable and again 3 and 7 days after presentation for a moderate exacerbation. Physical activity was recorded for 2 consecutive weeks after the exacerbation. 6MWT distance fell from a median 422m when stable to 373m on day 3 (p<0.001). Similarly, quadriceps maximum voluntary contraction fell from 32.6 to 29.7kg (p=0.026). Falls in 6MWT distance were associated with a rise in CRP level and increased Functional Assessment of Chronic Illness Therapy – Fatigue score. Light physical activity was undertaken for 2.18 hours per day during the first week post exacerbation and 1.98 hours per day during the second week (p=0.009). Patients who had attended pulmonary rehabilitation had smaller decreases in 6MWT distance than those who had not attended pulmonary rehabilitation (~35.0 vs. –114.9m [p=0.013]).

Comment: The effect of a hospital admission secondary to an infective exacerbation of COPD is well known. However, little is known about the patient’s experience in those with an exacerbation severe enough to need either or both steroids and antibiotics, but not hospital admission. Based on the London COPD cohort, which has been going since 1995, the authors report data from SenseWear armbands, 6MWTs and quadriceps maximum voluntary contractions. The information suggests that a pulmonary rehabilitation course may attenuate the adverse effects of an exacerbation. Bottom line: exacerbations managed in the community are associated with a decline in exercise capacity and reduced muscle strength.


Abstract

Independent commentary by Professor Lutz Beckert.

Professor Lutz Beckert is the Head of Department of Medicine of the University of Otago, Christchurch. He is also a Respiratory Physician at Canterbury District Health Board.

FOR FULL BIO CLICK HERE

Pulmonary rehabilitation as a mechanism to reduce hospitalizations for acute exacerbations of COPD

Authors: Moore E et al.

Summary: This was a systematic review and meta-analysis of eighteen studies assessing the impact of pulmonary rehabilitation on acute COPD exacerbations. Pulmonary rehabilitation was associated with a lower hospitalisation rate when compared with control groups in ten RCTs (0.62 vs. 0.97 hospitalisations per patient-year), and also a lower hospitalisation rate during the 12 months after versus before such a programme in five studies (0.47 vs. 1.24 hospitalisations per patient-year). Data pooled from three cohort studies showed that when compared with reference groups, pulmonary rehabilitation was associated with a higher hospitalisation rate (0.28 vs. 0.18 hospitalisations per patient-year).

Comment: Pulmonary rehabilitation reduces further hospitalisation after an initial exacerbation of COPD. The main question of this review is whether it has the same effect in all patients with COPD rather than just those who had a recent admission. The authors found strong supporting evidence in ten RCTs; the evidence was equally strong in trials comparing admission rates before and after a rehabilitation course. One cohort study described a reduction in the hospitalisation rate of 18% in the rehabilitation group, but greater than 27% in the ‘usual care’ group. Bottom line: on balance, we have good evidence that pulmonary rehabilitation reduces hospital admissions.


Abstract

Effectiveness of fluticasone furoate-vilanterol for COPD in clinical practice

Authors: Vestbo J et al., for the Salford Lung Study Investigators

Summary: In this real-world investigation, 2799 patients with COPD from 75 UK general practices were randomised to a once-daily inhaled combination of fluticasone furoate 100μg and vilanterol 25μg or to usual care (i.e. any combination of inhaled corticosteroids, LABAs and LAMAs). The mean annual rate of moderate or severe exacerbations was significantly lower with fluticasone furoate/vilanterol than with usual care (1.74 vs. 1.90 exacerbations per year [p=0.02]). No significant between-group difference was seen for the annual rate of COPD-related contacts to primary or secondary care, or for the rate of the first moderate or severe exacerbation or the first severe exacerbation in time-to-event analyses. Fluticasone furoate/vilanterol was not associated with excess serious pneumonia events. The numbers of other serious adverse events were similar between the groups.

Comment: Traditionally the clinical benefit of inhaler therapy in COPD has been demonstrated in well-controlled RCTs with the disadvantage that this excludes a large proportion of our usual population. The Salford Lung Study used patients enrolled in 75 general practices and randomised them to once-daily fluticasone furoate and vilanterol or usual care. The primary outcome was that the treatment group had 1.74 and the usual care group 1.90 annual exacerbations needing treatment with antibiotics, steroids or both, or unplanned healthcare utilisation. Bottom line: patients in general practice diagnosed with COPD may benefit from once-daily fluticasone furoate/vilanterol treatment.


Abstract
Progression from asthma to chronic obstructive pulmonary disease: is air pollution a risk factor?

**Authors:** To T et al., for the Canadian Respiratory Research Network

**Summary:** This research explored the impact of air pollution exposure on the risk of progression from asthma to ACOS (asthma-COPD overlap syndrome) in 6040 Canadian health survey respondents. Compared with respondents without ACOS, those with ACOS (n=630) had later onset of asthma, greater mortality and more frequent ED visits prior to COPD diagnosis. Each 10 µg/m³ increase in cumulative exposure to fine particulate matter (PM₂.₅) was associated with a significant increase in the risk of ACOS (adjusted HR 2.78 [95% CI 1.62, 4.78]), whereas the risk for cumulative exposure to 10 parts per billion of ozone was not significant (1.31 [0.71, 2.39]).

**Comment:** Patients with so-called ACOS have a more rapid lung function decline, more frequent exacerbations and poorer quality of life than patients with asthma or COPD alone. In this article, the Canadian authors explore the hypothesis that patients with asthma may develop ACOS secondary to air pollution. Based on more than 6000 individuals with a history of asthma diagnosed since 1996, the authors match the clinical outcome with measures of air pollution like PM₂.₅ and ozone. **Bottom line:** individuals with asthma exposed to air pollution have a nearly 3-fold increased risk of developing ACOS.


Abstract

Viruses are frequently present as the infecting agent in acute exacerbations of chronic obstructive pulmonary disease in patients presenting to hospital

**Authors:** Biancardi E et al.

**Summary:** PCR was used to detect viruses in 8811 nasopharyngeal aspirates obtained from the general population. PCR was used to detect viruses in 8811 nasopharyngeal aspirates obtained from the general population. The phase 3 AFFIRM COPD trial randomised 933 patients 1:1 to receive inhaled aclidinium/formoterol twice-daily or salmeterol/fluticasone 50µg/500µg twice-daily for 24 weeks. Compared with salmeterol/fluticasone, aclidinium/formoterol was significantly better for the primary outcome of peak FEV₁, and was noninferior to salmeterol. A cohort of almost 1000 patients had improved bronchodilation, equal symptom control, reduced exacerbations and fewer episodes of pneumonia. The accompanying editorial by Edward Kerwin is outstanding; he addresses the fact that the management of COPD has become a confusing ‘alphabet soup’ and suggests a simple, evidence-based approach on how to allocate and escalate therapy. **Bottom line:** the combination of aclidinium/formoterol improves airflow in COPD and has fewer side effects than standard treatment.


Abstract

Efficacy and safety of aclidinium/formoterol versus salmeterol/fluticasone

**Authors:** Vogelmeier C et al.

**Summary:** This is a well-conducted clinical audit administered by our colleagues in New South Wales. They used PCR to detect viruses in 8811 nasopharyngeal aspirates obtained from the general population. The phase 3 AFFIRM COPD trial randomised 933 patients 1:1 to receive inhaled aclidinium/formoterol twice-daily or salmeterol/fluticasone 50µg/500µg twice-daily for 24 weeks. Compared with salmeterol/fluticasone, aclidinium/formoterol was significantly better for the primary outcome of peak FEV₁, and was noninferior to salmeterol. A cohort of almost 1000 patients had improved bronchodilation, equal symptom control, reduced exacerbations and fewer episodes of pneumonia. The accompanying editorial by Edward Kerwin is outstanding; he addresses the fact that the management of COPD has become a confusing ‘alphabet soup’ and suggests a simple, evidence-based approach on how to allocate and escalate therapy. **Bottom line:** the combination of aclidinium/formoterol improves airflow in COPD and has fewer side effects than standard treatment.


Abstract

**Bottom line:** flu-like symptoms and a low CRP level may hint towards a viral cause of an exacerbation of COPD.


Abstract

**Bottom line:** individuals with asthma exposed to air pollution have a nearly 3-fold increased risk of developing ACOS.


Abstract

**Bottom line:** flu-like symptoms and a low CRP level may hint towards a viral cause of an exacerbation of COPD.


Abstract

**Bottom line:** flu-like symptoms and a low CRP level may hint towards a viral cause of an exacerbation of COPD.


Abstract
Treatment for multiple acute cardiopulmonary conditions in older adults hospitalized with pneumonia, chronic obstructive pulmonary disease, or heart failure

Authors: Dharmarajan K et al.

Summary: This retrospective cohort study of patients aged ≥65 years attending 268 US hospitals sought to determine the frequency at which those with a principal diagnosis of pneumonia (n=91,709), COPD (n=41,052) or HF (n=118,061) had other concurrent cardiopulmonary diseases. Among patients hospitalised principally for pneumonia, 18% received additional treatment for HF; 18% for COPD and 4% for both. Among patients with a principal diagnosis of COPD, 19% received additional treatment for HF; no additional treatments were administered for pneumonia. Among patients with a principal diagnosis of HF, 34% received additional treatment for pneumonia, 9% for COPD and 5% for both.

Comment: These American authors articulate the problem of patients presenting with comorbid conditions. Treatment guidelines, health pathways, clinical trials and textbooks are all derived for a distinct diagnosis or condition. However, in their cohort of about 90,000 patients admitted with pneumonia, about 18% were also treated for HF and 18% for COPD. Of the ~40,000 patients admitted with COPD, 19% also received treatment for cardiac conditions. As a Lancet review summarises, there is some hope that we will have evidence to manage COPD beyond the lungs. Bottom line: little high-quality evidence exists to guide treatment decisions for patients with several conditions contributing to shortness of breath.


Abstract

A randomized trial of long-term oxygen for COPD with moderate desaturation

Authors: The Long-Term Oxygen Treatment Trial Research Group

Summary: This paper reported on a randomised trial originally designed to examine the effect of long-term treatment with supplemental oxygen on time to death in patients with stable COPD with SpO₂ <88%. The trial was redesigned at 7 months (when 34 participants had been randomised) to include patients with stable COPD with SpO₂ ≥80% for ≥85% of time and <90% for ≤10 seconds during a 6MWT. Participants assigned to the supplemental oxygen group with resting desaturation received 24-hour oxygen and those with desaturation only during exercise received oxygen during exercise and sleep. The analyses included 738 participants followed for 1–6 years. There was no significant difference between the supplemental oxygen versus no supplemental oxygen arms for time to death or first hospitalisation (HR 0.94 [95% CI 0.79, 1.12]), all hospitalisations (rate ratio 1.01 [0.91, 1.13]), COPD exacerbations (1.08 [0.98, 1.19]), COPD-related hospitalisations (0.99 [0.83, 1.17]), quality of life measures, lung function parameters or 6MWT distance.

Comment: These authors systematically address another dilemma and frequent clinical scenario. We have good evidence that 15 hours of oxygen or more prolongs survival in patients with severe hypoxia. The cost of supplying oxygen to these patients is about $2 billion in the US. The current trial investigates whether oxygen supplementation to patients with saturations of 89–93% or exercise-induced hypoxia reduces mortality or hospital admissions. It was a complex trial that needed adjusting during the course and took more than 6 years to complete. Magnus Ekström in his editorial gives us the bottom line: long-term oxygen therapy should be prescribed for stable patients with prolonged, significant hypoxia (PaO₂ ≤55mm Hg, saturation <88%).


Abstract

Oxygen with cold bubble humidification is no better than dry oxygen in preventing mucus dehydration, decreased mucociliary clearance, and decline in pulmonary function

Authors: Franchini ML et al.

Summary: This research randomised patients with chronic hypoxaemia (66% with COPD) to receive dry (n=10) or humidified (n=8) nasal low-flow oxygen. Both groups experienced significant but similar decreases in nasal mucociliary clearance, with a significant association seen between impaired nasal mucociliary clearance and lung function decline. The proportions of macrophages, IL-8 levels and epithelial growth factor levels increased and IL-10 levels decreased, and no changes were seen in the proportion of ciliated cells or contact angle. Both groups experienced similar decreases in coughing and sleep symptoms. No significant between-group differences were seen.

Comment: Patients who use long-term nasal oxygen supplementation often suffer from drying of the mucosa causing ciliary dysfunction, alteration in mucus properties and impaired mucociliary clearance. These Brazilian researchers report on a randomised trial comparing the effect on mucociliary clearance, mucus properties and airway symptoms of usual oxygen or oxygen provided via an unheated bubble humidifier in 18 patients. After 3 months of standard or cold bubble humidification, the patients were systematically evaluated. Bottom line: cold bubble humidification does not adequately humidify inhaled oxygen and does not prevent slowing of mucosal clearance, mucus dehydration or worsening pulmonary function.


Abstract

Respiratory Research Review

Esbriet® Abredip Prescribing Information (API)

Esbriet (pirfenidone) 267 mg oral capsule is indicated for the treatment of idiopathic pulmonary fibrosis (IPF). Dosage and Administration: Please see Esbriet Data Sheet for information. Contraindications: Contraindicated in patients with a hypersensitivity to pirfenidone or any of the excipients. Patients taking furosemide and patients with a history of angioedema with furosemide. Precautions: Hepatic Function: Emissions in ALT and AST 3 x ULN have been reported. Liver function tests should be conducted prior to and during treatment. If significant elevations occur the dose of Esbriet should be adjusted, refer to dosage guidelines in Data Sheet. Caution when used in patients with mild to moderate hepatic impairment. Photosensitivity reaction/rash: exposure to direct sunlight should be minimised during treatment and patients instructed to wear sunblock and protective clothing. Dose adjustment or temporary discontinuation may be required, refer to dosage guidelines in Data Sheet. Angioedema: patients who develop signs or symptoms of angioedema while taking Esbriet should immediately discontinue treatment. Cigarette smoking and inducers of CYP1A2: exposure to pirfenidone is 50% less in patients who were smokers, concomitant use of strong inducers of CYP1A2 including smoking should be avoided. Pregnancy Cat B3: there are no data on the use in pregnancy. Paediatric: safety has not been established. Renal Impairment: Use with caution in patients with mild, moderate or severe renal impairment. Drug Interactions: Esbriet is contraindicated in patients taking furosemide and caution should be taken in patients taking inhibitors of CYP1A2 e.g. clarithromycin, amiodarone, propafenone or inducers of CYP1A2 e.g. omeprazole, ritonavir. Adverse Effects: Common only: see Data Sheet for full list: Uppers respiratory tract infection, urinary tract infection, weight decreases, nausea, diarrhoea, taste disturbances, dry mouth, headache, flu-like symptoms, skin rashes. Rare: diaphoresis, insomnia, dyspepsia, abdominal pain, anorexia, anorexia, pyrexia, dry skin, pruritus, liver function tests increase, agranulocytosis, blood test results abnormal, hair loss, photosensitivity reaction/rash. Laboratory test changes: see Data Sheet for full list: liver function tests abnormal, electrolyte changes.

Esbriet is contraindicated in patients with a hypersensitivity to pirfenidone or any of the excipients. Patients taking furosemide and patients with a history of angioedema with furosemide. Precautions: Hepatic Function: Emissions in ALT and AST 3 x ULN have been reported. Liver function tests should be conducted prior to and during treatment. If significant elevations occur the dose of Esbriet should be adjusted, refer to dosage guidelines in Data Sheet. Caution when used in patients with mild to moderate hepatic impairment. Photosensitivity reaction/rash: exposure to direct sunlight should be minimised during treatment and patients instructed to wear sunblock and protective clothing. Dose adjustment or temporary discontinuation may be required, refer to dosage guidelines in Data Sheet. Angioedema: patients who develop signs or symptoms of angioedema while taking Esbriet should immediately discontinue treatment. Cigarette smoking and inducers of CYP1A2: exposure to pirfenidone is 50% less in patients who were smokers, concomitant use of strong inducers of CYP1A2 including smoking should be avoided. Pregnancy Cat B3: there are no data on the use in pregnancy. Paediatric: safety has not been established. Renal Impairment: Use with caution in patients with mild, moderate or severe renal impairment. Drug Interactions: Esbriet is contraindicated in patients taking furosemide and caution should be taken in patients taking inhibitors of CYP1A2 e.g. clarithromycin, amiodarone, propafenone or inducers of CYP1A2 e.g. omeprazole, ritonavir. Adverse Effects: Common only: see Data Sheet for full list: Uppers respiratory tract infection, urinary tract infection, weight decreases, nausea, diarrhoea, taste disturbances, dry mouth, headache, flu-like symptoms. Laboratory test changes: see Data Sheet for full list: liver function tests abnormal, electrolyte changes.

From 01 January 2017 ESBRRIET will be a funded medicine for patients with IPF who meet pre-defined criteria. Prescription and doctors’ fees may apply.

Before prescribing, please review the Esbriet Data Sheet available at www.medsafe.govt.nz. API based on Data Sheet [26-09-2016]. Roche Products (New Zealand) Limited, Auckland. Ph 0800 656 464. www.roche.co.nz All trademarks mentioned herein are protected by law.

Esbriet (pirfenidone) 267 mg oral capsule is indicated for the treatment of idiopathic pulmonary fibrosis (IPF). Dosage and Administration: Please see Esbriet Data Sheet for information. Contraindications: Contraindicated in patients with a hypersensitivity to pirfenidone or any of the excipients. Patients taking furosemide and patients with a history of angioedema with furosemide. Precautions: Hepatic Function: Emissions in ALT and AST 3 x ULN have been reported. Liver function tests should be conducted prior to and during treatment. If significant elevations occur the dose of Esbriet should be adjusted, refer to dosage guidelines in Data Sheet. Caution when used in patients with mild to moderate hepatic impairment. Photosensitivity reaction/rash: exposure to direct sunlight should be minimised during treatment and patients instructed to wear sunblock and protective clothing. Dose adjustment or temporary discontinuation may be required, refer to dosage guidelines in Data Sheet. Angioedema: patients who develop signs or symptoms of angioedema while taking Esbriet should immediately discontinue treatment. Cigarette smoking and inducers of CYP1A2: exposure to pirfenidone is 50% less in patients who were smokers, concomitant use of strong inducers of CYP1A2 including smoking should be avoided. Pregnancy Cat B3: there are no data on the use in pregnancy. Paediatric: safety has not been established. Renal Impairment: Use with caution in patients with mild, moderate or severe renal impairment. Drug Interactions: Esbriet is contraindicated in patients taking furosemide and caution should be taken in patients taking inhibitors of CYP1A2 e.g. clarithromycin, amiodarone, propafenone or inducers of CYP1A2 e.g. omeprazole, ritonavir. Adverse Effects: Common only: see Data Sheet for full list: Uppers respiratory tract infection, urinary tract infection, weight decreases, nausea, diarrhoea, taste disturbances, dry mouth, headache, flu-like symptoms. Laboratory test changes: see Data Sheet for full list: liver function tests abnormal, electrolyte changes.

From 01 January 2017 ESBRRIET will be a funded medicine for patients with IPF who meet pre-defined criteria. Prescription and doctors’ fees may apply.

Before prescribing, please review the Esbriet Data Sheet available at www.medsafe.govt.nz. API based on Data Sheet [26-09-2016]. Roche Products (New Zealand) Limited, Auckland. Ph 0800 656 464. www.roche.co.nz All trademarks mentioned herein are protected by law.

© 2016 RESEARCH REVIEW

For more information, please go to www.medsafe.govt.nz